MATERIALS 4.0

LAB AUTOMATION FOR MATERIALS CHEMISTRY

This report is commissioned by the Henry Royce Institute for advanced materials as part of its role around convening and supporting the UK advanced materials community to help promote and develop new research activity.

The overriding objective is to bring together the advanced materials community to discuss, analyse and assimilate opportunities for emerging materials research for economic and societal benefit. Such research is ultimately linked to both national and global drivers, namely Transition to Zero Carbon, Sustainable Manufacture, Digital & Communications, Circular Economy as well as Health & Wellbeing.

HENRY ROYCE INSTITUTE

UNIVERSITY OF LIVERPOOL | MATERIALS INNOVATION FACTORY

UKRI Engineering and Physical Sciences Research Council

LAB AUTOMATION for MATERIALS CHEMISTRY

A roadmap for increasing UK prosperity from the use of robotic science in materials innovation.

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HEADLINE MESSAGES

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BACKGROUND

The fourth industrial revolution (Industry 4.0) continues to transform the UK's manufacturing sector. By harnessing the power of advances in digital technologies such as artificial intelligence (AI), machine learning, robotics, and virtual reality technologies it is creating new opportunities and economic growth. These "digital" techniques are not purely virtual. In addition to new classes of virtual asset, such as data and "digital twins", these new technologies have had a transformative effect on the physicality of manufacturing; the use of robots for multiple tasks; the layout and specification of factory units; the way that manufacturing staff work in those units; the sensor and data infrastructure of manufacturing plants etc. It is now clear that an opportunity exists to apply similar digital technologies, both virtual and physical, to the R&D and innovation process itself. The systematic application of digital technologies to innovation has, by analogy with Industry 4.0, become known as Innovation 4.0.

The focus of this paper is on a single element of the Innovation 4.0 opportunity, namely the use of advanced automation and robotics techniques within research, development and innovation for chemistry and advanced materials. The paper addresses how the Royce Institute and the wider leadership of EPSRC and UKRI could create significant economic benefits for the UK through an investment in lab automation for the chemistry sector. It is informed by strategic insights into the emerging landscape of robotic technologies, extensive engagement with commercial UK R&D organisations and specialist lab automation companies, and the insights of the research leadership of the Materials Innovation Factory in Liverpool.

This paper is structured so that this set of Headline Messages can act as a standalone document containing a summary analysis and set of recommendations. The full body of the paper includes: (1) an introductory overview of some key opportunities for digitising R&D; (2) a specific and detailed analysis of the dynamics of the UK chemical and pharmaceutical sector; (3) a synoptic analysis of current UK industrial context derived from in-depth interviews carried out for this paper; (4) a summary of existing activity by UK academics and the wider UK Government context and (5) a set of detailed recommendations.

For the benefit of non-experts who may be reading this paper, a short introduction to some of the main concepts involved in the safe and effective application of robotics and automation within academic and commercial materials chemistry labs is provided after section 5 as a Technical Annex. Some readers may find that the best way to read this paper is to follow these Headline Messages with the Technical Annex, before reading sections (1) - (5).

ANALYSIS

1. The UK materials chemistry industries (including chemical, pharmaceutical, rubber and plastic manufacturing) are a strategic part of the UK's manufacturing base, both in terms of scale and in terms of long-term innovative capacity. The Chemicals & Pharmaceuticals sector has an annual turnover of £62.8 Bn, with £18.3 Bn Gross Value Added, which is about as large as the Automotive & Aerospace sector. If rubber and plastics manufacturing are included, the turnover is £87 Bn, with £27 Bn Gross Value Added.

2. The chemicals industry has delivered long term gains in total factor productivity (a proxy for innovation). Its cumulative performance from 1995 – 2016 was better than financial services and pharmaceuticals. End user applications of the chemistry value chain include: Pharmaceuticals & medicines; Household and personal care products; Agrochemicals and fertilisers; Food and drink; Paper and pulp; Life sciences; Automotive; Aerospace and Construction. Geographically, the main manufacturing sites of the sector are located outside the prosperous southeast (e.g. North-West, Humber, Teeside).

3. The majority of R&D leaders in academic science, commercial research, product development, and innovation activities expect that over the next 5 - 10 years, digital techniques will become increasingly mainstream in R&D, including in the materials chemistry industries. These leaders believe that these technologies have the potential to deliver a step-change in the innovation efficiency of UK and global materials chemistry industries.

4. Laboratory work remains a crucial value creating activity for organizations in these industries. This lab work is not optional: it is how they meet customer needs; create resilience in their activities; innovate; create competitive advantage; secure IP; guarantee quality of manufactured goods; and justify advertising claims. Much of this lab work is currently manual. Its *efficiency* will not easily be improved without investments in digital technologies, and in particular, lab automation.

5. Lab automation is defined as, "… the use of robotic and automated platforms to perform repetitive laboratory technical tasks". This approach exploits industrial automation technologies, but it has additional and more stringent safety requirements, and also needs to automate different types of work pattern. When properly implemented, lab automation can address a wide range of different experimental requirements: automated running of routine product testing, e.g. sample stability; exploration of a space of alternatives, e.g. formulation optimisation; and open-ended or hypothesis led discovery. Lab automation can be used for research, product development and testing, and is also of high value for routine lab testing in a production environment for both quality control (QC) and quality assurance (QA).

6. Lab automation can simultaneously improve the reproducibility, traceability, reliability, and intensity of lab operations compared with current manual approaches. Even relatively modest improvements in each of these factors can deliver 2X to 10X improvements in the efficiency of the lab process which has been automated. Lab automation can therefore make a substantial contribution to improving the end-to-end innovation efficiency of SMEs, academic labs, and multinational corporations.

7. Although the sector invests £6 Bn in R&D (75% in pharmaceuticals), and employs ~ 40,000 FTE, it has seen lower levels of action on digital R&D compared with the stated ambition of its senior leadership. This reflects the significant barriers which need to be overcome for the widespread deployment of digital R&D in materials chemistry. Many organisations in the chemical and pharmaceutical sectors are looking for help in planning and implementing digitisation roadmaps for their organisations.

8. The vast majority of UK based materials chemistry companies have low levels of investment and expertise in digital R&D approaches. Partly this is due to the very high fragmentation of the sector: 92% of the 3,700 active companies in the sector have less than 100 employees. The sector as a whole is therefore systematically under-exploiting lab automation and missing out on the potential benefits of increased efficiency in their lab operations.

9. Based on the long term experience of many of the organisations interviewed for this paper, it has become clear that there are two main approaches to digitising R&D in the chemistry sector. The first approach focuses on the application of generic IT technologies to scientific and technical work. This approach is often championed by the IT directors and Chief Information Officers of client companies. It leads to engagements with multinational IT providers who have little, or no, real insight into the core operational issues found in chemical R&D labs. The second approach focuses on digitising the core value creating activities of R&D labs. Here the key task is to understand how best to deliver higher efficiency and speed from pre-existing company investments in lab real estate, lab equipment, and lab staff. Generic IT technologies do not address the core technical or managerial issues which are involved in improving the operational efficiency of a lab. At the core of what a lab is about, it is the deployment of automation and robotics that provides the biggest potential improvements in efficiency.

10. If lab automation is introduced in the right way, it not only delivers a quantifiable and rapid return on investment (ROI), it is also an excellent way to engage the creativity and energy of existing lab staff in moving the company towards more digitised R&D. Automated lab work addresses issues of experimental excellence, data quality, reducing the volume of waste chemicals, reducing the burden of repetitive manual tasks, and perhaps most importantly to create more space in their daily lab work for invention and discovery.

11. Companies who have been exposed to the benefits of lab automation naturally look for wider opportunities to use digital technologies to manage pre-lab work (e.g. more sophisticated approaches to the design of

experiments for automated lab work) and post-lab work (e.g. advanced AI and data analysis of data from automated lab work to create high value predictive models). Automating lab work is therefore an excellent way, and perhaps even the optimal way, to spearhead a move to more digitised R&D within companies in the UK chemical sector.

12. Current approaches to lab automation in chemistry have tended to focus on the development of large highly integrated platforms. These platforms require substantial capital investments to buy or build (£500K - £1M), and can only fully deliver value if they are managed and maintained by a team of lab automation specialists. This means that only a relatively small number of large companies and academic centres of excellence have invested in these platforms.

13. Critical to the adoption of new automation technologies has been the development of tools and testbeds that allow industrial users to make initial assessments of how these methods can transform their lab processes. Over the past 10 years or so a number of Open-Access facilities have been equipped with these testbed platforms (e.g. Materials Innovation Factory, CPI, Imperial College). This approach has provided a welcome means for a much wider group of UK companies and academics to benefit from the large investments and advanced skills which are required to maximise use of these large platforms.

14. Existing Open-Access facilities act as test beds for lab automation approaches, and this helps industrial users of the facilities to understand and mitigate the risks involved in new capital investment. This approach helps companies to understand their current level of “digital maturity” in their R&D organisation, and helps them to understand how to develop their capacity to absorb these innovations so they gain maximum leverage and impact from the emerging science and technology.

15. Although there has been a significant positive impact from increasing the access of companies to well managed large automation platforms, this has not created a ‘trickle down’ route for lab automation technology to become widely and routinely used in materials chemistry companies. Given the low level of in-house lab automation skills in many companies, large integrated platforms are high risk investments, and are often orders of magnitude too expensive for most companies in the sector. We estimate that less than 1% of the addressable market in the UK for automating lab work in the chemistry sector has been served.

16. Notwithstanding these limitations, the UK chemical sector could begin to transform its end-to-end innovation efficiency and significantly increase its speed of innovation if we took a radically different approach that allowed the UK to “democratise” the use of lab automation. In this context ‘democratising’ lab automation means that it is physically deployed in many more locations, not by creating a larger number of pay-as-you-go Open-Access facilities which is also a way of making automation democratically available.

17. A number of recent breakthroughs, in particular the development of ‘Loose integration’ strategies and mobile robotic platforms, can now deliver automation platforms which are fully modular, highly reliable, and relatively cheap. They are capital efficient because they can use existing lab spaces, and integrate many pre-existing pieces of lab equipment. For these reasons, this new approach can be deployed in many more settings than the current state-of-the-art in large integrated automation platforms.

18. Covid-19 lockdowns since March 2020 have had a major impact on lab usage. It is possible in offices and factories to work from home or apply social distancing. In chemistry labs it is hard to implement these restrictions without significantly reducing the overall capacity of the lab. Covid-19 has already led to a substantial loss of innovation capacity, which will lead to a cumulative ‘innovation deficit’ for UK companies in the sector.

19. Prompted by the Covid-19 lockdowns, there has now emerged a new interest in developing technological means for running lab activities more remotely. This approach would increase staff safety, improve company monitoring of regulatory and health and safety performance, help employees to work more flexible hours, help those with caring responsibilities, and also allow individuals with disabilities to drive experimental programs who would otherwise have difficulty with laboratory access.

20. The UK Government has already identified robotics as an area in which the UK lags its international competitors. To begin to address this, UKRI has invested in robotic science and innovation in the form of the ISCF Programme in Robotics for a Safer World. This £95 M investment is intended to develop novel automation and robotics techniques for use in extreme environments. The aim to use robotics for tasks that are: dull, dirty, dangerous, demanding, distant, and distributed. The bulk of this investment is focused on

nuclear decommissioning, with other focal activities in offshore (wind, underwater, ice), mining and space. To date, UKRI has not made any comparable investments in the development of lab automation techniques for chemistry labs. Now is a good time to transfer some of the skills developed in this ISCF program into lab automation for chemical labs.

21. One of the primary roles of the Royce Institute is to catalyse industrial collaboration and accelerate translation in materials research and innovation. This means that it is ideally placed to articulate and invest in lab automation for the chemical and pharmaceutical sector. It can invest in programs of research, innovation, and commercial engagement that accelerate the translation of ideas and innovation throughout the UK chemical and pharmaceutical value chain, from start-ups to SMEs and corporates.

RECOMMENDATIONS

To maximise the potential of Industry 4.0 to drive UK economic growth, in particular as part of a transformation of foundation industries such as chemicals, glass and steel manufacturing, we must also apply similar digitisation principles and technologies across the entire innovation value chain.

The unprecedented speed of discovery, scale-up, and deployment of vaccines for Covid-19 have been an inspirational lesson in the enormous value that can be created through radically increasing the speed of science and innovation. Using lab automation, robotics, and high performance computing, the UK can make a similar step-change in the speed of research, development, and innovation in materials chemistry and materials science. To accelerate the creation and exploitation of the new materials and chemistries we need for a net-zero world, the UK urgently needs to invest in Innovation 4.0 as well as Industry 4.0.

Based on the analysis presented in this paper we recommend that the Royce Institute / EPSRC establish a new UK centre of excellence in translational science and technology for chemical lab automation. This centre would need an investment of £20 M over 5 years, which would then leverage between £25 M and £40 M of private co-investment from a wide pre-competitive consortium of industrial partners.

The primary target for this centre of excellence is to catalyse a dramatic increase in the utilisation of lab automation across the chemical and pharmaceutical sectors, with a demonstrable increase in lab efficiency and value creation. This would address current market failures, create new standards, increase the number of jobs in UK companies, develop new UK high-tech skills, and create an export opportunity for UK manufacturers of lab automation equipment.

The work programme for this centre of excellence would be clustered under four headings: Science; Innovation; Skills Development; and Deployment.

[A] Science: Developing the UK science base for lab automation.

- The centre of excellence would lead the development of a coherent scientific research programme in lab automation. This portfolio of pure and applied research science could include, but would not be limited to, work on: AI & autonomous control of lab robots; novel feedback mechanisms; error recovery methods; gripper design; search strategies; human factors safety; positioning technology solutions; co-operative robotics.
- The centre would pioneer the use of the full range of lab automation approaches for chemistry, and chemical materials for advanced coatings, battery materials, circular economy and catalysis. These need to include lower cost and hybrid human-fixed platform approaches. Through outreach, other UK centres need to be encouraged to set up “carbon-copy” activities for their own chemistries, which often have quite similar workflows in detail, once the barrier to deployment, which is the real barrier, is overcome by proof-of-concept work at a centre of excellence.
- In addition, the centre of excellence would liaise closely with Royce Institute and EPSRC leadership to identify emerging needs in new academic science which are relevant to lab automation, which would then be funded through normal EPSRC peer review processes.

[B] Innovation: Catalysing a UK innovation ecosystem that resolves core technology challenges for chemical lab automation.

- The centre of excellence would lead a range of UK wide outreach activities with chemical & pharmaceutical companies, academics actively using lab automation, the KTN, KCMC, CPI etc, to articulate the common automation needs for the chemical and pharmaceutical sector.
- Using these common needs as technical targets, the centre of excellence would then design a portfolio of between 10 and 20 new open platforms for low cost modular unit operations and mobile robotic platforms. These platforms would be further co-developed between the centre of excellence and UK based manufacturers to ensure that a range of robust and low cost modules were available for purchase by chemical companies as standard catalogue items.
- The centre would invest in the development and widespread exploitation of existing open software standards for connectivity, data exchange and automation control (e.g. SiLA2 or OPC). It would also actively engage with equipment vendors to increase the use of these standards on standard lab equipment.
- The centre would create new web-native collaboration tools for managing lab automation. These would be designed so that open-source versions were made available, as well as fully serviced commercial implementations offered by suitable UK commercial partners.
- The centre would lead a range of UK wide outreach activities with existing and emerging manufacturers of automation solutions. It would actively create and share a dynamic map of the UK innovation ecosystem in this space as it evolved.
- Additionally, such efforts will also allow an assessment of the suitability of partial automation of existing practices, rather than fully automated labs which can be a major barrier to adoption when full costing can be hard to justify.
- From this set of innovation activities, the centre of excellence will also be able to develop novel approaches to Cobots. These approaches will need to be based on both qualitative and quantitative studies of human-robot interactions in realistic lab settings.
- The centre can reapply a range of innovation readiness assessment tools, such as the MIF's Digital Maturity framework for lab R&D, and the CPI's "Innovation Integrator" for process scale up development to help industrial partners to articulate their needs as part of developing innovation and research programs.

[C] Skills Development: Building leadership and human capital in chemical lab automation.

- Create a coherent lab automation skills development framework for use across the UK chemical & pharmaceutical sector.
- Catalogue existing training and learning courses at apprentice, undergraduate and post-graduate level, indexed to the skill development framework.
- Help the UK HEI sector to support the development of skills and careers in lab automation and associated disciplines for the UK chemical and pharmaceutical sectors. For example, by co-designing Masters level training courses, both full-time and part-time, in Chemical Automation, and novel undergraduate level degrees in Chemistry with Robotics/Automation.
- Create a new strategic "Leadership in lab automation" curriculum and deliver as a continuing professional development (CPD) opportunity.

[D] Deployment: Catalysing a UK business ecosystem.

- Using the new insights into common automation needs, and new open platforms for low cost modular unit operations and mobile robotic platforms, build partnerships with UK manufacturers that lead to new commercial lab automation platforms which are available at a cost basis of below £50K per unit.
- The centre of excellence will lead the development of adoption pathways to enable impact from the investments in this translational science activity.
- These adoption pathways will be co-created with existing networks and activity, including KTN, KCMC, and CPI, but they will also create new mechanisms. For example, introducing an 'innovation voucher' scheme (at a value of £2K - £5K per voucher), that UK chemical and pharmaceutical organisations who employ less than 100 staff can use with accredited UK organisations to perform "Line Walk" consulting support for early stage exploration of the value of lab automation.

[E] Centre of Excellence: Structure and Leadership.

- The proposed centre of excellence should be funded by BEIS and operate on a hub and spoke model which exploits the existing UK critical mass in physical and intellectual infrastructure which is located in established centres of translational physical science excellence.
- Much of the academic leadership in this field can be found in the North-West / North of the UK. Locating leadership across the North of the UK would therefore provide a way to align with current UK Government ambitions to 'level-up' research and innovation investment and activity, without any compromise on quality. It would also co-locate lab automation leadership in the region with the largest concentration of UK chemicals manufacturing activity.
- The proposed centre of excellence should adopt an 'Open by Design' industry engagement model (as exemplified at the Materials Innovation Factory / Royce Institute), and develop a wide ranging outreach activity with small, medium, and large companies in the sector, to include potential end-users, robotic innovators, and both existing and new automation equipment manufacturers.

[F] Adjacent innovation opportunities.

An important additional benefit from the creation of a more vibrant UK innovation and business ecosystem in lab automation would be the chance to open adjacent opportunities for loose integration and mobile researchers. Post-Covid, this technology could become an important and affordable practical lifeline for sectors that want to accelerate innovation whilst implementing new practices to deal with social distancing.

In our experience, these new lab automation technologies have wide cross-sector relevance in healthcare, medicine, food, oil & gas, and chemicals. Based on numerous discussions to date, we expect commercial applications of loose integration and mobile robotic platforms to include, but not to be limited to:

- Delivering 'Low-Touch' R&D lab operations to deal with Covid.
- Automated Contract Research Organisation (CRO) units.
- Small volume, high value, biotech manufacture.
- Long term product stability testing (e.g. for Pharma applications).
- Automated sampling in manufacturing plants: from line, to test and measurement, then disposal.

1. INTRODUCTION

This paper addresses how the Royce Institute and the wider leadership of EPSRC and UKRI could create significant economic benefits for the UK through a substantial investment in lab automation for R&D in the chemistry sector. It is informed by global strategic insights into the emerging landscape of robotic technologies, an extensive engagement with commercial UK R&D organisations and specialist lab automation companies, and the insights of the world leading translational research activity in computer aided chemical discovery and lab automation at the Materials Innovation Factory in Liverpool.

The preceding section (Headline Messages) is provided as a standalone output of the work. It summarises in brief the analysis and recommendations that are described in full in the main body of the paper (sections 1 - 5).

For the benefit of non-experts who may be reading this paper, a short introduction to some of the main concepts involved in the safe and effective application of robotics and automation within academic and commercial materials chemistry labs is provided as a Technical Annex.

Made Smarter

In 2017, the UK Government published the *Made Smarter Review* [1]. This report identified the following industrial digital technologies as key drivers of the fourth industrial revolution (also called Industry 4.0) that was then beginning to transform the UK's manufacturing sector:

- Additive Manufacturing,
- Artificial Intelligence/Machine Learning & Data Analytics,
- Robotics and Automation,
- The Industrial Internet of Things (IIOT) and Connectivity (5G, LPWAN etc.)
- Virtual Reality & Augmented Reality

Although not explicitly addressed in the *Made Smarter* Review, it is also the case that these technologies can be used to *Innovate Smarter*. In other words, to transform UK R&D, in the form of academic science, commercial research, product development, and innovation, through the application of digital technologies.

There is already strong evidence from commercial and academic pioneers in this space that this 'Innovation 4.0' approach can deliver a step-change in the productivity of UK R&D and innovation activities across many sectors of commercial, academic and medical research [2]. The approach also lends itself to transforming the scale, quality, and pace of translational research happening in existing world leading academic science facilities in UK universities.

In many ways, the fundamental output of most R&D lab activities is data. This data can be used in a wide variety of ways to create value for a company or academic institute: it can inform decisions; shape the direction of a product development activity; provide objective evidence of an invention for use in a patent filing; underpin a product claim; meet a regulatory or safety requirement; or it can be used as the basis for a scientific paper. For that reason, the primary focus of the remainder of this paper is on the application of automation and robotic techniques to laboratory activity in materials chemistry.

Without high volumes of high quality lab data, the potential benefits of advanced AI and machine learning techniques in creating breakthrough materials discoveries, or commercially valuable inventions and products will not materialise. It is also worth keeping in mind that for a transformation of R&D and innovation, the mindset required to implement and exploit lab automation to more efficiently create quality data is vital for a wider increase in innovation efficiency and industrial productivity.

Productivity

Productivity is a ratio used by economists to quantify the efficiency with which inputs are converted into outputs of value: Productivity = Output Measure / Input Measure. Increasing productivity means we get more from less ('More bang per buck'). There are various forms of productivity studied by economists, for example, labour productivity is the average value of goods and services per hour of work (i.e. GDP), and is dependent on both capital investment and technology.

Fundamentally, goods manufacturing and services are different because of their differential capacity for productivity improvement. Manufacturing has a high-capacity for productivity improvement because technological progress can lead to a rapid increase in labour productivity. In general, services have a lower capacity for productivity improvement because there are relatively few opportunities for technology to raise labour productivity in services. When considering productivity, it is normally assumed that a company will have tried to optimise its activities, this means a company's productivity is the minimum necessary input to deliver a certain level of output, given its level of capital investment, labour force, and technological knowledge.

Economists have established a link between innovation spend and the productivity of organisations. Investing in R&D tends to lead to improvements in the functionality of the core product, or improvements in the process by which those products are made [3].

Research and Innovation Efficiency

The ***efficiency*** of an R&D or innovation activity is also of interest for leaders of R&D organisations and those academics who study innovation. When considering the end-to-end efficiency of an innovation process, it is useful to employ the OECD definition of innovation: "…a new or improved product or business process (or combination thereof) that differs significantly from the firm's previous products or business processes and that has been introduced on the market or brought into use by the firm" [4]. In this context then, innovation efficiency refers to how well a company's research and development expenditure translates into new products, processes and economic value.

The end-to-end efficiency of the innovation process for a company is difficult to quantify and also difficult to increase. Although commercial innovation and R&D requires investment in capital, technology and highly skilled staff, its outputs continue to be dominated by human knowledge tasks whose productivity have been fairly immune to improvement through the application of technology. This is no surprise. R&D is essentially a service provided to a company by a mix of in-house and external service providers. The promise of modern digital technologies is that they can improve R&D efficiency.

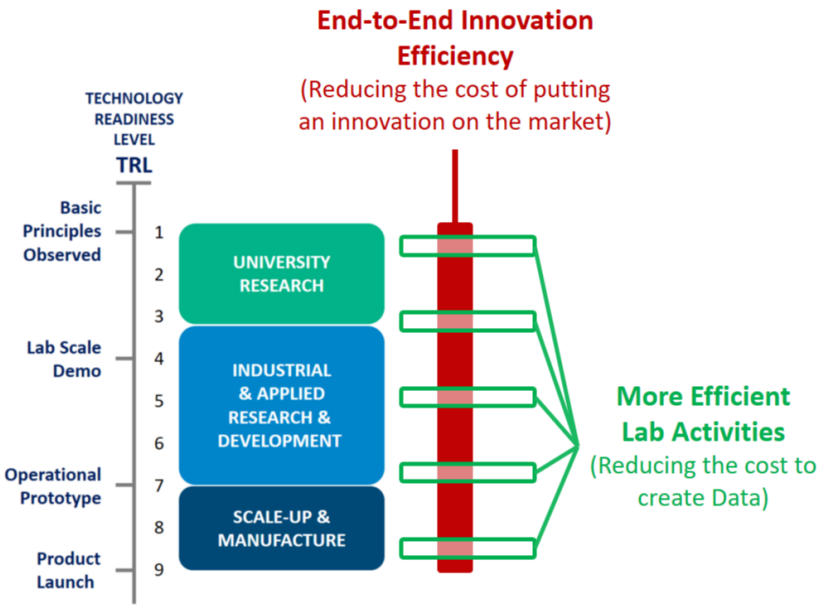


FIGURE 1: Two dimensions of innovation efficiency that are of relevance to academic and commercial organisations, and the UK economy as a whole.

End-to-end innovation efficiency is useful for a macroscopic level of analysis. For example, to address the efficiency of the complete R&D and innovation activity within a company, large Government lab, or academic facility. Perhaps contrary to expectation, the R&D efficiency of the global pharma industry (measured by the Number of drugs per billion US$ of R&D spending), has been in a precipitous decline for the past 75 years or so. This observation (known as Eroom's law) means that drug discovery is becoming slower and more expensive over time despite improvements in technology [5].

Of more interest to this paper is the efficiency of smaller units of R&D activity which are typically focused on the activities of a single lab. This unit of analysis will perhaps cover the work of between 5 and 10 scientists, technologists and lab technicians. For a small organisation, this size of lab may cover all of the lab work required for the totality of the company's R&D and innovation activities. For larger firms, the total R&D and innovation activity will be the aggregate of a number of these smaller labs. For a large multinational, their total corporate R&D activity may well be the aggregation of dozens or hundreds of lab units. As indicated in Figure 1, these lab activities work across all of the TRL levels of the innovation process, from 0 to 9, and they are also important in supporting ongoing manufacturing activities.

Labs and Offices

When compared to an office environment, a modern wet chemical laboratory space is very expensive to install and to run. On a per square metre basis, chemical labs are amongst the most expensive spaces that a company will ever build or lease. A lab construction or retrofit project needs to install specialist infrastructure for: general airflow management; fume hoods and air make-up; electrical supply for heating, lighting and ventilation; 3 phase electrical supply for specialist kit; backup and non-interruptible electrical supply; purified water systems; high purity gas plumbing; high density high speed data systems; safety technologies; staff access control; waste disposal systems; chemically resistant floor coverings and furniture.

The ongoing running costs for a lab are also much more expensive than for an office. The energy costs for a laboratory can easily be 2 to 3 times that of an office. Much of the waste created by a chemistry lab requires specialised waste disposal services to pick up, track, and dispose of the various waste streams. The financial deprecation of advanced scientific equipment will need to be borne by the operating costs of the lab activity. On top of these sources of cost, the highly skilled workforce required to obtain value from a lab adds to the cost of running a good quality R&D lab.

Digitising R&D

Given the high cost of capital investment for a chemistry lab, and the high staff costs, it is no wonder that R&D leaders are increasingly interested in exploiting digital technologies to improve the efficiency of their lab activities so they can maximise the value of lab outputs. Based on the long term experience of many of the organisations interviewed for this paper, it has become clear that there are two main approaches to digitising R&D in the chemistry sector.

1. **Generic IT Solutions:** The first approach focuses on the application of generic IT technologies to scientific and technical work. This approach involves the development and deployment of 'Electronic Lab Notebooks', 'Ontologies', 'Data Lakes', 'Artificial Intelligence', 'Distributed Cloud', etc. Often this approach will be championed by a company's IT director or Chief Information Officer.
2. **Automation:** The second approach focuses on digitising the core value creating activities of R&D labs. Here the key task is to understand how best to deliver higher efficiency from pre-existing company investments in lab real estate, lab equipment, and lab staff. Generic IT technologies do not address the core technical or managerial issues which are involved in improving the operational efficiency of a lab. At the core of what a lab is about, it is the deployment of automation and robotics that provides the biggest potential improvements in efficiency.

Lab Automation and Robotics

Lab automation can be defined as '…the use of robotic and automated platforms to perform repetitive laboratory technical tasks'. A number of different approaches for using robotic equipment are useful for research, product development and testing (i.e. at TRL 1-5). Lab automation and robotic techniques can also be of high value for routine lab testing in a production environment for both quality control (QC) and quality assurance (QA) (i.e. at TRL 9 and beyond). Lab automation can address a wide range of different experimental requirements:

- Automated running of routine product testing, e.g. sample stability.
- Exploration of a constrained space of alternatives, e.g. formulation optimisation.
- Open-ended or hypothesis led discovery.

When supplemented by direct to digital capture from manual experiments, and modern data management platforms, these use-cases cover a huge range of potential materials chemistry lab operations across the UK and globe.

Automated approaches to lab work have often been referred to generically as 'High-Throughput', e.g. High Throughput Screening (HTS). This nomenclature has had the unfortunate effect of focusing attention on the potential or actual increase in speed offered by automation. An increase in speed is only one of the multiple benefits that can be obtained by lab automation. It is often the least valuable of those benefits.

In many experimental situations, there are four independent dimensions on which lab automation can improve the quality and quantity of data coming from a lab activity:

- **Reproducibility:** By increasing the consistency and precision of a repeated task, lab automation can deliver a 2x to 5x improvement over the reproducibility of a comparable manual task. The higher consistency that is obtained from an automated process can often justify on its own the investment required to adopt automation. Benefits include: higher quality of results, removal of inter-operator variation, reduced waste, reduced need for duplicate testing.
- **Traceability:** Digital techniques are ideally suited for creating high-resolution and non-volatile records of the 'events' that happen through the time course of a lab based activity. Here digital data capture can provide a 5x or 10x higher quality of information versus human record keeping.
- **Reliability:** This is defined as the probability that an activity does not fail during a defined time under given functional and environmental conditions. If industrial robotic best practice is applied, then there is no reason why an automated process cannot achieve 95% - 99% reliability or uptime.
- **Intensity.** This is the number of tests / experiments / measurements performed per unit of time. Here lab automation can increase the speed of operation, it can parallelise operations, it can remove operator 'dead time', and it can increase the number of hours a lab space can be used per day when compared with manual lab work. These changes can easily achieve 2x to 5x improvements.

These four factors can be compounded (i.e. their effects are multiplied together not summed). This means that even a relatively modest improvement in **each** of these factors versus manual work can deliver very significant improvements in the overall quality and efficiency of the process that has been automated. Furthermore, if an automated lab workflow is driven with classical Design of Experiments (DoE) techniques, or more flexible forms of 'Autonomous' control, then both quality and efficiency can be further increased.

If lab automation is introduced in the right way, then it not only delivers a quantifiable and rapid return on investment (ROI), it is also an excellent way to engage the creativity and energy of existing lab staff in moving the company towards digital R&D. Instead of trying to convince an R&D chemist of the benefits of an abstract IT concept like a 'Data Lake' or an 'Ontology', the automation of lab work addresses issues of experimental excellence, data quality, reducing the volume of waste chemicals, reducing the burden of repetitive manual tasks, and perhaps most importantly how to create more space in the daily work of lab staff for creativity, invention and discovery.

Digital Maturity Framework

Based on experience at the Materials Innovation Factory, we have developed a digital maturity framework (Figure 2) for use in conversations with commercial partners who are interested in implementing digital techniques in their R&D activities.

This framework can be used for individual scientists to reflect on their own use of digital technologies, or to consider how a whole company measures up. Perhaps the best way to use this framework is at the level of a 'cellular lab'. Even for these relatively small operations, there are very few labs in the world which operate at a digital maturity of Level 4. In fact the vast majority operate at Level 0.

In general, chemistry sector companies have relatively low levels of investment and expertise in digital R&D approaches. Although these organisations are inspired by the academically leading activity they see in the world's best university groups, they are looking for help in planning and implementing a pragmatic digitisation roadmap for their organisation. The framework above was designed to address this need. It illustrates the wide scope and utility of digital R&D tools in materials chemistry R&D, and helps organisations to calibrate their current level of maturity and then articulate their future looking level of ambition.

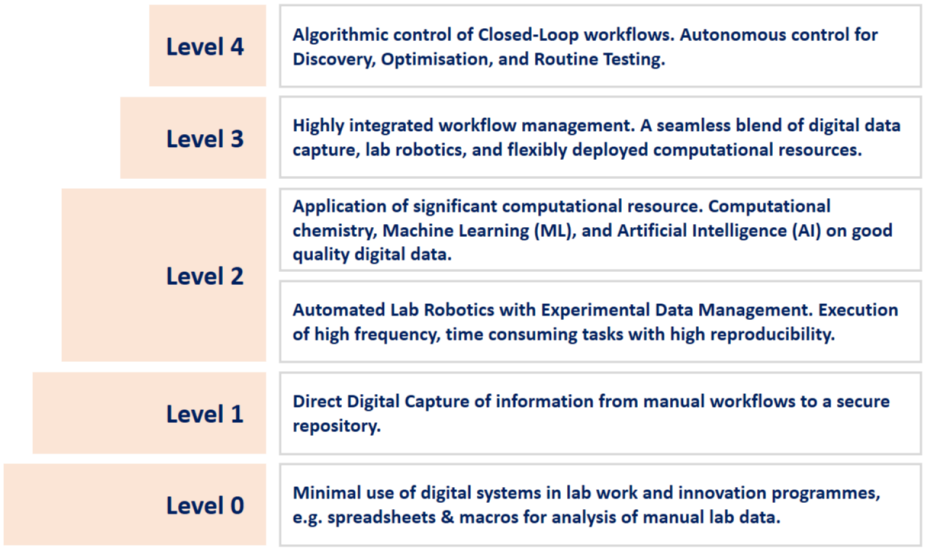


FIGURE 2: Digital maturity framework for chemical R&D activities.

This simple framework has now been used by multiple industrial organisations. Through our ongoing conversations with industrial innovators, we have found that lab automation is consistently seen as a crucial step to take in achieving higher levels of digital maturity for materials chemistry R&D.

Human Factors

The introduction of digital approaches into an existing R&D workforce is non-trivial. There are a number of critical micro-level and macro-level changes which need to be made to ensure successful implementation. For commercial researchers who are used to driving their programs 'one experiment at a time', or those who use paper lab-books to record observations, the impact of an increasingly digital approach on their work can be marked. Automated platforms and DoE approaches imply a major disruption to the working style of many scientists.

The introduction of lab automation in commercial organisations can fundamentally change the pace, scale and shape of their R&D programme. This drives the development of new skills. It therefore requires a step-change in ancillary R&D activities – particularly Modelling, Data Management and Data Science. Some of these changes can be made in parallel with the introduction of lab automation, or can usefully be catalysed by the introduction of automation.

From our experience, we have found that lab based chemists seem to engage more strongly with the concrete issues involved in automating a lab process than the more abstract issues they find in IT transformations. For many chemists, the conceptual leap involved in automating an existing manual process is far easier to manage than the more arcane issues they need to grapple with in modern lab information systems. For this reason, a strategic move to lab automation can be an ideal way to spearhead a wider change process for moving to digital R&D.

People change processes are not addressed in detail in this paper, but the senior leadership teams of R&D organisations who have successfully implemented digital approaches in R&D have found that it is ***never too soon*** to address how to win the hearts & minds of their staff as part of a digital R&D change process.

New IP Commercialisation Strategies

Modern scientific research activity creates a rich set of intellectual assets. These include know-how, trade secrets, databases, assays, published papers, partnerships, protocols, digital platforms, and patents. All of these assets can be used as the basis of commercial competitive advantage and economic spill-over from university research. In some sectors, such as pharma, chemistry, and bioscience, a patent remains a fundamentally important legal means to claim control over an invention. The granted patent gives the company a governmental recognition that for a limited time, the patented technology is the property of that company. However, the emergence of new digital platforms has begun to erode the importance of patents as a class of

asset. As speed to market becomes a valuable way for companies to succeed, the value of patents is likely to diminish over time.

One of the major IP commercialisation strategies which will increasingly be used by companies is the use of APIs built around closed, robustly engineered, digital assets. This aspect of IP control is not yet well understood in many commercial and academic chemistry teams, but this approach to IP control and exploitation will become a vital element in the coherent application of lab automation and Innovation 4.0 techniques.

Business Benefits

One of the reasons that Innovation 4.0 has great value creation potential, is that it can directly change the structure of existing commercial innovation processes. Digital techniques allow innovators to short-circuit some of their normal stage gates without increasing risk in the innovation process. Not only does lab automation increase the productivity of core lab processes, it also creates high quality data and structured digital assets which are of high long term value for later scale-up and manufacturing work.

Applying advanced digital techniques such as lab automation and robotics to research, product development and innovation opens up the following opportunities for commercial organisations:

- Speed: An ability to launch bigger innovations faster.
- IP: An opportunity to carve out wider and more robust patent positions.
- Innovation: The ability to develop superior, but harder to make, products.
- Scale-Up: Moving from lab or pilot plant scale to factory scale with no nasty surprises.
- Roll-Out: Consistent delivery of manufactured quality.

2. SECTOR CONTEXT

UK Chemistry Sector & Challenges

The global Chemistry and Advanced Materials industry is vast. It has a turnover of more than $3.5 Trillion per annum, employs about 10 million people, and accounts for about 2% of global GDP [6]. In the UK, the chemical and pharmaceutical sector is a major part of the UK economy. The sector has an annual turnover of £62.8 Bn, with £18.3 Bn Gross Value Added (2019 figures). If rubber and plastics manufacturing are included, the sector has a turnover of £87 Bn, with £27 Bn Gross Value Added (2019 figures) [7].

The chemical and pharmaceutical sector is a major high-value creating UK employer, with about 152,000 people directly employed and probably a total of 300,000 - 400,000 jobs which depend on the industry. This is comparable to the economic contribution of the life sciences, automotive, and aerospace sectors. End user applications of the chemistry value chain include: Household and personal care products; Agrochemicals and fertilisers; Food and drink; Paper and pulp; Life sciences; Automotive; Aerospace and Construction.

In total there are more than 3,700 companies working in the chemical and pharmaceutical sector. Table1 shows how these companies are distributed in size. It should be noted that in addition to the small number of very large corporations which are active in this sector, there is a large number of much smaller businesses. 92% of companies in the sector have less than 100 employees.

SIZE OF BUSINESS (Number of employees)	CHEMICAL SECTOR (Number of Businesses)	PHARMACEUTICAL SECTOR (Number of Businesses)
0 - 4	1699	420
5 - 9	375	55
10 - 19	300	45
20 - 49	280	45
50 - 99	190	25
100 - 249	110	35
> 250	80	50
TOTAL	3025	675

TABLE 1: Distribution of company size in the UK Chemical and Pharmaceutical sector (ONS) [8].

Scale and Productivity

Chemistry remains a core part of the UK's strategic manufacturing base, both in terms of scale and in terms of its long-term innovative capacity. In a recent talk to the Society for the Chemical Industry (SCI), Professor Richard Jones presents an analysis of both the total factor productivity growth of key UK sectors between 1995 and 2016 (which is interpreted by economists as a measure of the long term level of "innovation"), and the share of the UK economy GVA in 2016 that these sectors represented [9]. See Table 2.

It is well known that ***finance & insurance*** are important for the UK economy, but ***manufacturing*** as a whole is both a larger sector (10% of 2016 GVA) and of comparable long-term innovation performance (total factor productivity growth of 37%). Within manufacturing, the combined materials chemistry industries includes very large sectors such as ***chemicals & chemical products*** with a long-term total factor productivity growth of 63% which is comparable to ***Information & communication*** (~70%), and ***automotive & aerospace*** (73%).
Richard Jones makes the following comment:

> But the surprise – to many, I suspect – is the performance of the chemicals sector. Written off in the late 90's as the "old economy", the chemicals industry has delivered the steadiest gains in total factor productivity, its cumulative performance exceeding both financial services and pharmaceuticals. What's more, if we look at where the chemicals industry takes place, in the context of regional economic inequality

and the “levelling up” agenda of the government, we find that it is located outside the prosperous southeast, in Northwest England, the Humber and Teeside.

SECTOR	Total factor productivity growth 1995 - 2016	2016 share of the economy by GVA
Chemicals & Chemical Products	63%	0.65%
Pharmaceuticals	44%	0.75%
Rubber & Plastics	28%	0.8%
Transport equipment (Automotive & Aerospace)	73%	1.5%

TABLE 2: Total factor productivity growth between 1995 and 2016 and the share of the UK economy GVA in 2016 for selected UK sectors [9].

Chemicals R&D

The UK chemical and pharmaceutical sector continues to be a major investor in R&D, with annual R&D spending in excess of £6 Bn (2019), nearly 75% of which was for pharmaceuticals. R&D activity in chemicals and pharmaceuticals employs 39,000 full time equivalent staff (roughly 17,000 scientists and engineers, 12,000 lab technicians & assistants, and 11,000 in admin & clerical staff) [10]. Assuming that half of the scientists and engineers work in laboratories, then this is a total of about 20,000 R&D lab workers. In addition, there are a substantial number of laboratory staff employed in the chemistry sector who do not work in an R&D role (e.g. they work in QA / QC testing labs in factories and supply chain).

There is no detailed data available about the way that chemistry labs are organised across the sector. However, experience shows that very often chemical R&D work can be resolved into basic “cells” of activity of between 5 and 10 staff. Each of these cellular units will have a single focal activity: research, product development, process development, QC/QA, routine analysis etc. Assuming that the average size of a cellular lab activity in the UK chemical and pharmaceutical sector is 8 FTE, then the total lab activity of the sector across the UK can be thought of as a collection of between 2,500 and 3,000 cellular labs. This ‘cellular lab’ model is a useful way to keep a focus on the granularity of the lab work going on in the UK chemical and pharmaceutical sector. In particular, it is at the level of these cellular activities that a lab automation solution has to deliver value.

Role of Labs in creating value

Laboratory work is a core value creation activity for organizations in the chemical and pharmaceutical sector. The sector creates more than £18 Bn per annum in Gross Value Added (the value added over and above the costs of raw materials, capital and labour). Assuming that 20% of the added value is from lab based R&D and technical activities (based on fraction of personnel in R&D), then the GVA of lab work in the chemical and pharmaceutical sector is worth more than £3.5 Bn per annum.

In the chemical and pharmaceutical sector Lab work is not optional: it is how firms in the sector meet customer needs, innovate, create competitive advantage, secure IP, and justify advertising claims.

Much of this lab work remains manual.

Lab data is usually the outcome of a measurement, or a series of measurements, which have been made on a sample of some sort. In a Quality Control (QC) or Quality Assurance (QA) lab, the data is the result of a standard physical test or analytical chemistry measurement. In a product development lab tests will be made on samples which have just been made in the lab, or which have been taken out of long term storage in an oven or a fridge. In a research lab, the data may be measurements of more fundamental physical quantities, such as surface tension, pH, melting point, crystal structure, rheology, or density, on newly synthesised chemical entities which have never existed before.

The efficiency of many lab based activities can be improved by automation.

The simplest useful definition of the efficiency of a lab is, "... the number of data points obtained per unit of cost" (See technical Annex). An increase in lab efficiency creates additional value, which can then be harvested in a number of different ways: a reduction in lab operation costs; reduced chemical waste; an increase in speed of R&D and innovation activities; higher quality predictive modelling of product or process performance; faster regulatory approvals; building stronger patent portfolios; unlocking staff creativity etc.

Innovation Challenges

The innovation challenges which are currently being addressed across the chemical and pharmaceutical sector include the following: Sustainable Materials for Consumer Products; Sustainable Packaging; Advanced Materials for Health and Wellbeing; Advanced Materials for Composites; Formulation for the Future; Waste to Feedstocks; Industrial Symbiosis and Research Efficiency; Enabling the Hydrogen Economy; Advanced Materials for Batteries; Digitisation of Supply Chains and New Process Technologies.

Many of the benefits of lab automation for chemistry in the widest sense are also vital for chemical based materials that are important in advanced coatings, batteries, fuel cells, and other electrification technologies, as well as a very wide range of opportunities in sustainable manufacturing and circular economy applications enabled by catalysis. In these strategically important future looking technologies the UK has a near-term opportunity which is distinct from that of previous decades because in these areas the UK has some key global science and technology players. This broad view of 'chemistry' means that lab automation needs to include attention to automated workflows for heterogeneous catalysis, battery materials and thin film deposition.

Digital R&D in Chemistry

A market analysis of the UK materials chemistry sector's interest in digital R&D was carried out by an STFC led consortium in 2019 [11]. This analysis included an online survey, detailed 1-2-1 interviews, and a business engagement workshop. Respondents included 62 SMEs, 28 large corporates, and 17 intermediary organisations.

- There was real enthusiasm from respondents to co-invest in major UK Government funded innovation programs that sought to improve the application of digital tools to materials chemistry innovation.
- 72% of businesses stated that developments in new or improved materials were either very relevant, or critical, to their production processes.
- Most companies saw digital R&D approaches as important to their future, but they have uncertainty around how to adopt them: 48% said they had little or basic knowledge of how digital technologies can assist with this.
- The main barriers to digital adoption in R&D included: a lack of understanding of the technology; how best to frame the business case (18%); and lack of access to specialist expertise (18%).

More recent interviews conducted for this paper have supported the conclusions of this 2019 market analysis. Although many companies are interested in transforming their research, innovation and product development activities by implementing digital techniques, they want to avoid wasting time and money, and implement the things that will have the biggest impact. We also heard from companies who have engaged with very large IT vendors who claim that they can digitise R&D. In fact, these organisations seem to have little or no meaningful insight into the real challenges faced by R&D organisations in the chemical sector.

Large companies in this sector see strategic opportunities in applying digital techniques such as lab automation and robotics in their R&D processes, but they do not have easy routes to access specialist expertise and facilities and struggle to frame internal investment business cases. Many SMEs currently lack expertise and understanding of how digital technologies can help them transform their innovation activity.

The technical skill sets which are the common basis for chemical sector organisations do not have a significant overlap with the skills required for specifying and implementing lab automation or other digital R&D techniques. This skill and experience deficit exposes R&D organisations to some risks. Low self-confidence can lead companies to wait too long to get started, which leads to a long term reduction in their competitive position. Alternatively, initial overconfidence can lead to companies making expensive 'rookie' errors, after which they

become conservative. Both of these factors lead to UK companies being less competitive than comparable organisations in Europe, Asia and the US.

There is a generalised shortage of experienced staff in the UK who have a nuanced understanding of both the challenges of chemical R&D and real insights into the process of automating lab activities. We believe that the widespread adoption of digital approaches to R&D and innovation in the UK chemical sector cannot rely on self-directed learning. Investment decisions in this space are high-risk and prohibitively costly, in terms of elapsed time, CAPEX, OPEX & missed market opportunities.

Impact of Covid-19 (2020- 2025)

The series of UK Covid-19 lockdowns from March 2020 to the present have had a major impact on lab usage. It is possible in many office and factory environments to apply social distancing regulations, such as staying two metres apart. But in many chemistry labs, it has been hard to implement these restrictions without significantly reducing the overall capacity of the lab. Initial analyses by the Materials Innovation Factory and its commercial partners in May 2020 indicated that social distancing had reduced some lab activities to less than 25% of their pre-Covid capacity. This is a substantial loss of innovation capacity, which will lead to an 'innovation deficit', and an erosion of future profitability for the UK. We estimated that the total loss of portfolio value caused by Covid-19 related lab disruption could easily exceed £3 Bn.

Covid-19, and the closely related variants which are now emerging, are likely to create a cascade of social, medical, economic, and technological consequences. These impacts may last for multiple years. The widespread containment policies which were designed to control the pandemic will change how labs work. For organisations which rely on laboratory work to create value, the challenge is substantial: there is no easy way to run labs with social distancing measures in force [12].

Many organisations in the chemistry sector are now actively looking for technological means for them to run their lab activities more remotely. If organisations can reduce or remove a requirement for physical laboratory access, it would enable them to give more of their staff the means to run experimental lab protocols from home. In addition to mitigating the specific issues associated with Covid-19 lockdowns, this prospect would also: increase staff safety; improve company monitoring of regulatory and health and safety performance; help employees to work more flexible hours; help those with caring responsibilities; and also allow individuals with disabilities to drive experimental programs who otherwise have difficulty with laboratory access.

Global Trends

A number of global surveys over the past 5 years have indicated the growing interest in digital techniques by senior executives in the chemistry and advanced materials markets. In 2014, Accenture undertook a Global Digital Chemicals Survey of more than 150 top level executives in petrochemicals, agrochemicals, paints and coatings, plastics and fibres, specialty chemicals and basic and intermediate chemicals companies [Cited in 6]. For their business as a whole, these findings were emphatic:

- …executives strongly believe in the transformational effect of digitalization on their industry.
- 94% expect digital to revolutionize the industry
- 87% say that firms that don't embrace digital will lose their competitive edge and possibly face extinction

Similar responses were found in a 2016 Global Industry 4.0 Survey by PwC [13], which noted that the chemical sector has a history of investing in process control BUT a big increase in investment was planned, including:

- Digitisation of product and service offerings
- Digitalised product development & engineering

In 2017, the World Economic Forum and Accenture estimated that the cumulative global impact of digitising R&D in the chemical and advanced materials sector would be an additional value of $28-31Bn of value (between 2016 and 2025) [6].

Accessibility of Robotic technology

In an analysis made by Accenture in January 2020 on the state of digitalisation in Life Science R&D, they found that of the 128 senior life science innovation leaders they asked Where are you in your digital journey?, 40%

had not yet started, 37% were 'piloting' (many for 6 months or more), and 13% were scaling up. Only 10% of respondents claimed to already be digital [14]. Given that the life sciences sector has invested substantially more in lab automation and digital R&D than the chemical sector, and for a much longer time, it seems that even with a strongly articulated sense of urgency, the reality has fallen short of the ambition.

In late 2020, Accenture produced a report on their view of key technology trends [15]. One of these, which they call *Robots in the Wild*, notes that advances in sensors and computer vision, when combined with lower cost robot hardware will make automation more accessible for companies in almost every industry sector. The authors note that "...across 21 industries surveyed, 61% of executives expect their organizations will use robotics in uncontrolled environments within the next two years". For R&D activities, "Robots in the Wild" means mobile robotic researchers working in otherwise ordinary wet chemistry labs, and also often working collaboratively with lab staff.

Web native Productivity Tools

Productivity tools are the latest wave of software innovation which are of direct relevance to lucrative knowledge economy activities. Examples include:

- ***Frame.io***: for video production professionals
- ***Everlaw***: for legal discovery
- ***Figma***: for UX designers
- ***Onshape***: for CAD engineers
- ***Benchling***: for Life Science R&D

All of these platforms are designed to provide web native collaboration spaces for specific types of knowledge work. They each involve the imaginative unbundling and rebundling of functionality which is now found in spreadsheets, email, file sharing and collaborative editing platforms to deliver: "...some kind of richer canvas that mixes all of these together in ways that are native to the web and collaboration" [16]. There is no obviously available web native collaboration platform designed for use in chemical lab automation applications.

3. INDUSTRIAL INSIGHTS

The following section covers a range of different issues and opportunities which have emerged from fruitful and open interviews and conversations with UK leading lab automation innovators, academics active in the space, and both large and small scale end-users of lab automation solutions.

Robotic Technology in Chemistry Labs

Robotic and automated approaches to R&D have become increasingly viable because they are able to exploit technologies which have been developed and commercialised for use in factories. However, the ready availability of industrial automation equipment does not mean that it is a simple task to deploy automation in a lab environment. There are a number of reasons for this.

Firstly, labs do not work like factories. The dynamics of the work process in a chemistry lab has more in common with a craft workshop than a factory. Different 'workstations' or unit operations are distributed around the lab and skilled technical staff then string together the operations they need to get their desired outputs. Humans integrate the different tasks at 'run-time' not in advance. The flexibility that is inherent in this way of working is of high value in a lab operation. Installing a robotic solution that is *less flexible* than a team of human operators can therefore potentially reduce the efficiency of a lab's operations.

Secondly, the inherent safety issues associated with handling chemicals increases the overall level of hazards that have to be addressed in a robotic application. In a factory environment if a robot drops a part, then gravity will accelerate a hard and potentially heavy and/or sharp object to the ground. In a chemistry lab if a robot drops a sample, then the consequences can include an uncontrolled spillage of chemical reagents. This is potentially very serious, including possibilities for explosion, fire, spillage of teratogenic or bio-active agents, radioactive materials, toxic substances, and oxidising or corrosive materials.

Work Patterns

The work pattern of a lab therefore creates several distinct challenges when trying to deploy automation. The first is a need to selectively automate specific unit operations, which work within the larger manual activities in the lab. This process has already been happening in the field of analytical chemistry for more than 25 years. Modern analytical instruments such as gas chromatography, LCMS and nmr are now fitted with an "auto-sampler" which is a carousel or rack designed to hold a queue of samples in standardised glass vials or sample containers. The autosampler extracts a liquid or solid sample from each of the samples in the queue in turn, and for each one runs the required analytical method.

Within the wider range of activities found in chemistry labs, there is a paucity of low-cost, robust, automated unit operations.

Integration

The second challenge is to string together more than one automated unit operation into a completely automated workflow. These workflows either need to be controlled in a predetermined way, or if they are coupled into a closed loop, need to be managed by a more sophisticated algorithm to optimise an experimental system or autonomously create novelty.

Even with a large increase in investment in lab automation, over the next 5-10 years a substantial number of operations in chemical and pharmaceutical labs will remain manual. That is, they will rely on human control of kinematics, observation, data capture, and/or measurement. This means that even for organisations which invest heavily in lab automation, overall human control of the lab activity will remain crucial. One of the most important attributes that humans bring to a lab activity is their flexibility. In fact, as a lab becomes more automated, one critical thing to maintain is the flexibility that lab workflows already have. Overall, this means that for any materials chemistry organisation which is choosing an approach to lab automation, they need to carefully balance the advantages of highly efficient lab automation activities and the workflow flexibility offered by humans.

Cobots

In parallel with the introduction of lab automation, some R&D organisations have already begun to actively explore the opportunities that co-operative robots, or Cobots, offer in lab work. One example of a non-lab cobot application is within a car factory where a robot arm lifts a heavy wheel into position for attaching to an axle. A human operator can now apply and tighten the nuts holding the wheel in place. In a lab application the strength of a robot arm is not such an important advantage. It is the opportunity to replace the variation in human fine motor control with that of a robot that has higher potential utility. Here human-robot cooperation would create a different set of opportunities and a different set of issues.

Technical challenges

There are substantive technical and operational challenges associated with implementing automation in chemistry labs when compared with the application of lab automation in the life sciences. These challenges are wide ranging and in some cases fundamental. A non-exhaustive list of challenges includes:

- The wide diversity of material formats, including monolithic solids, granular or powdered materials, soft solids (pastes, gels, viscous, adhesive);
- The intrinsic safety hazards associated with corrosive, explosive, flammable, radioactive, and teratogenic materials;
- The lack of simple scaling relationships due to the physics of the materials;
- A lack of standardised storage and experimental formats compared with the near universal applicability of 96 well plate format and liquid pipetting in the life sciences;
- The lack of safety regulations governing scales of operation that are intermediate between small scale lab chemistry (<500 g) and pilot plants (>1,000 kg), including issues of solvent storage on automated platforms.

Commercial R&D Lab Automation Strategy

There are a number of quite distinct opportunities for lab automation across commercial R&D use-cases. These range from research tasks, in which a robotic system would be designed so that it could address a broad range of challenges, to much more focused product development applications in which a relatively limited number of tasks need to be repeatedly used for a much higher number of samples. These differences are highlighted in the following figure. In research applications, it is often worth trading off some throughput to retain high flexibility. In product development this trade off runs in the opposite direction (Figure 3).

At a strategic level it is often not possible to use a single lab automation system to achieve the outputs that are required for both research and product development activities. It is however possible to design a **modular** approach which can deliver functionality to both research and product development teams. Modularity is essential for flexibility and can help deliver system reliability because new modules can be tested independently before they are used in a workflow. A fully modular approach requires two things to be addressed simultaneously:

- that a coherent approach to the definition of automated modular Unit Operations is used (bottom-up)
- that a flexible means for integrating automated modular Unit Operations into an overall Workflow has been chosen (top-down).

Both of these considerations need to be held in mind during the strategic planning phase of lab automation investments. Unit Operations and Workflows operate at very different levels of granularity, however, they are inextricably connected. This means that decisions which are made about the way a Unit Operation is automated and the integration strategy that is used are never 100% de-coupled. Decisions about how to automate a Unit Operation need to be made in light of the overarching integration approach, and vice-versa.

In addition to control mechanisms, integration is largely to do with logistics, materials handling, and data flow. Decisions about logistics can have profound effects on the overall success of lab automation. Even seemingly unimportant design decisions about the logistics of material flow can have enormous effects. The size, shape, material properties, and unit cost of the containers used in an automated system can make or break an implementation:

	RESEARCH	PRODUCT DEVELOPMENT
Experimental Objective	Screening	Optimisation
Flexibility	High	Low
Speed	Medium	High
Repetitiveness	Medium	High
Precision (Data Granularity)	Medium	High
Outputs	*Inventions, Insights, Models, Patents.*	*New Products, Process Diagrams, Specifications.*

FIGURE 3: Automation strategies for Research and Product Development applications.

Sources of Competitive advantage

For many commercial organisations, the following high-level segmentation of lab activities has been found to be useful for articulating partnership and collaboration opportunities for innovations in lab automation. Two activities in particular, Make and Characterise, provide interesting opportunities for collaboration and for establishing pre-competitive industry-academic consortia. In practice, many Make activities are found to be widely used or generic across a given industry sector. Having an automated method for these activities does not necessarily confer competitive advantage. The Characterise activities are even less specific, and are often generic across the whole of the physical and biological sciences. However, this is not the case for Performance Testing. Very often this type of testing addresses the actual utility of a prototype product in the market application (or a proxy test of that application).

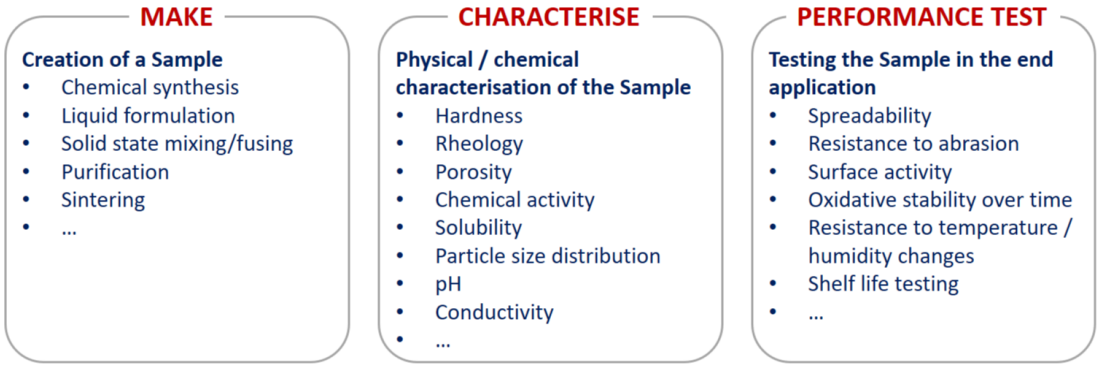


FIGURE 4: High level classification of lab unit operations for automation.

Creating an automated solution for a performance test is an opportunity for a company to create competitive advantage: usually, it will only be a direct competitor who would have an identical need.

Note that although individual unit operations within the Make and Characterise steps can be automated separately, it is often found that trying to automate both at the same time is very efficient. Otherwise the danger is that the overall process can only proceed at the speed of the slowest process. In some cases it may be an adjacent data analysis step that actually slows down an end-to-end process. For example, some types of experimental data characterisation (like powder diffraction) is not fast enough to keep up with the data creation.

This three part classification is a useful way to explain the benefits of a high level automated or autonomous control algorithm. Figure 5 shows schematically how a ‘closed loop’ design can be used to further optimise how

a set of Make - Characterise - Performance Test units can be exploited. The addition of automated control adds considerable speed to the end-to-end process, and provides an opportunity for fully autonomous control (e.g. to achieve level 4 of the digital maturity model in Figure 2).

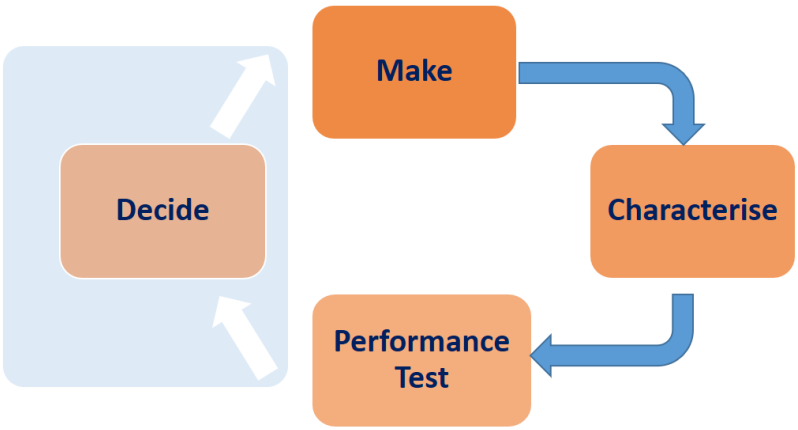


FIGURE 5: Adding an algorithmic Decide step into an existing Make - Characterise - Performance test loop creates a 'closed-loop' that significantly speeds up the end-to-end process.

Investment Case for Automation

As companies in the chemical and pharmaceutical sector become interested in lab automation, they often want to build in-house understanding of the area through engagement with an existing open-access capability at a centre of excellence such as the Centre for Process Innovation or Materials Innovation Factory. These facilities are funded in such a way that a company can easily gain access to expert teams and fully serviced platforms which have a high cost of capital outlay, high service and running costs, and a high concentration of specialised skills.

Inevitably, companies begin considering how they might develop in-house lab automation facilities and skills. Broadly speaking there are three approaches to implementing in-house lab automation in a commercial chemistry lab. The first is to buy an off-the-shelf tightly integrated platform, the second is to procure a bespoke tightly integrated platform, the third is to use a fully modular approach using loose integration.

Each of these have advantages and disadvantages and quite distinctive investment and payback profiles. In some cases, a company will need to invest in the creation of an in-house lab automation team to minimise risks of a particular approach.

Tightly integrated platforms

The maturity of lab automation in the life sciences has created a significant market for tightly integrated lab automation platforms. These platforms automate a series of Unit Operations required for a particular workflow. In life sciences, the almost universal use of 96 well plates and liquid handling means that a lab can shift its manual plate pipetting/handling onto an automated commercial platform with low risk. These platforms can handle a wide range of life science tasks: UV/Vis quantification of DNA and RNA; particle sizing; viscosity; stability; microscopy; buffer exchange and dilution; and pH measurement. These platforms are designed for use with small volume samples of aqueous solution (0.1 – 200 mL).

If a chemistry workflow can be handled in a 96 well plate format, then these platforms are a good way to automate. However, if the physical properties of the sample are very different from aqueous solutions, then these approaches are unproven. In addition, adding non-standard processes into these off-the-shelf platforms is very difficult.

In parallel with life science platforms, these are a number of tightly integrated platforms available for chemistry workflows such as synthesis and product formulation.

A number of large end-users of lab automation have invested heavily in bespoke tightly integrated platforms. Although this approach is necessary for specialised lab automation requirements, these projects are inherently high-risk. Very often the automation supplier will only ever build a single unit. The platform is a prototype, and can often have significant post-build issues that need ironing out. A company looking to successfully commission this type of platform will need significant in-house expertise in lab automation, IT interfacing, and procurement, to set up these large design and build projects. There is only a small market for very large high capital automation platforms (i.e. that cost >£300 K). The number of active integration companies reflect this. This approach can only ever touch a tiny part of the addressable market for lab automation.

One of the issues which is found with tightly integrated platforms is that they often preclude opportunities for expansion or flexibility.

Loose integration

Loose integration adopts a different approach to lab automation. Rather than trying to tightly integrate all Unit Operations within a single confined unit, the loose integration approach is designed to exploit existing lab space, benching, services, and pre-automated Unit Operations. The Workflow is then implemented by the use of a mobile robotic researcher.

This approach allows an end-user company a lot of flexibility in choosing the number of, location of, and type of Unit Operation. The approach allows an automated Workflow to evolve over time – as new Unit Operations are added, upgrades, or replaced. This approach also requires a much shorter and less expensive design phase, which can be more easily broken into a sequence of discrete phases.

	TIGHTLY INTEGRATED OFF THE SHELF PLATFORMS	TIGHTLY INTEGRATED BESPOKE PLATFROMS	LOOSE INTEGRATION
Summary	**Optimised for a small number of workflow**	**Optimised for a small number of related workflows**	**Highly flexible, deployable for multiple workflows**
CAPEX	Medium - High	High	Low - Medium
Flexibility	Low	Medium	High
Reliability	High	Medium	High
Data Platform	Often closed	Mixed	Open
Ease of Integration with other lab activities	Medium	Medium	High
Safety	Designed to exclude human proximity	Designed to exclude human proximity	Unit operations exclude human proximity. Lab level systems designed to stop on human proximity
Procurement	Buying an off the shelf system from a selection of competitive suppliers	Requires a long and costly design study prior to the build commencing.	Can specify and buy in a modular way.
Unit Operation Innovation	Limited	Fully customisable	Unlimited

TABLE 3: Comparison of tightly integrated versus loose integration approaches to lab automation.

One of the consequences of these different approaches to implementing in-house lab automation is a very different spend profile. For an off-the-shelf tightly integrated piece of lab automation, the end-user company needs to secure a significant quantity of in-house Capex funding to make the purchase. Buying an off the shelf system from a selection of competitive suppliers is a normal commercial procurement process, but given the limited number of potential vendors, it can be difficult to properly weigh up different solutions. A reasonable quality off-the-shelf platform for chemical lab uses can easily cost between £300 K and £800 K.

The purchase of a bespoke platform has a similar total cost to an off-the-shelf platform, but the process is inherently higher risk, and needs more in-house expertise to successfully manage the process. In these projects the design study phase can easily be 25% to 30% of the total costs. Trying to save costs by shortening the design phase often leads to a poor quality design, and ultimately a platform that does not meet the expectations of stakeholders.

A fully modular approach using loose integration has a very different spend profile. Now the focus will be on purchasing modules that each have an accelerating effect on lab work. A series of smaller purchases is lower risk for most commercial organisations, and this approach allows decision makers to see the returns on their investments, before committing any further funding.

Mixed Human - Fixed Unit Operation based Workflows

In many research applications of lab automation, both academic and commercial, a 'mixed' workflow that combines a 'fixed' platform or unit operation with human operations can be a powerful way to exploit lab automation. In these applications, it is the combination of relatively inexpensive off-the-shelf automated dispensing or measurement kit with clearly articulated hypotheses and Design of Experiment (DoE) approaches that facilitates discovery and invention. This approach is well-illustrated by the work carried out by the Rosseinsky group with Johnson-Matthey to discover new Fischer-Tropsch catalysts [17,18]. This example shows that even in an established area of catalyst science, with a congested IP landscape, a mix of human work, robotic techniques, and parallel diffraction measurements could create new commercial IP [19].

Mindset + Skills + Money

Successful implementations of lab automation rely on a combination of the right mind-set, the right skills, and the right level of investment. Real-world implementations of lab automation are highly diverse, they reflect the specific problem which is being addressed, the mindset of the person or organisation who has implemented the solution, the level of skills they have, and also the amount of money which was invested. These is no one size that fits all. A more highly democratised use of automation in chemistry labs will include cheap immobile robots designed to do one or a few tasks, more usable software platforms for designing materials discovery experiments, mobile robotic systems for sale or to hire, open-access facilities, and automated or smarter flow-chemistry units. A key task, which we have identified here, but not resolved, is the need to map out the full landscape of options for areas of interest across the chemical and pharmaceutical sector to prioritize the barriers which need to be removed.

Market Demand and Penetration

The global market for life sciences laboratory automation is already large ~$21 Bn (2018). Some analysts project growth in this market at an annual growth rate (CAGR) of 6.8%, leading to a total market size of $29 Bn by 2023. About half of this market is in consumables. When they are excluded, the hardware, equipment, and software component of the market is projected to reach $17 Bn by 2023 [20].

The UK chemical and pharmaceutical sectors have a wealth of potential application areas for lab automation in research, product development, innovation, and standard testing for advanced materials, chemistry, and formulation. However, we estimate that the current penetration of lab automation in this sector is less than about 1% of the total addressable market.

There are a number of important reasons for the big difference in the market sizes of life science and chemical sector lab automation. The life sciences are a relatively modern industry compared with chemistry. In addition, relatively early on in the development of the sector, and particularly from the early 1980s, there was a strong standardisation in the industry around the use of 96 well microplates as a basic format for experimental work. This standardisation has influenced the whole trajectory of lab automation in the life sciences sector. It is now easy to buy low cost automated microplate handling equipment as commodities. The microplate format is ideal for handling very small volumes of aqueous solutions of highly soluble molecules. The chemical and pharmaceutical sector has a much wider set of demands in materials handling, most of which cannot be handled with off the shelf 96 well microplate equipment.

The market for lab automation in chemical and pharmaceutical sector would greatly benefit from the creation of *de facto* materials handling standards and the creation of a set of common assay or synthesis platforms.

Data Management for Automated systems

Classical science places the human scientist at the heart of all lab processes. They decide what they will do, set up apparatus, select reagents, study possible methods, implement the lab methods themselves and record in a hard bound lab notebook what they did: quantitative and qualitative observations they made through the

process and final measurements. Inherent within this classical lab science paradigm is a dichotomy between 'scientific measurement data' and the ancillary data that may be recorded by a lab worker.

From the mid-1980s, initial uses of digital imaging and lab auto-sampling, led to changes in the way that lab data was captured. Data and information was managed with a hybrid of lab notebooks (often with pasted-in print-outs of images, computer code and chromatograms), and rudimentary digital archiving on disk or tapes. These archives were designed for long term stability, not for real time interrogation. In analytical chemistry labs from the late 1980s, we began to see the adoption of LIMS systems to support lab quality systems – often based on structured relational databases. Automation in the form of 'auto-samplers' become an integral component of mainstream analytical chemistry platforms such as GCMS, LCMS, and nmr spectrometry.

After a long series of breakthroughs in chemistry, combined with equally important breakthroughs in computer technology, the internet and lab automation allowed a new approach to chemical synthesis and formulation. For example, Unilever invested in a scientific data management system for robotic experiments from 2003. This system retains a clear distinction between three data types:

- Maintenance, hardware and software versions, and modifications (not recorded)
- Telemetry - data on the operation of platforms (patchy recording)
- Measured scientific data (batch records in relational database)

This approach is fundamentally a batch processing approach for collecting and analysing scientific data.

The Future of Data management in Digital Labs

The future of data management in a fully digital lab environment will be based on a different data model. This approach goes far beyond the concept of an 'electronic lab notebook' (ELN).

The complexity of modern automated labs, direct to digital instruments, and the pervasive deployment of IoT technologies, means that in a modern lab it is no longer useful to retain a separation of data types nor to base data collection strategies on a batch processing model. The availability of cheap and effectively limitless storage and new open source high speed data capture and database technologies will allow a new 'data streaming' paradigm to be implemented. In this approach <u>everything that happens</u> in a digitally enabled lab creates a stream of event data: where each event is time stamped and uniquely identified (What, When, Where, How, Who, Why). Possible events include:

- Changes in ambient temperature, pressure, or light levels.
- Human lab activity or human instigated start/stop events.
- Barcode reads from samples.
- Maintenance or configuration changes.
- Telemetry recorded during robotic experiments.
- Complete time stamped manual process data streams.
- Measured end points in robotic systems.
- Re-configurations of a workflow.
- Cobot interactions (Human + Robot).

For high information content event data, such as that generated by a digital lab, a three stage pipeline is applied for stream data processing [21]. From initial data production (e.g. wireless sensors, analytical instrument, card swipe) the data streams typically pass through three-stages: collection, ingestion and storage. Analysis workflows then proceed by setting up 'data streams', which can be analysed in real time, OR analysed offline in batch mode. This approach builds from 'Fast Data' (as opposed to 'Big Data') technology platforms which have already been created for real time trading, FinTech, and Social Media applications. This approach will be essential in any complex and fully digitised lab environment. In this environment, AI will be used widely as a real time means to help optimise experiments and the efficiency and output of the lab.

Typically there is very little feedback between data scientists and lab automation scientists, yet to achieve the stream data processing paradigm, a close collaboration is required. The stream approach explicitly includes both descriptors of the experimental data, but also a 'fingerprint' of the facility where they have been collected, the standards used, and recalibration processes. There is currently no settled definition of "good practice" that addresses all of these issues, but rather a moving target of constantly evolving best practice.

Upskilling

As part of the development of a modern culture of data science in the R&D and innovation activities of the chemical and pharmaceutical sector, it will be essential for existing lab staff to develop new skills. In the context of lab automation, this means that staff will need to learn how to collaborate with robotic engineers and data scientists to obtain the most value from robotic and automated lab unit operations.

For a technical skill area like lab automation, it is useful to define 4 levels of expertise, moving from the most inclusive to the most expert.

- ***Aware:*** (Target is 100% of an R&D population). Sufficient expertise to recognise the main elements and core concepts involved in a skill area and discuss these factors with others.
- ***Operational:*** (Target is 20 - 30% of an R&D population). Allows the person to be directly involved in making decisions about, and drive actions in, the skill area.
- ***Expert:*** (Target is 5 - 10% of an R&D population). A person at this level can personally perform the majority of the practical and theoretical activities required in the skill area.
- ***Master:*** (Usually no more than 1 - 2% of an R&D population). A person operating at this level of expertise will be able to make significant innovations and developments in the field and lead strategic investment decisions.

Note that for lab automation the core skill that most chemists need to learn is not generic computer programming, but rather the ability to analytically understand, represent, and innovate the lab workflows they are working with. This type of analytical workflow thinking is more commonly found in engineering disciplines than in chemistry. Both 'pseudocode' and diagrammatic approaches are useful ways for chemists to develop this new skill. This workflow approach is also crucial for the wider application of digital R&D approaches.

The experience of both academic research leaders and UK company R&D teams is that it is extremely difficult to recruit data scientists to the field due to competition from better paid jobs, and to recruit industrial robotics experts into the adjacent field of lab automation. In fact in many cases the intellectual burden of solving lab automation problems falls onto existing lab scientists. It would help the UK chemical and pharmaceutical sectors if the UK HEI sector could gear up to support the development of skills and careers in this space. For example, to formulate and deliver Masters level training courses, both full-time and part-time, in Chemical Automation, or some novel undergraduate level degrees in Chemistry with Robotics/Automation.

Most UK companies in the chemical and pharmaceutical sectors do not currently have enough in-house capability to successfully implement a coherent lab automation strategy. However, this does not mean they cannot benefit from lab automation. Rather than trying to develop a fully in-house activity, it is better for most organisations to develop their capability through partnering with external organisations. This approach allows companies to learn faster and at lower risk than doing everything in-house. This partnership approach does not imply that a company will have a weaker competitive position. A partnership based route to implementing lab automation will give companies a way of designing and leading a network of partners to achieve the innovations they need to make. Partnering allows companies to access skills and innovation assets they do not own and cannot afford. If implemented properly, for most companies a partnership led approach will create more value, more quickly, than doing it on their own.

Many companies in the UK are able to leverage UK Government R&D and innovation funds. This leveraging of external R&D funding can help a company to:

- Increase the speed, efficiency and agility of its innovation activities.
- Support longer investment horizon projects than they are normally able to support.
- Access science capabilities through partnering that act as a multiplier to company resources by attracting Government and third-party cash.
- Access capabilities that would be impossible with their own R&D external budgets alone.

Standards and Open Platforms

Standards are a powerful means to stimulate innovation and industry sector level improvements in efficiency.

In lab automation the SiLA 2 standard has emerged over the past decade as the primary standards activity in lab automation [22]. The move to open standards in lab automation is working against a general inertia in the chemical and pharmaceutical sectors. In particular, many equipment vendors continue to see a competitive advantage in keeping a tight control over data capture, control, data formatting etc.

In parallel to SiLA, interconnectivity standards have also emerged for PLC controlled industrial automation systems, most notably OPC. This is a platform independent interoperability standard for secure and reliable exchange of data and information between automation equipment from multiple vendors. The OPC Foundation is responsible for the development and maintenance of this standard [23].

Recently, there have been a number of 'open source' platforms developed for low-cost lab automation. For example, Opentrons has a 96 well plate handling robot platform with a base cost of $5,000 [24].

Modularity

One of the topics that was repeatedly raised by interviewees was a need for fully modular lab automation solutions. Modularity provides a means for a company to implement an automation investment strategy piece by piece. With each newly bought module independently adding value, but also knowing that in addition they can tie together the modules at some stage in the future to deliver an additional value. Standards underpin modularity, as does a clear identification of the most common lab tasks that need automating. Neither standard development, nor the creation of a roadmap of required automated modules are likely to happen spontaneously. Here is an opportunity for a UK Government funded intervention to address this market.

Public-Private Consortia

Although many organisations in the chemical and pharmaceutical sector are interested in finding out about, and potentially joining, Public-Private innovation consortia, any UK Government investment in lab automation for the chemistry and advanced materials sectors will also need to address the high level of fragmentation of the sector (>3,000 companies). To date there has been no central 'clearing house' for identifying and articulating sector wide opportunities and challenges and this has held back the pace of innovation and deployment of lab automation in the UK versus the life science sector.

Currently the UK does not have a well recognised national centre of excellence in lab automation for the materials chemistry industries. This is one reason why the uptake of lab automation in materials chemistry continues to trail behind the uptake of automation in the life sciences. The progress of scientific research in the area, the rate of innovation of new and widely applicable technologies, and the rate of deployment of solutions into industry are all behind where they need to be to see automation make a substantial impact on lab efficiency and value creation for the UK materials chemistry sectors.

4. WIDER UK CONTEXT

UK R&D Roadmap

In 2018, total R&D investment in the UK was £37.1 Bn, which is about 1.7% of UK GDP. Of this total, public funding (including government, research councils and the devolved higher education funding councils) was £9.6 Bn, about 26% of the total of UK R&D funding.

In 2017, the UK government committed itself to achieving a total UK level of investment in R&D to 2.4% of GDP by 2027 and 3% in the 'longer-term' (this target includes both public and private sector investment). The March 2020 budget set out plans to increase public investment in R&D to £22 billion per year by 2024-25.

Most of the UK's public expenditure on R&D comes from the Department for Business, Energy and Industrial Strategy (BEIS), which funds a non-departmental public body called UK Research and Innovation (UKRI). The investment in UKRI is allocated via seven research councils, Research England, and Innovate UK. In 2019/20 UKRI received a total of £7.46 Bn of UK government funding.

In addition to disciplinary research councils, which focus on traditional academic disciplines such as engineering, physical sciences, biotechnology, biological sciences, arts, humanities, environment, social sciences, UKRI also invests in collaborative R&D via the UK's innovation agency (Innovate UK) and major cross-disciplinary investments such as the Industrial Strategy Challenge Fund [25].

Place Investment Strategy

In July 2019, the UK Government estimated that an additional £12 Bn per annum of private R&D investment would be needed to hit the 2.4% of GDP on R&D target. The UK Government has introduced a number of programs to encourage R&D investment (tax relief), improve knowledge exchange between universities and industry (KEF), and support investments into scaling up innovative businesses (British Business Bank).

At the time of writing, the UK Government is finalising policies on how it can use R&D expenditure to 'level up' the UK across the regions outside of the south-east of England. They have also committed to publishing a Place Strategy for UK R&D to further capitalise on regional science and innovation strengths [26].

Translational Research

In biomedical science over the past 20 years, the largest funders of academic research have begun pushing the recipients of funding to address the translational potential of their work. Examples include the US National Institute of Health (NIH) Common Fund, with an annual budget in 2016 of $675 million budget, which is targeted at developing new research tools and translational studies. By combining proof of principle studies with therapeutic development, the aspiration of translational biomedical research is to accelerate the time that it takes for basic discoveries to be deployed in the clinic.

Translational studies in biomedicine are also used to stimulate interdisciplinary collaboration, which are used to identify gaps in understanding, and open up directions for new basic science research. It is widely understood that funding for translational research should **not** be seen as an alternative to basic research, but rather a parallel funding stream designed to exploit the fruits of basic research.

Although the term translational research is much less commonly employed in describing work in the physical sciences, in fact many societal grand challenges also require collaborative, interdisciplinary translational research to find solutions. Although there are many hurdles involved in the full scale commercialisation or exploitation of a new insight or invention the earliest stage of this process provides a good generic definition for translational research: 'Turning a science based discovery into a tangible solution to a real world problem' [27].

Richard Jones FRS is a professor at the University of Manchester, and a highly informed commentator on UK science and innovation policy. In May 2019, Jones published a long and detailed analysis on UK productivity, science and innovation policy, and the need to rebalance the UK's innovation system to increase R&D capacity outside London and the South East [28]. Jones argues that despite the strength of the UK academic science base, the wider innovation landscape suffers from three faults:

- It is too small for the size of the UK economy, as measured by R&D intensity,

- It is particularly weak in translational research and industrial R&D,
- It is too geographically concentrated in the already prosperous parts of the country.

From his analysis, Jones identifies the need for public investment in translational research facilities, which he argues will (a) attract private sector investment, (b) bring together clusters of public funded research and business funded R&D, (c) create new institutions for cross-disciplinary skills development, and (d) create networks of expertise.

This approach, argues Jones, requires translational research centres to be built on existing academic strengths and localised industrial needs, and this provides a new intervention model for raising productivity levels in both high technology, and so-called foundational sectors of the economy. The analysis by Jones echoes that of Pisano and Shih [29], who argue that it is the development and maintenance of a shared body of knowledge, capabilities, relationships and skills – what they call an 'industrial commons' that is vital for regional and national economic growth. In this approach, the role of a translational research facility is not only to track the needs of local industry, but also to underpin and catalyse the development of new industrial sectors.

Collaborative R&D projects that involve organizations from both public and private sectors are a proven driver of innovation. This approach forms the foundation of industrial R&D investment by both the UK Government, largely through Innovate UK funding, European Union funding e.g. Horizon2020, and internationally available funding such as the Gates Foundation.

There are three broad types of knowledge which are relevant to industrial research, innovation and production:

- Firm-specific knowledge, which is the basis of how a firm specialises and competes;
- industry-level knowledge, which is shared by most or all firms in an industry, and
- generic, largely scientific, knowledge, which is relevant across many industries and public sector activities.

These three classes of knowledge include the development of widely applicable approaches and technologies, nurturing of longer time-scale science and technology development, actively de-risking of new technologies, creating and curating of widely applicable and expensive infrastructure, and interfacing between university knowledge bases and industrial users [30].

The second and third of these activities are effectively what Jones, Pisano & Shah call 'industrial commons'. To date, there has been insufficient investment in the UK into creating either 'industry-level knowledge' or 'generic, largely scientific, knowledge', for use in chemical and pharmaceutical sector lab automation. There is a clear need in the UK to develop a translational research centre in lab automation, built on existing academic strengths, and the UK wide industrial needs of the chemical and pharmaceutical sectors.

Routes to Impact

Traditionally, throughout the 19th and 20th centuries, the impact arising from university research in the physical sciences was through the education and development of individuals, and through the publication and dissemination of peer reviewed papers. Much of the knowledge transfer from leading researchers to more junior staff was achieved through their PhD training – which was effectively an apprenticeship in research technique. In the 21st century, non-academic impacts from academic research have continued to increase in importance, and several additional routes to impact have become common.

Now impact from academic scientific research routinely arises from:

- **People:** human capital development through PhD and Postdoc activity,
- **Publication:** knowledge development and dissemination through papers, books, and monographs, and
- **Patents:** discrete commercial opportunities through licences and/or spin-outs of inventions).

An even newer route to impact for commercial, economic, academic and societal benefits is the development of Platforms: digital assets that allow users to benefit from specialised scientific and technical knowledge, anywhere in the world, and at any time. To date the systematic creation and exploitation of Platforms from world-class physical science research in most universities is in its infancy. Properly engineered platforms not only create new impact opportunities, they have a positive feedback effect on the pace and quality of research in the core research groups.

Key Trends and Emerging research

In 2019, the Royal Society of Chemistry undertook a large scale road mapping exercise called *Science Horizons* [31]. This project involved in-depth engagements with more than 700 academic researchers globally to understand key trends and emerging research areas in the chemical sciences and those areas of science and innovation impacted by chemistry.

The main output of the Science Horizons activity was that, 'Finding paths to sustainable prosperity is the priority for governments funding research and development (R&D) globally'. In addition, the report identified 3 advances in scientific research which would be crucial for meeting this global R&D agenda:

(i) Solutions to global & industrial challenges. Researchers expect significant advances in the chemical sciences to underpin new technological solutions to major societal challenges.
(ii) Leading-edge questions. Researchers are tackling an incredibly broad range of questions relating to the structure, properties and interactions of matter across multiple length scales and levels of complexity (atoms to ecosystems).
(iii) Frontier techniques. Under this heading the Science Horizons report concluded that:

> Advances across a staggering range of techniques are enabling researchers to reveal the structure and properties of matter at unprecedented resolution in space and time. Scientists and engineers are pushing the frontiers of: measurement & imaging; sensors & screening and modelling & simulations. Data and digital technologies are central to these areas as researchers gather and analyse data from increasingly complex studies, going on to use data and digital technologies in new ways to make predictions and discoveries, and to deliver new insights and products.

The report noted the sense of excitement that existed in their group of respondents about the potential of new digital techniques was tempered with scepticism. The large cohort were yet to be convinced of the transformative opportunity that big data, AI and robotics represented for scientific discovery. This note of caution reflects public concern about the impact of digitisation on jobs and ethical considerations.

Following the publication of their *Science Horizons* report, the Royal Society of Chemistry convened an advisory forum in 2020 to further explore the long-term promise of and concerns about the use of data and digital technologies for scientific discovery [32].

Some selected findings from this paper:

- Digital technologies have huge potential in chemistry-using industry sectors. They will increase efficiency and sustainability across the chain from sourcing raw materials, to product development and manufacturing, to distribution, consumption and end of product life.
- Harnessing digital technologies for science R&D will enable scientists to deliver new benefits for society and the economy faster.
- Digital technologies will enable and challenge human scientists to go faster and to think at a higher level. They will extend human ambition and creativity, enabling multidisciplinary teams to solve bigger problems.
- For the foreseeable future human input and supervision will be essential in harnessing data and digital tools for scientific discovery in a way that is efficient, effective and ethical.
- Leadership and strategic vision, combined with insights from active researchers, will be key to ensuring we seize the opportunities at the chemistry-digital frontier.

The *Science Horizons* (2019) and *Digital Futures* (2020) reports from the Royal Society of Chemistry are high quality contemporary summaries of both the state-of-the-art and future prospects for academic activity in digitising chemistry, including lab automation and its associated digital technologies.

UK Academic Lab Automation Activity

Over the past few years there has been a marked increase in the level of investment of academic chemistry departments in the UK into lab automation. Following is a non-exhaustive list of teams who are using high end lab automation for chemical R&D:

- Richard Bourne, University of Leeds [33].

- Anna Slater, University of Liverpool [34].
- Centre for Rapid Online Analysis of Reactions, Imperial College [35].
- Camille Petit, Imperial College [36].
- Varinder Kumar Aggarwal, University of Bristol [37].

In addition, there is a smaller number of UK academic teams who have invested in the development of pioneering approaches to elements of chemical lab automation, both in terms of hardware innovations and new software platforms. These teams include the Cronin lab at the University of Glasgow [38], and both the Cooper and Rosseinsky groups at the Materials Innovation Factory / Leverhulme Research Centre for Functional Materials Design at the University of Liverpool [39 & 40].

The research of the Cronin group is '...motivated by the fascination for complex chemical systems, and the desire to construct complex functional molecular architectures that are not based on biologically derived building blocks'. A subset of the group focuses on digital chemistry. This team '...is focused on combining the use of automated feedback mechanisms, algorithmic control of chemistry and the use of robotic systems with real time reaction monitoring to enable the exploration of chemical systems which lie on a parameter "knife-edge" where stochastic effects can have large influence in the outcome of reaction networks'.

The Materials Innovation Factory at the University hosts the Cooper and Rosseinsky groups and the Leverhulme Research Centre for Functional Materials Design. Its vision is to, "…drive a design revolution for functional materials at the atomic scale by fusing chemical knowledge with state-of-the-art computer science in a world leading interdisciplinary team". The Centre works on fusing leading-edge synthesis concepts from the physical sciences with ideas from the forefront of computer science. It employs experts in robotics, engineering, management and social science. Instead of targeting specific materials or their applications, the goal of this centre is to change the way that materials chemists approach their design problems [41].

One of the seminal outputs of the Cooper group at the Leverhulme Research Centre for Functional Materials Design which has high relevance for this paper is the development of a revolutionary Artificial Intelligence (AI) driven mobile robotic researcher [42]. This system can work independently in a chemistry lab for extended periods. In the first example of this technology, a lab technician takes 3 hours to set up the lab, and then a mobile robot works 24/7, for 8 days, completing 700 experiments without any further human input.

The Materials Innovation Factory has also benefitted from an investment into lab automation from the Henry Royce Institute, and is the research area lead for the institute on Digital Materials Discovery [43].

It is worth noting that the three highlighted academic groups are amongst the best funded in the UK. This reflects both their exceptional track record, and the reality that to date the financial and intellectual entry barrier for making progress on chemical lab automation is exceptionally high. One of the key opportunities for UK academia is to also 'democratise' this area of science, so that there is a much broader pool of UK academics who are interested in and able to contribute to this emerging area of science. As noted earlier, the UK really needs a centre of excellence that has experience in applying a full range of technology solutions (simple units, larger fixed platforms, and mobile platforms), with optimal interactions with human scientists and technicians.

Having a place that pioneers the use of the full range of lab automation approaches, including lower cost and hybrid human-fixed platform approaches, would allow other UK centres to set up "carbon-copy" activities for their own chemistries, which often have quite similar workflows in detail, once the barrier to deployment, which is the real barrier, is overcome by proof-of-concept work at a centre of excellence.

ISCF Robotics for a safer world

The UK Government has already identified robotics as an area in which the UK lags its international competitors. To begin to address this, UKRI has invested in robotic science and innovation in the form of the ISCF Programme in Robotics for a Safer World [44]. This £95 M investment is intended to develop novel automation and robotics techniques for use in extreme environments. The aim to use robotics for tasks that are: dull, dirty, dangerous, demanding, distant, and distributed.

To date this program has invested £95 M with about £80 M of match funding. The first area of investment has been in collaborative research and development demonstrator projects led by UK companies to '...encourage business growth by improving robotics and AI capabilities, and testing their ideas in real-world extreme environments'. The second major investment has been in four University based research hubs. These hubs

have had £44.5 M investment from the UK government with additional funding from commercial organisations. The bulk of the UK government investment in the hubs has been in nuclear sector university consortia. These investments include £12.2 M in the Robotics and Artificial Intelligence for Nuclear (RAIN) consortia and £11.6 M in a National Centre for Nuclear Robotics (NCNR).

The main focus of the ISCF Robotics for a safer world challenge is in extreme and hazardous environments. The director says “The challenge is to turn that promise into reality and increase productivity in the workplace, while keeping people safe in these extreme environments”.

There are five ‘environments’ that have been targeted for investment in this ISCF challenge.

- Nuclear
- offshore (wind, underwater, ice)
- space
- mining
- cross-cutting (technological developments or cross-industry applications).

The bulk of this investment is focused on nuclear decommissioning. The investment in robotics for space applications is £12.6 M. To date, UKRI has not made any comparable investments in the development of lab automation techniques for chemistry labs. Now is a good time to transfer some of the skills developed in this ISCF program into lab automation for chemical labs.

5. RECOMMENDATIONS

To maximise the potential of Industry 4.0 to drive UK economic growth, in particular as part of a transformation of foundation industries such as chemicals, glass and steel manufacturing, we must also apply similar digitisation principles and technologies across the entire innovation value chain.

The unprecedented speed of discovery, scale-up, and deployment of vaccines for Covid-19 have been an inspirational lesson in the enormous value that can be created through radically increasing the speed of science and innovation. Using lab automation, robotics, and high performance computing, the UK can make a similar step-change in the speed of research, development, and innovation in materials chemistry and materials science. To accelerate the creation and exploitation of the new materials and chemistries we need for a net-zero world, the UK urgently needs to invest in Innovation 4.0 as well as Industry 4.0.

Based on the analysis presented in this paper we recommend that the Royce Institute / EPSRC establish a new UK centre of excellence in translational science and technology for chemical lab automation. This centre would need an investment of £20 M over 5 years, which would then leverage between £25 M and £40 M of private co-investment from a wide pre-competitive consortium of industrial partners.

The primary target for this centre of excellence is to catalyse a dramatic increase in the utilisation of lab automation across the chemical and pharmaceutical sectors, with a demonstrable increase in lab efficiency and value creation. This would address current market failures, create new standards, increase the number of jobs in UK companies, develop new UK high-tech skills, and create an export opportunity for UK manufacturers of lab automation equipment.

The work programme for this centre of excellence would be clustered under four headings: Science; Innovation; Skills Development; and Deployment.

[A] Science: Developing the UK science base for lab automation.

- The centre of excellence would lead the development of a coherent scientific research programme in lab automation. This portfolio of pure and applied research science could include, but would not be limited to, work on: AI & autonomous control of lab robots; novel feedback mechanisms; error recovery methods; gripper design; search strategies; human factors safety; positioning technology solutions; co-operative robotics.
- The centre would pioneer the use of the full range of lab automation approaches for chemistry, and chemical materials for advanced coatings, battery materials, circular economy and catalysis. These need to include lower cost and hybrid human-fixed platform approaches. Through outreach, other UK centres need to be encouraged to set up “carbon-copy” activities for their own chemistries, which often have quite similar workflows in detail, once the barrier to deployment, which is the real barrier, is overcome by proof-of-concept work at a centre of excellence.
- In addition, the centre of excellence would liaise closely with Royce Institute and EPSRC leadership to identify emerging needs in new academic science which are relevant to lab automation, which would then be funded through normal EPSRC peer review processes.

[B] Innovation: Catalysing a UK innovation ecosystem that resolves core technology challenges for chemical lab automation.

- The centre of excellence would lead a range of UK wide outreach activities with chemical & pharmaceutical companies, academics actively using lab automation, the KTN, KCMC, CPI etc, to articulate the common automation needs for the chemical and pharmaceutical sector.
- Using these common needs as technical targets, the centre of excellence would then design a portfolio of between 10 and 20 new open platforms for low cost modular unit operations and mobile robotic platforms. These platforms would be further co-developed between the centre of excellence and UK based manufacturers to ensure that a range of robust and low cost modules were available for purchase by chemical companies as standard catalogue items.

- The centre would invest in the development and widespread exploitation of existing open software standards for connectivity, data exchange and automation control (e.g. SiLA2 or OPC). It would also actively engage with equipment vendors to increase the use of these standards on standard lab equipment.
- The centre would create new web-native collaboration tools for managing lab automation. These would be designed so that open-source versions were made available, as well as fully serviced commercial implementations offered by suitable UK commercial partners.
- The centre would lead a range of UK wide outreach activities with existing and emerging manufacturers of automation solutions. It would actively create and share a dynamic map of the UK innovation ecosystem in this space as it evolved.
- Additionally, such efforts will also allow an assessment of the suitability of partial automation of existing practices, rather than fully automated labs which can be a major barrier to adoption when full costing can be hard to justify.
- From this set of innovation activities, the centre of excellence will also be able to develop novel approaches to Cobots. These approaches will need to be based on both qualitative and quantitative studies of human-robot interactions in realistic lab settings.
- The centre can reapply a range of innovation readiness assessment tools, such as the MIF's Digital Maturity framework for lab R&D, and the CPI's "Innovation Integrator" for process scale up development to help industrial partners to articulate their needs as part of developing innovation and research programs.

[C] Skills Development: Building leadership and human capital in chemical lab automation.

- Create a coherent lab automation skills development framework for use across the UK chemical & pharmaceutical sector.
- Catalogue existing training and learning courses at apprentice, undergraduate and post-graduate level, indexed to the skill development framework.
- Help the UK HEI sector to support the development of skills and careers in lab automation and associated disciplines for the UK chemical and pharmaceutical sectors. For example, by co-designing Masters level training courses, both full-time and part-time, in Chemical Automation, and novel undergraduate level degrees in Chemistry with Robotics/Automation.
- Create a new strategic "Leadership in lab automation" curriculum and deliver as a continuing professional development (CPD) opportunity.

[D] Deployment: Catalysing a UK business ecosystem.

- Using the new insights into common automation needs, and new open platforms for low cost modular unit operations and mobile robotic platforms, build partnerships with UK manufacturers that lead to new commercial lab automation platforms which are available at a cost basis of below £50K per unit.
- The centre of excellence will lead the development of adoption pathways to enable impact from the investments in this translational science activity.
- These adoption pathways will be co-created with existing networks and activity, including KTN, KCMC, and CPI, but they will also create new mechanisms. For example, introducing an 'innovation voucher' scheme (at a value of £2K - £5K per voucher), that UK chemical and pharmaceutical organisations who employ less than 100 staff can use with accredited UK organisations to perform "Line Walk" consulting support for early stage exploration of the value of lab automation.

[E] Centre of Excellence: Structure and Leadership.

- The proposed centre of excellence should be funded by BEIS and operate on a hub and spoke model which exploits the existing UK critical mass in physical and intellectual infrastructure which is located in established centres of translational physical science excellence.
- Much of the academic leadership in this field can be found in the North-West / North of the UK. Locating leadership across the North of the UK would therefore provide a way to align with current UK Government ambitions to 'level-up' research and innovation investment and activity, without any compromise on quality. It would also co-locate lab automation leadership in the region with the largest concentration of UK chemicals manufacturing activity.
- The proposed centre of excellence should adopt an 'Open by Design' industry engagement model (as exemplified at the Materials Innovation Factory / Royce Institute), and develop a wide ranging outreach activity with small, medium, and large companies in the sector, to include potential end-users, robotic innovators, and both existing and new automation equipment manufacturers.

[F] Adjacent innovation opportunities.

An important additional benefit from the creation of a more vibrant UK innovation and business ecosystem in lab automation would be the chance to open adjacent opportunities for loose integration and mobile researchers. Post-Covid, this technology could become an important and affordable practical lifeline for sectors that want to accelerate innovation whilst implementing new practices to deal with social distancing.

In our experience, these new lab automation technologies have wide cross-sector relevance in healthcare, medicine, food, oil & gas, and chemicals. Based on numerous discussions to date, we expect commercial applications of loose integration and mobile robotic platforms to include, but not to be limited to:

- Delivering 'Low-Touch' R&D lab operations to deal with Covid.
- Automated Contract Research Organisation (CRO) units.
- Small volume, high value, biotech manufacture.
- Long term product stability testing (e.g. for Pharma applications).
- Automated sampling in manufacturing plants: from line, to test and measurement, then disposal.

TECHNICAL ANNEX

Basic Concepts in Lab Automation

The application of lab automation and robotics to the work of a chemistry lab requires the development of new conceptual and technical skills for many chemists (human Operators). The transformation from manual to automated chemistry lab operations requires human Operators to: represent real lab equipment and technical processes in machine readable languages and structured diagrams; learn new analytical tools for understanding and recording lab processes; expand R&D teams to include day to day working with automated Operators (i.e. robotic engineers, robotic modellers and robotics data scientists).

There are five key concepts which chemistry researchers need to understand in order that they can begin to appreciate the benefits and issues associated with lab automation systems:

Lab Unit. A discrete piece of lab equipment, which is capable of performing one or more operations. Examples include: a balance, a stirrer, a reaction vessel, an auto-titrator, a rotary evaporator, a rheometer, a GC-MS.
Unit Operation. This is a concept widely used in Chemical Engineering to describe a basic step in a process. Unit operations usually involve a physical change or chemical transformation from INPUT(S) to OUTPUT(S). Examples include: separation, crystallization, evaporation, filtration, polymerization, isomerization, mixing, and measurement. Each unit of operation can be designed as being a distinct module within a sequence (or workflow).
Workflow. A well defined sequence of Unit Operations, designed to achieve a given outcome in a lab environment. These workflows can be formally defined in a Standard Operating Procedure (SOP), or be more loosely defined as part of a research or discovery process.
Integration. The high level means by which a set of Unit Operations are linked together (physically, logically, and data-flow) in a sequence to make a workflow possible.

Lab Unit

A Lab Unit is designed to help a lab Operator (either human or automated) to do a particular type of task. The operational performance of a Lab Unit is constrained by the laws of physics and chemistry. These fundamentals need to be understood in the design and construction of lab units to ensure accuracy of operation. For example, a standard glass burette delivers accurately measured volumes of aqueous solutions, but the accuracy of a burette reading needs to take into account the meniscus caused by surface tension and the temperature at which the apparatus was calibrated and is now being used. The most accurate modern analytical balances use high resolution electromagnetic force restoration (EMFR) sensors as the key transduction mechanism in the measurement process. A good understanding of the physics of EMFR is therefore vital for the design and construction of a high quality balance.

Unit Operations

The best way to think of a Unit Operation is as a modular step in a process, in which a change or transformation is made within a single Lab Unit between an INPUT state and an OUTPUT state. What happens within the Unit Operation is under the control of an Operator (either a human or a robot/computer). The logic of what happens within a Unit Operation can usefully be represented in a flow diagram of key tasks or steps. A Unit Operation will often be a module within a larger logic diagram called a Workflow. A Unit Operation can be manually controlled, or it can be controlled by a robot/computer, i.e. can be automated.

Many Unit Operations in lab chemistry remain controlled by human Operator (i.e. manually). The control measures undertaken are also often informed by human Operator analysis of the recorded outputs. An example of this is human Operator control in determining the volume of a chemical to add to a mixture in response to a visual inspection of colour change - such as a strong acid - strong base titration using a phenolphthalein indicator. The indicator changes colour in a pH range between 8.3 and 10. It is pink in basic solutions and clear in acidic solutions. In a strong acid-strong base titration, this pH transition is sharp (within a fraction of a drop of the actual neutralization point because the strength of the base is high). You add acid until the indicator just turns from pink to colourless (this actually happens at pH 8.3, but the graph is so steep here that there is minimal error). This is an example of a Unit Operation, in which the process is controlled through (human) monitoring of some key physical or chemical condition or conditions. The process runs until a preset or pre-defined ***condition*** has been observed.

Logically, this manual acid-base titration is an example of a ***while*** loop. You keep checking the condition you are monitoring (observed colour of the solution), and while it hasn't met the pre-defined end point you perform the next step.

This control loop can be written in an analytical description called "pseudocode" (i.e. using the structural conventions of a computer programming language).

```
START
       Precondition: Starting Colour is Pink
       WHILE Colour is not equal to Colourless
              Add a drop of Acid to the Flask
END
```

The logic can also be represented as an activity diagram of the process.

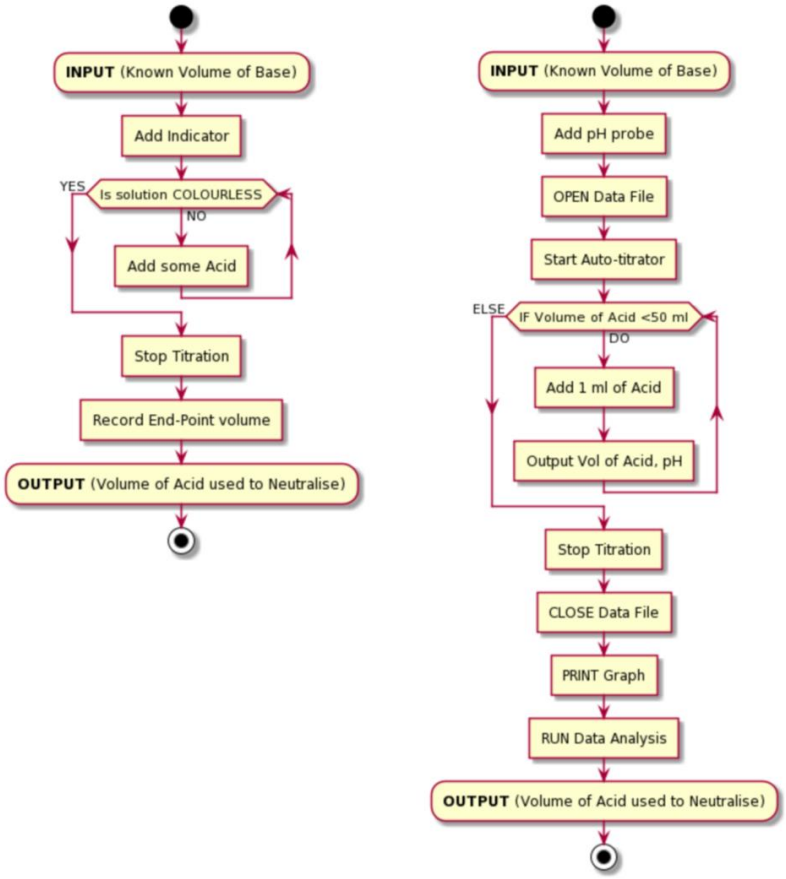


FIGURE 6: The task list for a manual titration unit operation (left), and a comparable task list for a computer controlled titration (right).

When a manual Unit Operation is automated, i.e. put under the control of a computer, it will retain the same INPUTS and OUTPUTS, but very often the process within the Unit Operation will be transformed.

For example, the pH of a solution can be directly monitored by a pH electrode. Now, the titration process is completely different. The acid is added continuously under computer control of a motor driven syringe, and the measured pH is recorded as a function of the added volume of acid. The first derivative of the titration curve shows even more clearly the volume of acid used at the endpoint. Raw data is measured pH versus delivered volume. The end point is not indicated by a colour change, but by a mathematical analysis of the raw data.

The INPUTS and OUTPUTS of the unit operation match those of the manual analysis. But what happens in between is very different. Now the tasks within the Unit Operation include explicit computer instructions to open

data files, save data, analyse data etc. The new automated operation introduces important new things to think about in the associated experimental kit: Analogue to Digital (AD) conversion of signals, sampling rates, systematic errors, mechatronic failures, random electronic noise, and data output formats.

Unit Operations (and also Workflows) are core concepts for lab automation and robotics – and more widely in digital R&D. A key new skill for chemists working with lab automation and robotics, is to be able to both WRITE a task list and workflow in pseudocode, and READ one in a diagram.

Modularity

Ensuring that each Unit Operation is a distinct module within a larger workflow is one of the key means available in lab automation and robotics to deliver flexibility and reliability. Each module can be tested independently before use in the workflow. Top Down and Bottom Up considerations need to be held in mind during the design phases of lab automation and robotics projects. Some high level considerations

- Create Unit Operations that do one thing and do it well.
- Create Unit Operations that can work together.
- Create Unit Operations to handle standardised material & container formats.

Wherever possible, it is best to try and use existing commercially available automated Unit Operations if they are robust, fit-for-purpose, of a reasonable cost (both initial CAPEX and ongoing revenue for consumables), and can easily be interfaced to your chosen integration approach.

There are two generically useful models for creating new Unit Operations:

- Automating an instrument: wrap a non-automated scientific instrument into an automated Unit Operation.
- Multiplexing: move from serial operation into a multiplexed format enabling multiple operations simultaneously.

Automating an Instrument

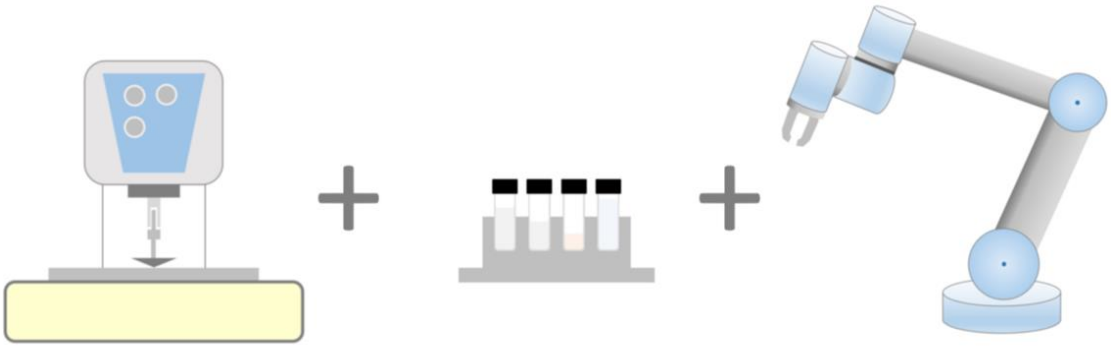


FIGURE 7: A schematic example of how an existing rheometer, plus an off the shelf robotic arm, can be used to create an automated rheometer Unit Operation.

This is often about better, more reproducible, material handling & sample preparation. The “measurement” remains at the same speed and resolution as the manual process. Complex manipulations that scientists do effortlessly in a manual way need to be translated into a foolproof mechanical operation. This approach does have some issues. Often the ‘wrapped’ instrument will fail faster than you expect due to the higher throughput nature of automated operations. Most high-quality scientific instruments are not designed to work at throughput rates 5x or 10x of that possible with manual lab operation. Warranties can easily be invalidated when you integrate. If an error occurs in an automated Unit Operation you have built yourself, it is often not obvious which kit is at fault.

Multiplexing

One well known method for automating a process, is to replace a serial set of measurements or operations with a multiplexed or parallelised version. In general to achieve this change the original resolution of the serial

measurement is lessened in order to create the vastly increased speed. This approach is ideal for screening with tiny amounts of material.

FIGURE 8: A schematic example of how an existing serial measurement, made using a point imaging device such as a microscope, can be implemented in a 96 well plate format that can be scanned on e.g. a flatbed optical scanner.

Workflows

A Workflow is a well-defined sequence of Unit Operations. What happens within the Workflow is under the control of an Operator (either human or automated). The logic of what happens within the Workflow can usefully be represented in an activity diagram. At the level of a Workflow, especially one that is controlled automatically, Data Management has to be designed and implemented before you start.

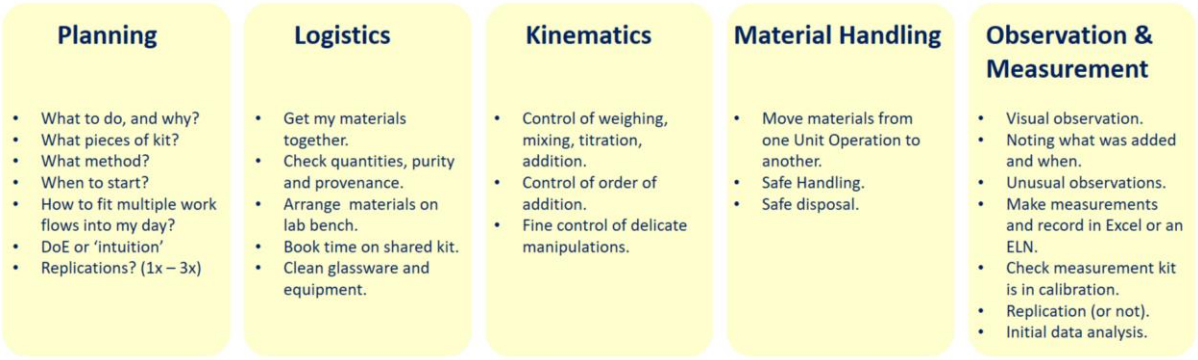


FIGURE 9: The end-to-end process of lab work will involve planning, logistics, kinematics, handing, and observation steps. There is often little advantage in attempting to include all of these processes in an automation approach. More frequently a few key unit operations or joined up elements of the workflow will be automated to make a substantial improvement in the efficiency of the activity.

A particular lab workflow is usually part of a larger end-to-end technical or scientific activity. The edges (the before and after) of a Workflow are defined by humans. At present, the majority of Unit Operations used in chemistry lab workflows remain manual: that is they rely on human control of kinematics, observation, data capture, and measurement. This means that even, with significant investment in lab automation and robotics, elements of human control will remain crucial.

Unified Modelling Language (UML)

Unit Operations & Workflows are a good place to start for chemists who are new to lab automation and robotics for two reasons:

- They are an abstraction of a very concrete set of physical activities that use physical substances and artefacts.
- They also lend themselves to being visualised.

However, rather than drawing these diagrams in Powerpoint (which is possible) it is much better to WRITE them in a simple and logical 'script' syntax and get the computer to automatically create a diagram from that script. To be most useful these script need to be written using a well-defined language, without an overly complex syntax, and hosted in an interactive environment, so that an edited script leads to an immediate change in visual output.

Diagrams of a workflow are a natural thing for a team of chemists to work with. As well as being numerate, chemists generally have a better than average ability to visualise in 2D/3D (this is required for structural formulae, stereoisomers, and Jablonski diagrams etc). The automated visualisations are a way of getting lab staff to focus on the relationships and complex ideas that need to be captured in the workflow (rather than drawing diagrams manually with endless resizing and aligning of rectangles).

The Unified Modelling Language (UML) is a general-purpose modelling language used in the field of software engineering [45]. It is intended to provide a standard way to visualise the design of a system. UML offers a way to visualise the architecture of a system in diagrams. It can represent:

- Discrete activities
- Individual components in the system
- How the components (software & hardware) interact with other components
- How the system runs
- External user interfaces.

UML is particularly useful for documenting the design of a complex system. PlantUML is an example of a UML scripting language and diagram creation engine [46]. PlantText is a very clean implementation of PlantUML [47]

UML is not the only language that is used to model business processes - another widely used framework is Business Process Modelling Notation [48].

Integration

Integration is the means by which a set of Unit Operations is linked together in a sequence to make a workflow possible (physically, logically and in terms of data-flow). Unit Operations and Workflows operate at different levels of granularity, however, they do connect with each other. Decisions which are made about the way a Unit Operation is automated and the strategy for integrating it into a workflow are never completely decoupled. In addition to control mechanisms, integration is largely to do with logistics, materials handling, and data flow. Different approaches have advantages and disadvantages, including Safety issues.

Manual lab workflows emerge from the spatial layout of the lab, the tasks that need performing (e.g. the Standard Operating Procedure), the equipment roster, individual habits of scientists and social relationships. It is essentially a 'craft' activity. Kit is 'loosely integrated' by the way that the staff use it. Re-jigging the lab layout does not usually help. It is also expensive and disruptive.

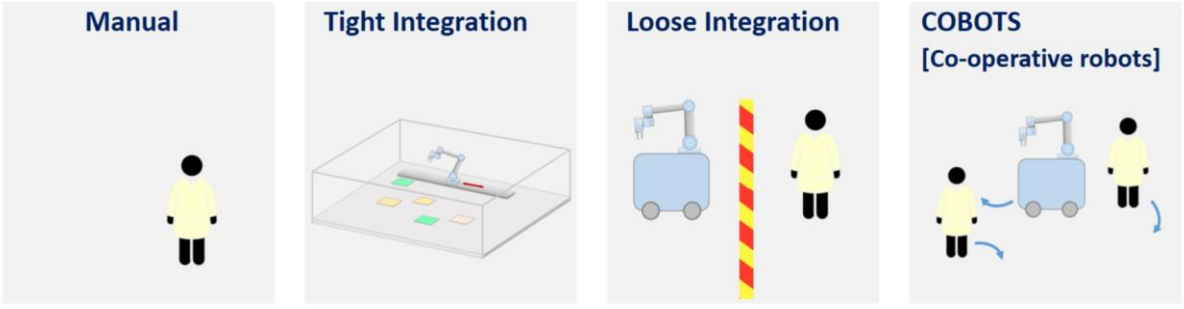


FIGURE 10: Four generic means to integrate automated unit operations into automated workflows.

Tight Integration

This approach requires high-level engineering skills in both hardware and software integration. Usually, the aim is to build a unit that integrates the series of operations in a compact stand-alone enclosure for use in a lab environment. Pre-compiled together into a unit.

Loose Integration

This approach follows a different approach that seeks to integrate at 'run-time' rather than to 'pre-integrate'. It aims to exploit existing lab space, benching, services, and Unit Operations. It does not attempt to tightly integrate existing Unit Operations into a single larger platform. Provides a number of opportunities to exploit much higher level of flexibility in the number of, location of, and type of Unit Operations which are integrated together. Allows a Workflow to evolve over time – as new Unit Operations are added, upgrade, replaced. Requires a much shorter and less expensive design phase.

Co-operative Robots (or Cobots)

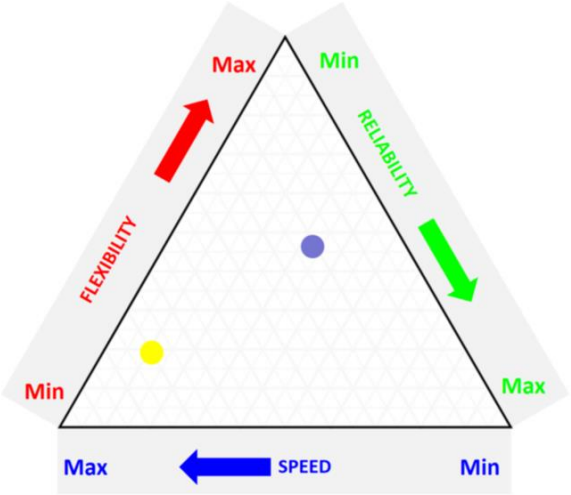
This approach takes the Loose Integration idea to its logical conclusion and explicitly uses human operators as part of the integration strategy.

Three considerations are important in choosing an integration approach.

Flexibility: This is the ability to re-configure a workflow without major downtime and/or CAPEX costs. Re-configuration can be used to improve quality: replace an existing Unit Operation with one of a higher specification; add a Unit Operation to create a new set of workflows; duplicate a Unit Operation to improve throughput by removing a bottleneck.

Reliability: The reliability of a system can be defined as "...the probability that it does not fail during a defined time under given functional and environmental conditions". A big factor in reliability is the robustness of the system: "A product or process is said to be robust when it performs as intended even under non-ideal conditions…"

Speed: The number of unit operations or samples processed per unit of time. If the average speed of the manual process is assigned as a speed of 1, then the aim of lab automation is to achieve speeds of between 2 and 10.



It is not possible to build a Lab robotic system at a reasonable cost which is simultaneously Flexible, Reliable and Fast. Integration is therefore always a trade-off between these three requirements. Flexibility can often be achieved cost effectively if designed in at the start. Reliability can be achieved through careful design and high quality construction. Achieving high-speed operation is always expensive.

If flexibility and reliability are of higher value than speed then Loose Integration can deliver both together. For Research applications this is often the most important consideration. If reliability and speed are of higher value than flexibility, then Tight Integration can deliver both together. For Product Development this may be more important.

Lab automation systems can only ever partially automate an end-to-end lab operation (there are always "edges"). Choices have to be made about which elements of the overall process are worth automating now, which could be automated but are too complex to attempt yet, and which are best done by humans. These choices begin with evaluating Unit Operations -

No fully automated workflow can exist without two conditions having been met:

1. **that each and every Unit Operation in the workflow has been automated,**

2. **that a means for integrating these Unit Operations into an overall workflow has been implemented.**

Modularity and System Complexity

Whereas non-modular lab automation systems can be designed and built to do a single task, it is only when a rigorous approach to modularity and integration are designed that a lab automation approach can deliver utility across a wide range of use-cases.

Managing demands of system complexity using modularisation is both a creative process and an important decision that can have profound accelerating or decelerating effects on lab automation and robotics implementation. The design rules encapsulated in the UNIX system are one widely applicable set of heuristics which are useful for designing complex computer systems [49]. A subset of these rules can be modified and used in lab automation and robotics:

- You often can't tell in advance how a Unit Operation (or Workflow) is going to spend its time. Bottlenecks occur in surprising places, so don't try to second guess and put in a speed hack until you've proven that is where the bottleneck is.
- Measure. Don't tune for speed until you've measured, and even then don't unless one part of the process overwhelmingly slows down the rest.
- Fancy methods are usually slow when the number of replicates, N, is small.
- Fancy methods are less reliable than simple ones, and they are much harder to implement. Use simple methods unless there is a compelling reason not to.
- Physical material handling and data dominates. If you've chosen the right way to store materials, organised how these things move, and chosen the right data structures, the rest will almost always be self-evident.

Using the UNIX rules approach, we can describe some useful high level considerations for designing modular Unit Operations: create Unit Operations that do one thing and do it well; create Unit Operations that can work together; create Unit Operations to handle standardised material & container formats; wherever possible use existing commercially available automated Unit Operations if they are robust, fit-for-purpose, of a reasonable cost (both initial CAPEX and ongoing revenue for consumables), and can easily be interfaced to your chosen integration approach.

Reducing Experimental Variation

In many commercial experimental workflows, there will be a large number of independent sources of variation. These could include some or all of the following:

- Natural variation in raw materials or ingredients.
- Variations in the production process.
- Storage, sampling, age of sample, supplier.
- Intra-person and Inter-person variation in experimental technique.
- Order of addition.
- Control of Process.
- Measurement protocol selected for use.
- Precision and accuracy of the measurement device.

Many of these sources of variation can be dramatically reduced by using lab automation.

Formulation as an experimental challenge

One of the challenges of manual experiments is in simplifying or narrowing the process to make it manageable for human Operators to undertake in a realistic timeframe. This often means that the number of variables for a given experiment are reduced. The implementation of lab automation and robotics helps to remove these barriers, enabling more variables to be investigated and therefore influencing experimental design approaches. Figure 11 shows in schematic form a typical industrial formulation challenge, exemplified in the formulation of a carotenoid into a food emulsion.

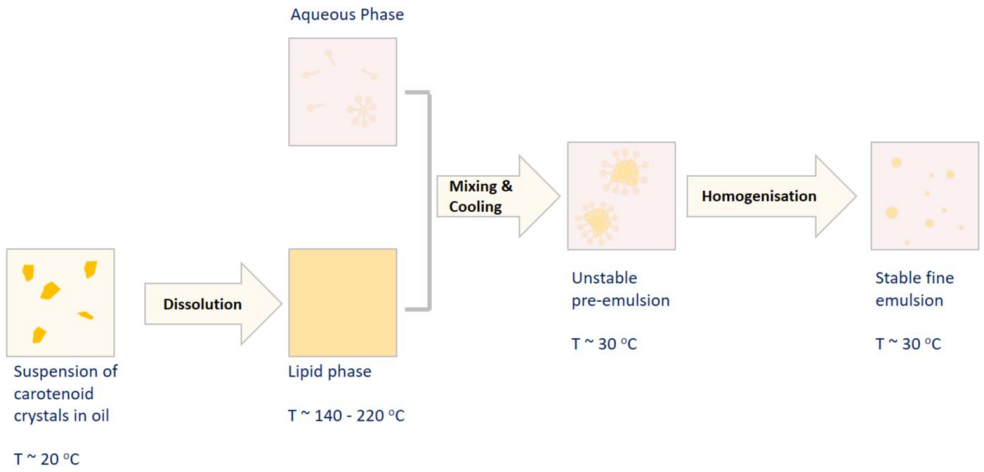


FIGURE 11: The formulation of a carotenoid into a food emulsion (redrawn from [50]).

The table to the right shows the different variables in this formulation scheme. The total number of experiments required to explore all variables would require a full factorial design with more than 100 million formulation prototypes to fully understand the response of the system to variables. Pragmatically, about 12 could be made. In practice then, a bench scientist applies their scientific understanding to reduce the complexity to a manageable number of manual experiments, i.e. between 10 and 20.

Parameters	Ideal Levels	Pragmatic bench experiment
Carotenoid structure.	5	1
Concentration of carotenoid in oil.	1	1
Temperature of oil.	3	1
Oil composition.	5	1
Rate of dissolution.	1	1
Agitation rate.	1	1
Temperature of lipid phase.	3	1
Composition of surfactant	9	1
Concentration of surfactant	3	1
Temperature of aqueous phase	1	1
Other solutes (type/concentration)	1	1
Mixing conditions (agitation rate)	3	1
Rate of addition	2	1
Rate of cooling	2	1
Temperature of unstable emulsion	3	1
Ratio of lipid to aqueous phase	3	1
Concentration of caretenoid	3	3
"Storage" time	3	2
Agitation speed	3	2
Homogenization time	3	1
Homogenization temperature	1	1
Configuration of homogenizer (disperser device)	2	1

Taking the pragmatic approach relies on making assumptions about things that we often know little about. The net effect is to end up 'optimising' the system for a single carotenoid, in a single oil phase, with a single process.

A more sophisticated experimental design (known as D-optimal) would look at the main factors alone, and would require 540 experiments. This is still a lot to do for a human Operator – but is now possible for an automated Operator (i.e. a robot).

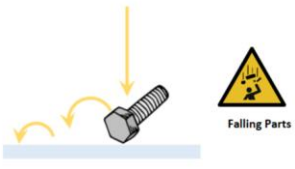
Workplace Health, Safety and Welfare

The following three figures demonstrate some of the health, safety and welfare considerations in the operation of robotics in a chemistry lab.

Hard, Heavy or Sharp Objects

PRIMARY HAZARD

Gravity driven acceleration of a hard (and potentially heavy and/or sharp) object to the ground.

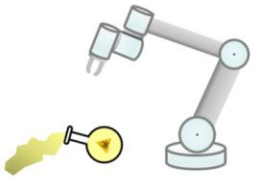


Human Proximity to Moving Parts

PRIMARY HAZARD

High speed or high torque movement of arm into human.

Automated Chemical handling



PRIMARY HAZARD

Uncontrolled spillage of chemical reagents – and potentially explosive, unpredictable, and very serious series of consequences.

The health, safety and welfare considerations are also dependent on the integration approach (tight, loose or cooperative robots).

Tight Integration (Closed Platform)

These platforms are physically closed with metal enclosures and glass doors/windows. Risks include:

- Intrinsic chemical risks
- Spillages / solvents
- Robotic arm movements

Loose Integration (Mobile Robotics)

These 'systems' are composed of one or more mobile robots in a wider chemical lab environment. Risks include:

- Intrinsic chemical risks
- Spillages / solvents
- Robotic arm movements
- Human-robot collision

Cooperative Robots (Cobots)

These 'systems' are composed of one or more mobile robots with human operatives working together in a wider chemical lab environment. Risks include:

- Intrinsic chemical risks
- Spillages / solvents
- Robotic arm movements
- Human-robot collision

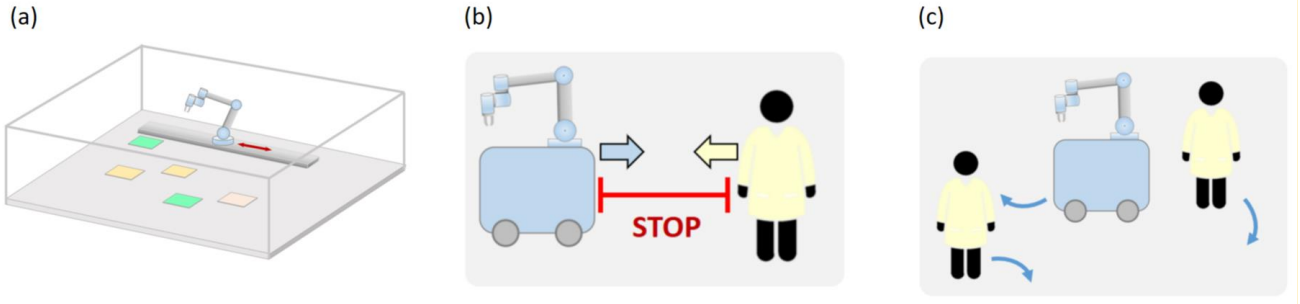


FIGURE 12: Safety approaches for tight integration, loose integration, and Cobots.

Robustness

A big factor in the reliability of a lab automation is the robustness of the system, this means that the system performs as intended even under non-ideal conditions. These non-deal conditions can often be difficult to

predict, and they include expected or unexpected variations which are external to the automated system, plus the intrinsic variation (noise) in its own operation.

The Robust Design Methodology (RDM) is an approach that makes a systematic effort to achieve insensitivity to noise factors [51]. It is founded on an awareness of the widespread sources of variation in an operational system. It has four factors -

- A cornerstone of robust design methodology is a keen awareness of variation in all aspects of the operation of a designed product.
- Noise factors are often expensive (or impossible) to control - the goal in robust design is to create insensitivity to noise factors.
- Robust design does not in itself prescribe the use of certain methods applied in specified steps.
- RDM is useful from concept generation to the production of a product.

Lab Efficiency

The fundamental output of most labs is data. This data can be used in a wide variety of ways to create value for a company or academic institute: it can inform decisions; shape the direction of a product development activity; provide objective evidence of an invention for use in a patent filing; underpin a product claim; meet a regulatory or safety requirement; or it can be used as the basis for a scientific paper.
Lab data is usually the outcome of a measurement, or a series of measurements, which have been made on a sample of some sort which is dependent on the type of lab. In a Quality Control (QC) or Quality Assurance (QA) lab, the data is the result of a standard physical test or analytical chemistry measurement. In a product development lab tests will be made on samples which have just been made in the lab, or which have been taken out of long term storage in an oven or a fridge. In a research lab, the data may be measurements of more fundamental physical quantities, such as surface tension, pH, melting point, crystal structure, rheology, or density, on newly synthesised chemical entities which have never existed before.
For all three of these cases, and many more, the simplest useful definition of the efficiency of a lab is, "... the number of data points obtained per unit of cost".

The Value of Data

There are a multitude of different ways to use the technical data which is obtained from a lab. How a specific organisation uses data to create value will reflect its overall aims and the details of the domain in which it is active. It is therefore impossible to create a universally applicable mapping of data to value. However, within a particular organisation, the mapping of data to value creation does not change rapidly, and in general it will not be changed by an increase in the efficiency of data creation in a lab. This means that for a particular lab operation, an increase in the efficiency of data creation through the introduction of some automation will lead to a direct increase in value to the organisation (i.e. both the data and its costs are equally fungible). The important conclusion of this is that:

> ***All other things being equal, an increase in lab efficiency leads to a direct increase in value creation capacity.***

This means that it is important to be able to compare the efficiency of a current lab operation versus a changed set of operations, e.g. through the introduction of lab automation.

A calculation of efficiency needs to be able to account for the very diverse range of factors which impinge on the experimental work of a modern chemistry lab. Our aim is to be able to make comparisons between the efficiency of existing manual lab activities and automated versions of those same activities. In this context, the increase in efficiency is the primary means to show that an investment in lab automation can create a meaningful return on investment (ROI).

Data Quality

In estimating efficiency, it is naive to use the number of data as the primary output measure of a lab. It is far better to weight each data point by a quality factor. Perfect data, with perfect traceability, would have a weighting of 1.0. Real lab data always includes error and has some indeterminacy with respect to traceability. It is intuitively reasonable that a small number of higher quality data are equivalent in value to a large number of lower quality

data. Higher efficiency is not just about increasing the number of data, but about increasing the information content of the data that is collected.

Factors which need to be included in the "error" rate for each data point include accuracy (how close to the truth), precision (reproducibility of the measurement) and traceability (does the data point actually refer to that sample ID or not?). All three of these are susceptible in various ways to human shortcomings which depend on the actual test or measurement protocol, the overarching set of lab procedures applied, and individual differences in human skill.

As an example, if a key measurement is surface tension, then an error rate of 0.05 or 0.1 can be achieved using a series of steps: an automated pendant drop shape analysis; high purity reagents and water; clean glassware; a well-trained operator; and good lab notebook practice that conforms to good practice or international standards (such as GLP or ISO9001). This would mean that each measured data point had a "weight" of 0.95 to 0.9. A cruder industry standard test or measurement may be more susceptible to higher inter-operator variability, and this would lead to a lower value for each data point.

In the following we assume that a given lab has created "*N"* data points in the defined period of analysis. After weighting each data point by its quality, the key output of the lab is the quality weighted number of data, "N_Q".

Data Cost

The aim is to be able to estimate the cost of acquiring the data in the period of analysis, "*Cost* (*N*)". This is a simple sum of three types of cost: *Capital*, *Staff* and *Services*.

> ***Capital:*** Capex depreciation for the scientific equipment used, the lab furniture, and the real estate cost as an equivalent lease per sq metre per unit of time (these are all slowly varying costs).
> ***Staff:*** The cost of the time that staff actually spend in the lab or on planning or reporting activities that are essential to their lab activity (i.e. not on peripheral non-lab activities). The best unit to use is cost per hour of lab staff time, without unspecified overheads e.g. exclude the cost of general company admin staff or management.
> ***Services:*** The activity's variable cost, which will include consumables (reagents, glass ware, etc), waste disposal, cost of service infrastructure (electricity, gases, water, IT infrastructure) and software costs.

Lab Efficiency

With an estimate of N_Q and *Cost* (*N*) in hand, both estimated on the same period of analysis, we can estimate the lab efficiency:

$$Efficiency = N_Q \,/\, Cost\ (N).$$

This equation can be applied to a before and after set of circumstances, e.g. before implementing an automated workflow, and afterwards.

Worked Example

To illustrate the use of the efficiency calculation we present a hypothetical case based on the experience of the lead author and partners.

Scenario
A cellular lab employs 8 FTE of staff to perform a set of routine product characterisation measurements as part of a larger Product Development activity. The lab workflows include manual making of samples, measuring the sample rheology and pH of a sample over a range of temperatures, putting samples on and recovering samples back from long-term storage in an oven and fridge.

Current Situation: The lab employs 8 staff, who each work 8 hours per day. Of this they each lose 1 hour per day on non-experimental activity, leaving 7 hours per day for lab work. Each sample requires 0.5 hours of technician time to make a measurement. On average 560 samples are measured each week with an average quality of 0.7. Each sample creates a consumable cost of £3. The average hourly cost of the lab staff is £26.60. The cost of infrastructure (including CAPEX) is £3,000 per working week. Using these values we can calculate the efficiency of the lab.

Staff Costs	Infrastructure	Consumables	Cost (*N*)	N_Q
£7,447	£3,000	£1,680	£12,127	392

Current Efficiency = N_Q / *Cost* (*N*) = 392 / £12,127 = 0.0323 £$^{-1}$

New Situation: New lab automation equipment is purchased to automate the rheology and pH measurement. The capital cost of the kit is £300,000. This cost is deprecated over 5 years, meaning that there is an additional cost of infrastructure of £1,153 per week. This automation increases the speed of analysis by 2.5X, so that on average now a sample takes 0.2 hours of technician time to make a measurement. Assuming that the consumable cost remains at £3 per sample, and that staff costs remain the same, and that the automated platform has a reliability of 0.8, the lab can now measure 1120 samples per week. There has been a marked improvement in data quality, from 0.7 to 0.9, due to improved reproducibility versus manual method, use of a barcode scanner for reading sample IDs and reducing traceability mistakes, and use of automated data capture reduces human transcription errors. Using these values we can calculate the efficiency of the lab with the inclusion of the new automation platform.

Staff Costs	Infrastructure	Consumables	Cost (*N*)	N_Q
£7,447	£4,153	£3,360	£14,960	1008

Automated Efficiency = N_Q / *Cost* (*N*) = 1008 / £14,960 = 0.0674 £$^{-1}$

Notwithstanding the increases in the consumable and infrastructure costs for the automated solution, the efficiency of the automated lab is 2 times that of the manual lab.

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