Review of Low-cost Self-driving Laboratories: The "Frugal Twin" Concept

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Abstract

This review proposes the concept of a "frugal twin," similar to a digital twin, but for physical experiments. Frugal twins range from simple toy examples to low-cost surrogates of high-cost research. For example, a color-mixing self-driving laboratory (SDL) is a low-cost version of a costly multi-step chemical discovery SDL. We need frugal twins because they provide hands-on experience, a test bed for software prototyping (e.g., optimization, data infrastructure), and a low barrier to entry for democratizing SDLs. However, there is room for improvement. The true value of frugal twins can be realized in three core areas: hardware and software modularity, human-inspired vs. hardware-centric vs. human-in-the-loop design, and state-of-the-art software (e.g., multi-fidelity optimization). We also describe the ethical benefits and risks that come with the democratization of science through frugal twins. In future work, we suggest ideas for new frugal twins, SDL educational course outcomes, and a classification scheme for autonomy levels.

Keywords: automation, robotics, education, lab of the future, machine learning

1. Introduction

Self-driving laboratories (SDLs) are autonomous experiment-performing systems that have the potential to accelerate the discovery of solutions for key societal needs such as zero-carbon processes, food and agriculture, fuels, clean energy, energy storage, drug discovery, and structural materials [1]. SDLs have the potential to increase experimental reproducibility [2] and improve researcher productivity by automating tedious, repetitive tasks. This requires scientists to learn new skills related to the supervision, modification, and maintenance of autonomous systems related to both hardware (e.g., liquid handlers, robotic arms) and software

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(e.g., optimization algorithms, workflow orchestration, data infrastructure). It allows scientists to focus on higher-level cognitive tasks, such as hypothesis formulation, experimental design, and data interpretation, which are not easily automated [3].

The idea of accelerated discovery through automation has been called by several different names: SDLs [3–8], materials acceleration platforms (MAPs) [9], Lab 4.0 [10–12], Internet of Laboratory Things [13–15], Robot Scientists [16], the Autonomous Research System [17], and autonomous experimentation systems [18]. While each of these terms has its own nuances, for this work, we use the term SDL, which refers exclusively to fully autonomous[1] research systems used to accelerate materials discovery without human intervention.

SDLs that are used to solve societal challenges are considered to be materials acceleration for societal solutions (MASS) [1]. However, SDLs have yet to reach a critical MASS [1], or in other words, autonomous laboratories have yet to become commonplace and common sense. This widespread adoption requires widespread accessibility, implying lower costs, the ability to reconfigure and expand, and a joint effort to make easy-to-understand examples and systems for more advanced research tasks available. Since the introduction of SDLs in 2016 by Nikolaev et al. [19], many low-cost SDLs have been developed. Stach et al. [18] provide a community perspective on SDLs in the context of academia, industry, government laboratories, and funding agencies, and supply a descriptive table of selected SDLs across a variety of applications including chemical vapor deposition [19], flow- [20] and vial-based [21] chemistry, oil-in-water emulsions [22], additive manufacturing [23], thin films [7], quantum materials [24], and solid-state materials [25]. Many review and perspective articles have been contributed [1, 3, 4, 9, 18, 26–42], for which a list of 27 recent reviews is given in Table 1 of Xie et al. [42].

What sets our review apart from others is that we explicitly focus on low-cost SDLs, i.e., frugal twins of high-cost SDLs. We hope that this attention to the importance of low-cost SDLs will shift perspectives on educational and research capabilities of low-cost systems and provide a common reference point for building new solutions.

While the notion of low-vs-high cost setups is both a subjective and contextual problem, in the case of educational tasks, the cost limitations are usually more prohibitive, as indicated by the large fraction of educational SDLs specifically described as low-cost, under 1000 USD [43–45]. This is in part because the final objectives are often based around learning outcomes rather than specific research objectives.

In both contexts, there is a range between costs that can be covered from business-as-usual "spare" monetary resources vs. costs that require dedicated support from grants and other funding sources. For example, the National Science Foundation places a threshold of 5000 USD to differentiate between consumables and equipment, above which a purchase must be "adequately justified" on a grant proposal. [**?**] An example such as Opentrons robotics (7̃500 USD starting cost) likely fits more clearly into the "dedicated support" category for many education-oriented systems and somewhere in-between "spare resources" and "dedicated support" for research tasks. Of course, the context depends on a multitude of other factors including the specific research group and institution.

In this review, we describe what frugal twins are and why we need them (Section 2). Next, we describe how frugal twins are being used in education and research applications (Section 3). However, there are many ways we can leverage frugal twins more effectively and make them better (Section 4). This includes things like modularity, new design approaches, and incorporating state-of-the-art (SOTA) software. We highlight the ethical benefits and risks associated with frugal twins including citizen science efforts and potential for misuse (Section 5). Finally, we describe ideas for new frugal twins, suggest potential SDL course outcomes, and discuss how to classify autonomy levels in SDLs (Section 6). To encourage a continuing discussion,

[1]Automation refers to the use of technology to perform tasks with minimal human intervention, while autonomy implies the ability of a system to operate independently, making decisions and taking actions without human control.

we also provide a list of public, community-driven discussions (Section 7).

With an emphasis on chemistry and materials science applications and as part of a broader focus on MAPs and MASS, we walk through topics relevant to low-cost SDLs (Figure 1). First, we describe the development of "frugal twins" that capture the core principles of real-world systems at an education-friendly cost, and present areas where the community benefits from low-cost twins (Section 2). Next, we delineate how educational outcomes and autonomy can equip the next generation of scientists with industry-relevant skills (Section 3). We detail how modularity for hardware and software plays an important role in reducing redesign costs for future systems (Section 4.1). In a similar vein, we show that using a hardware-centric approach when developing SDLs can reduce system complexity by leveraging existing hardware in unconventional ways and describe trade-offs between design approaches (Section 4.2). Furthermore, the acceleration factor of discovery can be enhanced through high-throughput and parallelized systems (Section 4.3.1). Finally, cloud experimentation (similar to cloud computing, but for experiments) decentralizes hardware, computing, and domain expertise, reducing the barrier-of-entry for SDLs and enabling robust and efficient batch optimization (Section 4.3.4).

2. What are frugal twins, and why do we need them?

Inspired by the digital twin, a virtual counterpart of a physical entity, we introduce the concept of the frugal twin, a low-cost counterpart of a physical entity [46]. The digital twin is designed for simulation, modelling, and evaluation, which can offer insights into the physical entity, typically a priori to the inception of the physical entity [46]. Likewise, a low-cost SDL is the frugal twin of a high-cost SDL. Frugal twins offer a low-risk environment for rapid prototyping and also provide benefits in terms of education, citizen science, and research grade systems.They range within a trade-off spectrum of cost/research capabilities, where the balance between the two factors determines their usefulness for particular research activities (Section 2.1). Specific examples of these trade-offs are shown for materials science and chemistry in Figure 2. A summary of various low-cost SDLs is provided in Table 1.

2.1. *Trade-offs between cost and research capabilities*

The appropriate balance between cost and research capabilities for a useful low-cost SDL is largely governed by access to resources and the desired research goal. Much research at the forefront of its field relies on expensive analytical instrumentation to be able to obtain sufficient information about experiments. For instance, compound characterization typically requires the use of analytical techniques including nuclear magnetic resonance spectroscopy (NMR) and high-performance liquid chromatography coupled with mass spectrometry (HPLC-MS). However, the acquisition and operation of these techniques can cost hundreds of thousands of dollars, rendering their procurement and maintenance a challenge. Here, sacrificing research capabilities for lower costs is infeasible, as low-cost ($\leq\sim$10000 USD) alternatives to NMR or HPLC-MS do not currently exist on the market. Even if such alternatives were available, their reliability and accuracy compared to the standard techniques would be paramount. There are primarily two ways to reduce the cost of a frugal twin, which are to reduce its research capabilities, or to reduce its accuracy and precision. In Figure 2, we outline two trade-off examples for a frugal twin in the context of a materials science and a chemistry experiment. Although some of these examples are not standalone SDLs, they all have the potential for integration into an SDL for varied research purposes. The SOTA research capability in the materials science example is the ability to 3D print various metal alloys at extremely high temperatures, which can be accomplished by the FormAlloy metal 3D printer [50].

As cost decreases, the more frugal instruments' capabilities stray further away from the SOTA research capabilities (Figure 2). The arc melter can form alloys at high temperatures, but cannot 3D print them. The next drop in costs renders

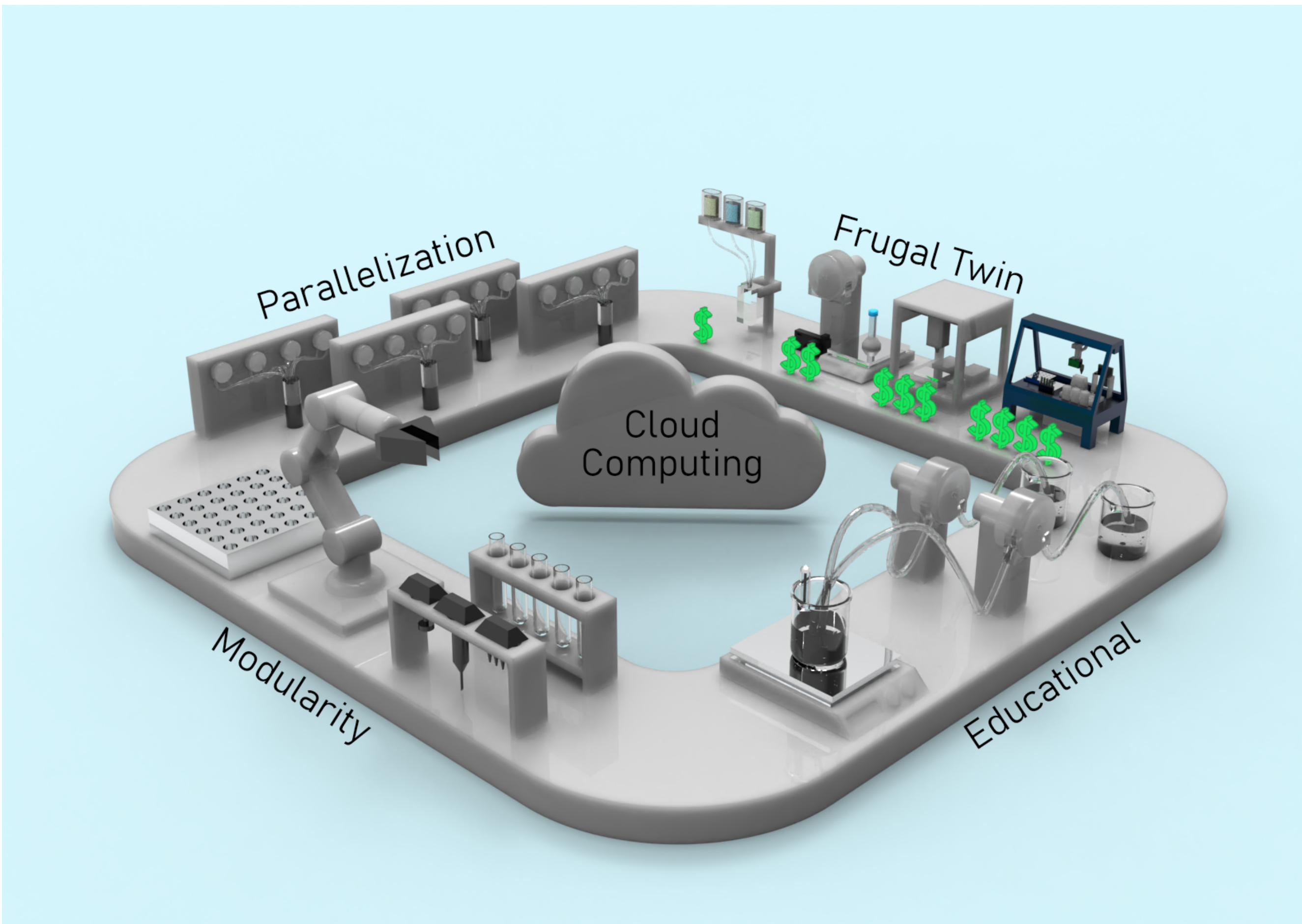

Figure 1: Key themes of low-cost self-driving labs: frugal twins, education, modularity, parallelization, and cloud computing.

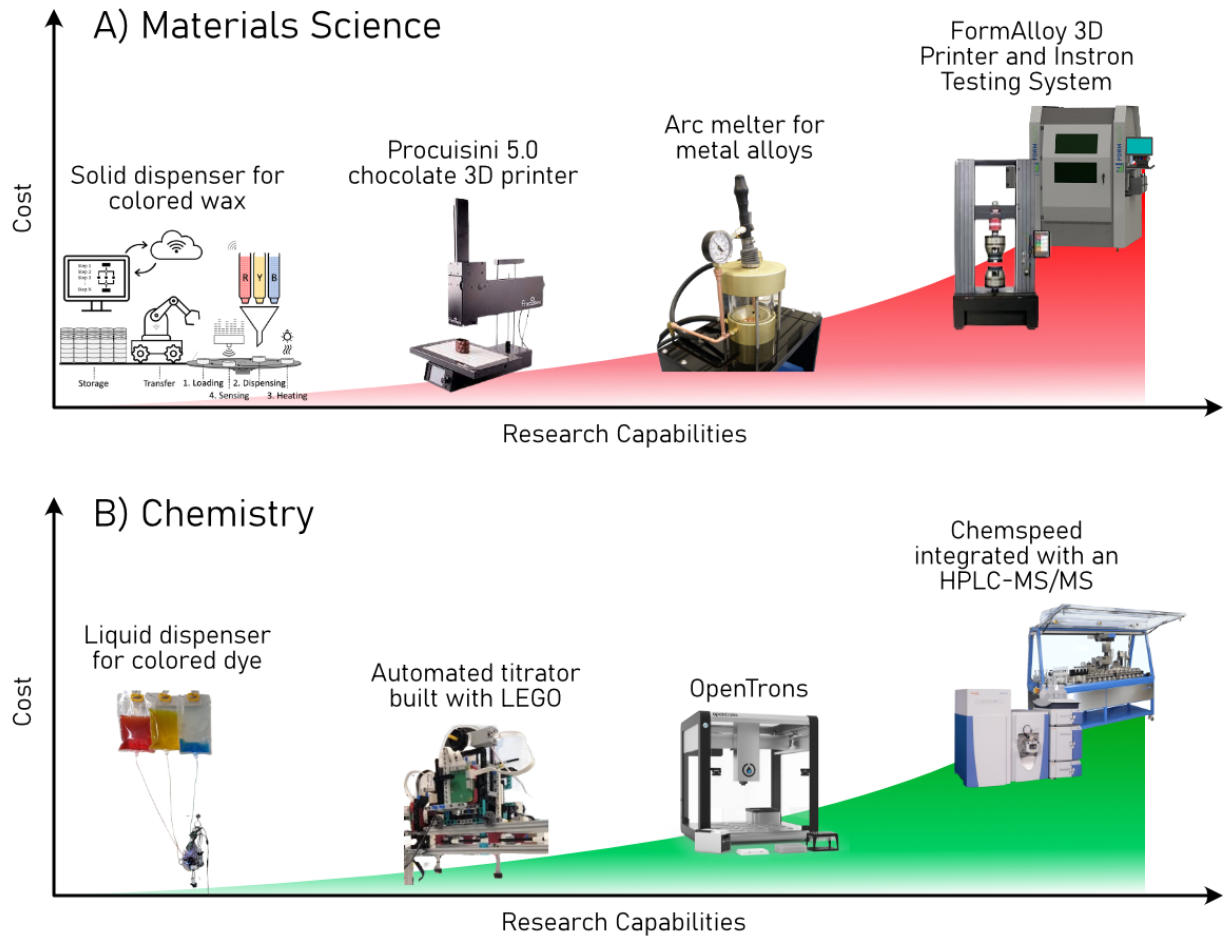

Figure 2: Spectrum of frugal twin capability vs. cost trade-off. A) From left to right: solid dispenser for colored wax [47], Procuisini 5.0 chocolate 3D printer [48], arc melter [49], FormAlloy metal 3D printer [50], and Instron electromechanical universal testing system for metals [51]. B) From left to right: liquid handling for dye mixing [47], automated titrator built from LEGO [52], OpenTrons [53], and Chemspeed integrated with an HPLC-MS/MS [54, 55]

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Table 1: Low-cost SDL summary. Estimated costs in USD.

Name	Field	Purpose	Cost	REF
"The Chemputer"	Chem. synthesis	Chem. discovery	30 000	[56]
An autonomous portable platform for universal chemical synthesis	Chem. synthesis	Chem. discovery	10 000	[57]
Networking chemical robots	Chem. synthesis	Cloud experiments	500	[58]
Additive Manufacturing Autonomous Research System (AM ARES)	Mat. Sci.	Print characteristics	1000	[17]
Crystallization Robot	Mat. Sci.	Random number generator	3000	[59]
Accelerate Synthesis of Metal–Organic Frameworks	Mat. Sci.	MOF crystallinity optimization	830	[60]
A chemical synthesis robot for nanomaterials	Mat. Sci.	Morphology optimization	15 000	[61]
LEGO low-cost autonomous science (LEGOLAS)	Education	Titration	300	[52]
Scientific Inquiry in Middle Schools	Education	Titration	250	[43]
Automatic titrator for intro chemistry labs	Education	Titration	934	[62]
Automatic titration for teaching chemistry	Education	Titration	4160	[63]
Autonomous titration for chemistry classrooms	Education	Titration	600	[64]
Automated pH Adjustment with Robotics and Machine Learning	Education	Titration	650	[65]
MIT students remotely control an autonomous robot across the country	Education	Color-matching	10 000	[66]
Bayesian Optimization Bartender (BOB)	Education	Color-matching	200	[67]
Closed-loop Spectroscopy Lab: Light-mixing (CLSLab:Light)	Education	Color-matching	50	[68]
Evolution of oil droplets in a chemorobotic platform	Formulations	Evolutionary dynamics	1000	[69]
A microfluidic platform to explore chemical evolution	Formulations	Evolutionary dynamics	5000	[70]
Evolution of protocells in a configurable 3D-printed fluidic platform	Formulations	Evolutionary dynamics	2000	[71]
A curious formulation robot for discovering novel protocell behavior	Formulations	Evolutionary dynamics	1000	[22]

the instrument only capable of toy problems: the Procuisini 5.0 3D chocolate printer can form and 3D print various chocolate compositions. Lastly, the "Hello World" of a materials science SDLs at the lowest cost shown is the solid dispenser for colored wax, capable of producing candle wax in customized colours [47]. Likewise in the context of chemistry, the glssota research capability is to perform multi-step, multi-batch synthesis and characterization, which could be accomplished by a Chemspeed integrated with an HPLC-MS/MS. At a significantly lower cost, the OpenTrons system shown can perform single-step, multi-batch synthesis and limited characterization techniques, focused primarily on biological applications [53]. The automated titrator built from LEGO, one step lower in cost than the OpenTrons, can no longer perform synthesis but only multi-batch liquid dispensing, and uses a pH probe for characterization [52]. Lastly, the cheapest SDL in a chemistry context is a liquid handler for dye mixing, tasked with obtaining a customized color as characterized by a light sensor [58, 67, 68, 72].

2.2. *Rapid, low-risk prototyping and proofs of concept for research*

SOTA SDLs are a feat of both science and engineering, which are often complex and expensive, making them challenging for rapid prototyping. Their frugal twins can enable researchers to easily prototype and engage in an iterative loop to explore new design concepts, gain new knowledge, refine and validate existing designs, and easily share information within the group of researchers [73]. This approach is known as relaxed requirement prototyping, leveraging the trade-off between model accuracy and cost [73]. In addition, the application of advanced optimization algorithms for SDLs can be directly integrated and tested on the frugal twin.

Nevertheless, preliminary evidence acquired from a low-cost SDL can serve as proof of concept for solving an analogous research problem which justifies the funding of a high-cost SDL. They may have lower accuracy and reliability but still serve as evidence of feasibility for the proposed research, as well as answering some of the relevant research questions. In addition, the low-cost SDL can act

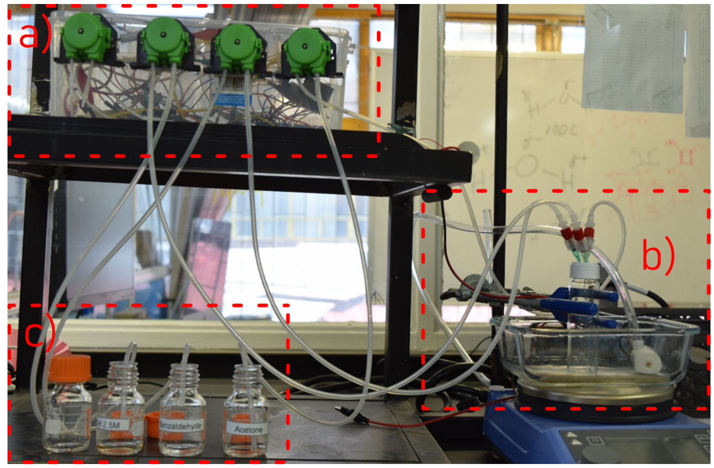


Figure 3: MIK-I, a low-cost automated synthesis workflow platform. a) Peristaltic pumps controlled by a Raspberry Pi, b) synthesis reactor, c) reagent bottles.

as a proxy for estimating the acceleration factor an SDL can offer in comparison to manual experimentation.

An example that compellingly captures how a frugal twin can promote rapid prototyping and educate students to learn transferable skills in a low-risk setting is a project from the Aguilar Granda group at the National Autonomous University of Mexico. Researchers ordered components to build "The Machine" [74]. However, prior to assembling this final SOTA research tool, they built another system, MIK-I, with the purpose of familiarizing themselves with automated synthesis platforms. MIK-I is the frugal twin of "The Machine", with a total cost of approximately 350 USD (Figure 3). This low-cost system is capable of handling liquids of different physicochemical properties such as density, viscosity, and surface tension. As a proof of concept, the researchers successfully performed a crossed aldol condensation autonomously (Figure 4). The primary goals of MIK-I were to familiarize the students with low-level hardware and to anticipate and troubleshoot problems when building "The Machine": e.g., the calibration necessary for handling liquids with a wide range of physicochemical properties.

2.3. *Education, and Citizen Science*

SOTA SDLs can pose a troublesome opportunity cost for researchers, due to the high training bur-

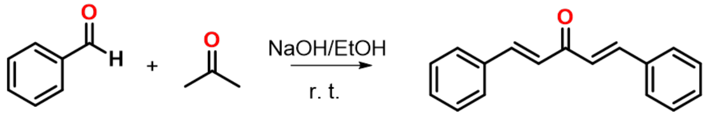


Figure 4: The scheme for a general crossed aldol condensation reaction as a proof of concept.

den and potential high cost of mistakes. One of the solutions is the frugal twin, where new users can play-test and familiarize themselves with the frugal twin to learn transferable skills for the SOTA SDLs. Low-cost SDLs create an environment conducive to experiential learning via trial-and-error, which acts as a stepping stone for new users with limited robotics and programming experience that is important for the design, setup, and operation of SDLs. Effectively democratizing access to SDLs requires overcoming both financial and technical barriers, by providing detailed schematics, parts lists, assembly instructions, code documentation, and troubleshooting guides.

3. How are frugal twins being used in education and research?

In this section, we offer an in-depth overview of low-cost SDLs in materials science and chemistry designed for education (Section 3.1) and research (Section 3.2). From these examples, there are many lessons to be learned and areas to be improved, which are later discussed in Section 4.

3.1. Designed for Education

Two pertinent educational topics are examples of autonomous titration setups (Section 3.1.1) and minimal working examples of SDLs (Section 3.1.2).

3.1.1. Titration

Titrations are one of the most ubiquitous experiment types in a high school or undergraduate chemistry curriculum. The automation of a titrator allows many students, including students with certain disabilities who may otherwise be excluded, to further their understanding of chemistry, while simultaneously providing an opportunity to learn about electronics [75] (Figure 5). A variety of features can be incorporated around an automated titrator such as a web interface for remote work, a liquid (acid/base) dispenser using a solenoid valve or peristaltic pump, a pH probe for characterization, a pH indicator with computer vision, voice activation via digital assistants such as Siri, and a LEGO framework for modularity and high-throughput [52, 62, 63, 75, 76]. As an educational tool, automating a previously manual procedure is engaging, encourages critical thinking, and provides an additional layer of complexity. Typically, students develop their own heuristics, such as adding large amounts of titrant at the start of the experiment and slowly reducing the addition of titrant until the endpoint is reached, with the goal of optimizing for efficiency and accuracy. However, with the integration of several robotic components, students can easily quantify and test multiple titration strategies for optimal efficiency, accuracy, or both [64].

The applicability of skills acquired from educational settings to research and industry settings is critical [77], and modification of a titration experiment presents a direct example of this transferability. For instance, Pomberger et al. [65] designed their titration apparatus with high-throughput batch samples, and active machine learning (ML) to model the pH response of multi-buffered polyprotic systems, which is a challenging yet important task for many chemical labs and industrial plants. For context, educational titration setups with a single-buffered system like the ones mentioned above can be accurately described by the Henderson–Hasselbalch equation [65]. However, this does not hold for multi-buffered polyprotic systems [65]. Although the multi-buffered polyprotic problem has greater complexity, students can learn to adapt solutions to fit their needs and work around limitations. By exploiting the benefits of modularity (outlined in Section 4.1), students can choose from several optimization algorithms such as ML, proportional-integral-derivative control, and model predictive control [65]. Although automated solutions improve efficiency and robustness, an educational apparatus should also provide the option for a student to be put back in the loop (i.e., manual mode) because it can provide the student with more direct interactions with the

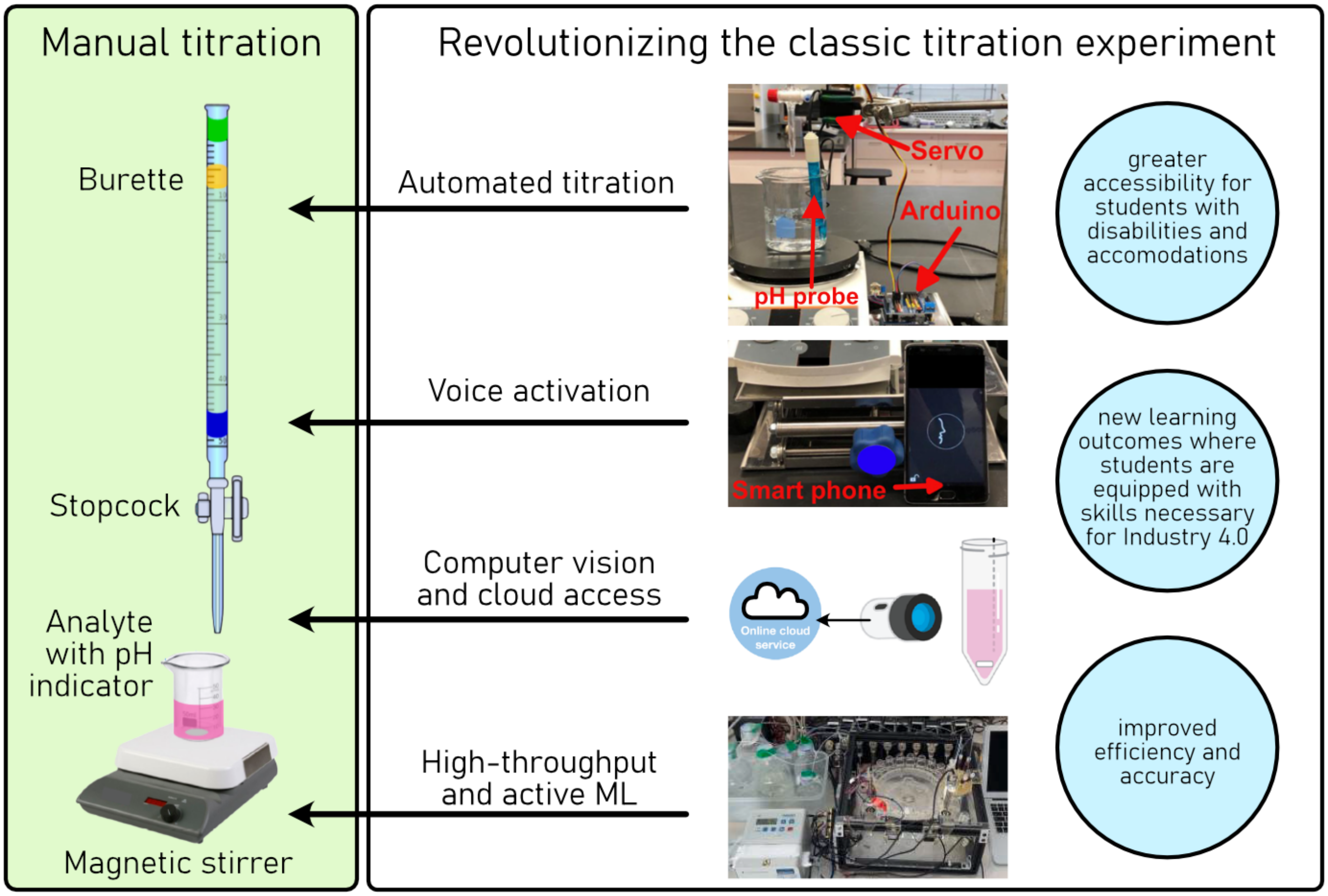


Figure 5: Example of a titration setup that can be equipped with automation, voice activation, computer vision, high-throughput capabilities, and machine learning. Adapted with permission from [62, 63, 75, 76]. Copyright 2016, 2019, 2021 American Chemical Society. Adapted with permission from [65] under the Creative Commons Attribution license (CC-BY). Copyright Elsevier 2022.

hardware.

3.1.2. CLSLab minimal working examples

Recently, Baird and Sparks [68] developed a system known as Closed-loop Spectroscopy Lab: Light-mixing (CLSLab:Light) as a teaching and prototyping platform that presents a color-matching task for mixtures of red, green, and blue light-emitting diodes (Figure 6). The demo utilizes light rather than matter while retaining the principles of SDLs. Taking language from the software community, it is a "minimal working example" of an SDL. The primary benefits of this device are that it costs under 100 USD, requires less than an hour of setup time, and takes up minimal desk space, compared with more costly, time-intensive, higher-footprint (and, of course, more chemistry-relevant) liquid handlers such as Opentrons [53], Sidekick [78], evoBOT [79], OpenLH [80], OTTO [81], and OpenWorkstation [82]. While CLSLab:Light is not an SDL for materials discovery, these features make it an ideal candidate for classroom settings, where each student or team can obtain hands-on experience. Additionally, the platform can be used to prototype concepts such as creating a network of geographically distant experiments and implementing advanced optimization topics such as batch (Section 4.3.1) and multi-fidelity optimization (Section 4.3.2). Over a dozen tutorials and examples for basic optimization, advanced optimization, device communication, and data ecosystems are given in the Closed-loop Spectroscopy Lab documentation.

CLSLab:Light has also evolved as an example and suggestion of SDL best practices: the software is modular, open-source, well-documented, and robust against deprecation. Build instructions and a video build tutorial are provided, with parts lists designed to be modular and robust to supply chain issues [72]. Some additional features of the CLSLab:Light platform that help students to learn and implement best practices are summarized in Table 2.

Recently, Baird and Sparks [72] explored the commercialization of CLSLab:Light as an at-cost kit with two successful rounds of crowdfunding via the GroupGets platform (see Campaign #1112 and Campaign #1129), totaling 39 kits; many kits have already been used in classroom settings at the University of Toronto, Massachusetts Institute of Technology, and the University of Chicago. For continuing discussion related to packaging open-source hardware as commercial kits, see Discussion #124.

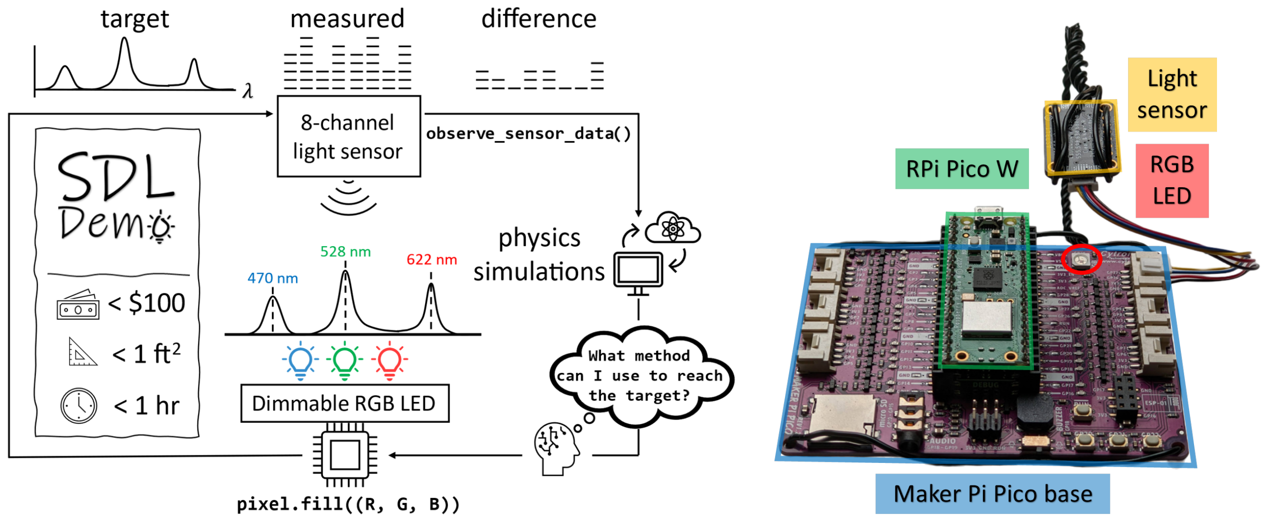
CLSLab:Light has already seen success, but domain-specific communities (biology, chemistry, solid-state materials science) will benefit from their own minimal working examples. Baird and Sparks [72] have explored the development of extensions that adapt the instructive lessons from CLSLab:Light to other domains. Using the modular software and hardware components, the platform has been extended to a liquid-based color-matching task (Closed-loop Spectroscopy Lab: Liquid-mixing (CLSLab:Liquid)) using the prototypical example of mixing red, yellow, and blue food coloring dyes (Figure 7). In sharp contrast to biology and chemistry applications, low-cost examples of SDLs for solid-state materials science are effectively non-existent. To address this gap, an idea for a solid-state materials science extension involving the melting and mixing of colored wax powders is described in Section 6.1.

3.2. Designed for Research

Typically, low-cost setups are not regarded as research tools because of their lack of accuracy, precision, and capabilities. However, many research groups are developing low-cost SDLs for reasons such as full control over the end-to-end design (Section 3.2.1), and ease of parallelization (Section 3.2.2).

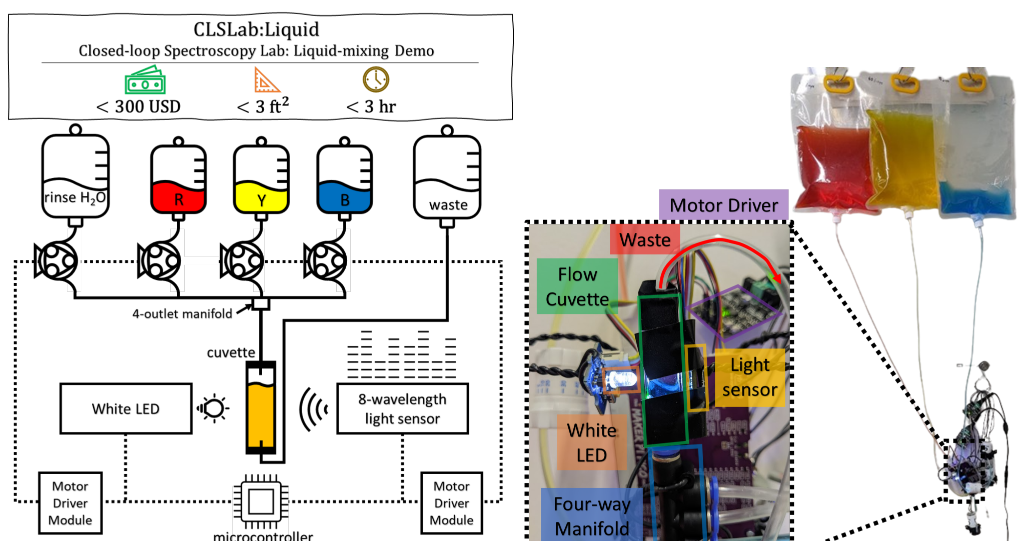
3.2.1. End-to-end design

Instead of purchasing expensive and inflexible commercial systems to produce an SDL, building a low-cost SDL from scratch gives the researcher full control over the system. This concept of building a complete system from beginning to end is referred to as end-to-end design. Cronin et al. [84] demonstrates this process through several examples over the last decade. Enabled by Moore's law, where electronics become cheaper over time, and the growing opportunities available from the ??, custom scientific apparatus can now be built at low



(a) (b)

Figure 6: The CLSLab:Light demo. (a) A summary schematic of CLSLab:Light. b) An annotated image of the CLSLab:Light. (a). Adapted with permission from [83]. Copyright Elsevier 2023.



(a) (b)

Figure 7: The CLSLab:Liquid demo. (a) A summary schematic of CLSLab:Liquid. (b) An annotated image of the CLSLab:Liquid [47].

Table 2: Summary of best practice topics (Topic) that address development pain points (Pain Point). Related resources/-tools (Resources) and corresponding implementations in the CLSLab:Light framework (CLSLab:Light) are also given. In other words, the Resources column links directly to the tools while the CLSLab:Light column typically links to various places in https://github.com/sparks-baird/self-driving-lab-demo. *Detailed setup instructions for MQTT and MongoDB are provided in Baird and Sparks [72].

Topic	Pain Point	Resources	CLSLab:Light
Version control	Keep detailed, accessible, and efficient snapshots of your code at any point in time	Git, GitHub	GitHub repo/history
Project Generator	Streamline setting up modular code for a new project while conforming to best practices	PyScaffold, cookiecutter-pypackage	PyScaffold and initial commit
Python packages	Make installation and setup easier for users	PyPI (pip), Anaconda	PyPI via setup.cfg
Unit tests	Catch bugs and ensure functionality	pytest	tests folder
Continuous integration	Regularly and automatically validate code, run tests, and publish new versions	GitHub actions	actions via ci.yml
Secure wireless communication	Safely communicate within and between software and hardware	MQTT	MQTT* host/client
Data management	Store data that is "Findable, Accessible, Interoperable, Reusable" (FAIR)	MongoDB, SQL	MongoDB* main.py
Installation-free notebook tutorials	Make it easy for users to learn, test, and adapt the functionality	Google Colab, Binder	Tutorials page
Documentation web host	Host a website with your documentation for free	Readthedocs, GitHub pages	Readthedocs site
Documentation builder	Package your documentation, tutorials, and API as web-friendly HTML files	Sphinx, Jekyll	Source files, conf.py

costs. However, although low-cost electronic and hardware components offer a wide range of unique capabilities compared to fully developed systems, they generally require significant time and effort to design, engineer, and test.

Nevertheless, with a specific, unique, and focused research problem, Gutierrez et al. [69] take advantage of the full control over the end-to-end design of a novel, custom-built chemorobotic platform. This system is capable of exploring a diverse range of oil-droplet formulations which was designed to improve the understanding of evolutionary dynamics. Many low-cost components such as a RepRap 3D printer, camera, Arduino microcontroller, and 3D printed parts are used to gain the desired functionality for this specific experimental task [69]. Later, this robot was redesigned with a 3D printed arena for droplet mixing which could be easily transformed into different environments, adding a new independent variable to experimentation [71]. With high-throughput experimentation and automation, it is not crucial for the robot to be extremely accurate or precise, due to the ease of performing multiple replicates to reduce the uncertainty of results. In this oil-droplet system, several replicates are performed and the uncertainty measured and accounted for before drawing conclusions from general trends [71]. Full control over the design of the experimental apparatus is invaluable for niche research problems, where science knows no bounds.

The modular Geneva wheel platform engineered by Salley et al. [85, 86] is another example of a low-cost SDL designed end-to-end to leverage the advantages of low-cost components and custom parts. Due to its modular nature, it can be easily reconfigured for the synthesis of polyoxometalates (POMs), gold nanoparticles, lanthanide-based Mo-POMs, or other coordination compounds [61, 85–88]. From this system, an important takeaway is that "automation can only be so cheap before significant frustration is experienced."[84] In this example, Cronin et al. [84] replace very cheap aquarium pumps with motor-controlled stepper pumps, which offer better control and accuracy over the liquid dispensing while still remaining quite cheap.

Although the "Chemputer" is not as low-cost as our other considerations, it is worth mentioning because of its end-to-end design for universal chemical synthesis. The Chemputer integrates not only custom 3D-printed parts and electronic components such as syringe pumps, but also interfaces with existing chemistry instruments that may already be in the lab such as hotplates, photoreactors, flow reactors, a rotary evaporator, benchtop NMR spectrometers, and in-line spectrometers (UV-Vis, ART-IR and ESI-MS) to perform organic synthesis and characterization [89–98]. Although the Chemputer can perform closed-loop discovery with a wide range of research capabilities, it can cost over USD 30 000 with a setup time of 1 week, which is not accessible for most citizen science and smaller research groups. Manzano et al. [57] develop the "mini-Chemputer", which reduces the barrier of entry from USD 30 000 to USD 10 000, and 1 week to 1 day of setup time. Having full control over the end-to-end design of this system enabled the Cronin group to develop both the many different research capabilities of the Chemputer, and the low-cost, portable mini-Chemputer.

3.2.2. Ease of parallelization

A network of chemical robots is a useful tool for performing decentralized, cloud-based, batch optimization of an experimental campaign. Caramelli et al. [58] build a simple chemical robot using several peristaltic pumps for liquid handling, a glass reaction vial, a webcam for reaction analysis, and a pcDuino board for electronic control. Due to its simplicity and low cost, the hardware is easily replicated, which enables parallelization of experiments to increase throughput. The following experiments described below exploit some of the advantages of building a network of robots: collaborative azo dye chemical space exploration, real-time control of an oscillating reaction, a reproducibility assessment of inorganic cluster crystallization, and gameplay-driven chemical discovery [58].

First, the robots were able to communicate by uploading results to the cloud and screening for results from other robots via Twitter. This system prevents robots from duplicating others' reactions and allows them to explore more efficiently as a team. Using a network connection, multiple, physically-separated robots can be synchronized in real time. Caramelli et al. [58] use the chemical oscillator based on the Belousov-Zhabotinsky (BZ) reaction to showcase real-time control performance. The oscillation period is synchronized in real time between robots with an uncertainty of 2 s.

Reproducibility in the context of parallelization is necessary for accurate data acquisition. In one experiment, the network of robots collaboratively explores the conditions for the crystallization of tungsten POM clusters. Crystallization is a stochastic process, which makes it challenging to determine its ideal conditions, particularly on smal scale. Nevertheless, the network of robots found six sets of conditions that offered reproducibility between 11.8 – 50%, which may be deemed acceptable for a stochastic process on small scale.

Lastly, success in gameplaying offers the insight that large amounts of data enabled by powerful computation can push ML models to reach superhuman performance [99]. Highly robust and reproducible materials chemistry SDLs can generate large amounts of data with low-cost experimentation and parallelization. Caramelli et al. [58] demonstrate that two robots can compete against each other in a well-defined game to discover novel colors in the context of an azo coupling reaction. The rules are simple: novel results are rewarded, and common results are punished. Each time that a loser emerges at the completion of a game, the loser can change strategies by redefining their reaction space. The goal of the gamification of such an experiment is for the model to develop an optimal strategy to maximize the objective without human guidance. The success of this simple experiment provides the groundwork for similar SDLs to solve more complex problems though a low-cost and parallelized approach.

4. How do we make frugal twins better?

We describe ways to continue improving and leveraging the strengths of frugal twins in terms of hardware and software modularity (Section 4.1), human-inspired vs. hardware-centric vs. human-in-the-loop design approaches (Section 4.2), and synergizing frugal twins with ?? software tools and algorithms (Section 4.3).

4.1. Modularity

Modularity refers to the assembly of a cohesive system or device that has discrete, self-contained modules which can be easily interconnected and replaced. Each module performs a specific function or task, and they can be combined or modified independently. This approach allows for flexibility, scalability, and ease of maintenance, as well as facilitating the reuse of components in different applications. In this section, we explore modularity in the context of both low-cost hardware (Section 4.1.1) and open-source software (Section 4.1.2).

4.1.1. Hardware

MacLeod et al. [34] emphasize “the characteristic features of modern robots that make them useful for flexible automation [which] include large working areas, many degrees of freedom, high positioning accuracy and repeatability, intrinsic safety, and easy programming (Figure 8). Versatile multi-axis robots that can interact with both liquids and solids offer the flexibility to automate a wide range of experiments.” Although low-cost SDLs cannot generally afford such characteristics, the emphasis on is leveraging cost-effective and creative strategies to automate a diverse range of experiments within their limitations.Gutierrez et al. [69] demonstrate their use of modular design to effect simple reconfiguration where parts can be easily redesigned, replaced, and tested. Their oil-water droplet robot can be readily reconfigured for adding new chemicals and other formulation-based studies in a variety of simple ways [22, 69, 70]. For example, the 3D printed polypropylene evolutionary arena can be interchanged with different designs that have pillars, caves, or other arrangements [71]. The well-plate array for sample preparation can also be switched with a Geneva wheel that automates drying and cleaning, increasing experimental throughput [22]. Another flexible concept for simple reconfigurations is Reactionware, which refers to low-cost 3D printable reactors for custom reactions and volumes [95, 100, 101].

Given that devices inevitably break down at times, incorporating modularity into SDLs reduces

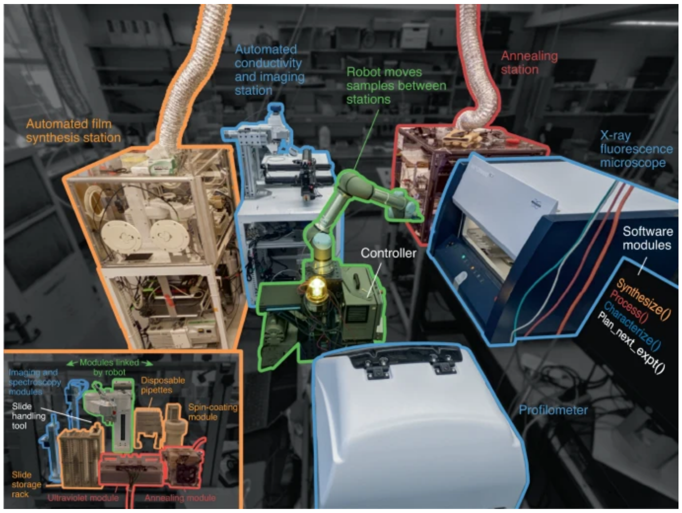


Figure 8: Flexible automation for SDLs where components can be rearranged and replaced around the central robot arm. MacLeod et al., Flexible automation accelerates materials discovery, *Nature Materials*, published 2022, Copyright © 2021, Springer Nature Limited.

the time and cost of maintenance. If one component breaks, then only that small portion of the instrument needs to be repaired or replaced. In addition, with smaller modular parts, debugging is simplified since each individual component can be tested separately, quickly determining the points of failure.

An SDL should be composed of a core infrastructure capable of interchangeably adapting to domain-specific requirements such as but not limited to liquid handling, solid dispensing, and thin-film manufacturing. This is more cost-effective than building a fixed, domain-specific system capable of performing all the desired tasks for only one given type of experimentation. After the first discovery campaign is completed, the cost of redesigning an inflexible SDL for further work could be much higher than for a modular system. To make the most of modularity in the context of low-cost SDLs, it needs to reduce the redesign cost for future systems.

4.1.2. Software

While existing efforts to enforce SDL hardware modularity are valuable, in practice, it is still in its infancy. Some lessons can be taken from modern software development, such as functional and object-oriented programming (i.e., organized use of functions and classes), the single responsibility principle (each module has a single, well-defined responsibility), and related concepts like version control (semantic versioning, commit history, backups, and rolling back to previous versions). These principles are applied out of necessity to optimization and workflow orchestration software ecosystems with large user bases such as Meta's Adaptive Experimentation (Ax) Platform (`https://ax.dev/`) and Agnostic's Covalent workflow orchestration platform (`https://www.covalent.xyz/`). In some cases, these best practices have also been applied to chemistry and materials informatics optimization and workflow orchestration packages. For example, Gryffin uses a custom Python class (`Gryffin`) in an object-oriented programming fashion ([102]). An object can be instantiated based on the `Gryffin` class with user-specified configuration parameters. After instantiation, built-in class methods perform operations such as `recommend` and `build_surrogate` on the object.

Likewise, `alab_management` and `Bluesky` utilize classes. For example, `alab_management` offers base classes for devices and tasks. A user need only create a custom class for a specific device or task once that can be reused, and copy-pasting of "boilerplate" code is unnecessary. `Bluesky`, designed with synchroton facilities in mind, use "motors" and "detectors" to clarify the difference between hardware that performs tasks based on inputs (e.g., temperature controllers, sample changers) and characterization hardware that produces research data (e.g., photodiodes, CCD cameras, spectrometers).

While the hardware associated with low-cost SDLs may not be as performant as high-cost examples, the same SOTA software that is deployed on a high-cost SDL can be deployed to a low-cost SDL with minimal effort. This enables both rapid, low-risk prototyping (Section 2.2) and opportunities to integrate low-cost and high-cost experiments via multi-fidelity optimization (Section 4.3.2). A more general discussion of ?? optimization with workflow orchestration tools and algorithms is given in Section 4.3.

4.2. Design Approaches

In this section, we describe three different design approaches for SDLs. The most common of these for automation is the human-inspired approach (Section 4.2.1) because of the intuitive translation between human and robotic motion. Alternatively, hardware-centric design (Section 4.2.2) is becoming more prevalent due to taking better advantage of the potential of hardware components. However thirdly, at times, it is more cost-effective and practical to keep the human in the loop (Section 4.2.3) for the main objective of accelerating scientific discovery. Each of these approaches is conceptually summarized in Figure 9. At the end of Section 4.2.3, we describe the role of frugal twins in bridging gaps between these seemingly disparate design philosophies.

4.2.1. Human-inspired

When most people think of robots, they think of human-inspired robotic design (Figure 9b, Figure 9e), where robots perform tasks anthropomorphically. For example, robotic arm setups [21, 34] are often used to mimic human behavior. While there are benefits, this design approach exhibits its own set of trade-offs. We define human-inspired design as:

> Designing systems that mimic human behavior to accommodate traditional experiments

For example, robots can be made to use existing, human-centric lab equipment without modification [21]. However, without complex sensing capabilities such as computer vision, a hard-coded system is sensitive to slight perturbations in absolute positions and orientations. This often requires extensive routine calibration and is tedious to implement when integrating new scientific instrumentation. The introduction of computer vision to recognize particular objects can introduce greater flexibility, but suffers from the larger startup cost of the vision algorithm and may not elegantly handle all possible situations. Additionally, glassware is an essential component of any chemistry lab, but it is incredibly challenging for computer vision to recognize transparent objects [103].

An alternative that combines the benefits of hard-coded routines and complex computer vision decisions is to use fiducial systems such as AprilTags [104, 105], which are used by Xu et al. [103], Wang et al. [106] (Section 4.2.1). These can be thought of as QR codes or bar codes attached to pieces of equipment to help with relative positioning. However, the true value is not simply to identify hardware with unique IDs; an AprilTag in conjunction with the AprilTag detection software allows for the "[computation of] the precise 3D position, orientation, and identity of the tags relative to the camera." More recent work also enables flexible fiducial markers to be placed on circular, annular, and other shaped objects [107] such as vials. Likewise, Krogius et al. [107] demonstrate the use of nested, recursive layouts for high dynamic range. While there are challenges associated with mimicking human behavior, there remain excellent use cases for the human-inspired approach.

4.2.2. Hardware-centric

Replicating human behavior is often a difficult task because robotic arms come into play for tasks like sample transfer, a task that humans excel at but robots do not. An effective alternative to the human-inspired design approach exists which we refer to as hardware-centric design. Seifrid et al. [3] state:

> [It] is critical to understand that adapting experimental procedures that were designed for human experimenters is not as simple as transferring those same actions to an automated system, and there may be more efficient ways to achieve the same goal in an automated fashion.

For example, Abolhasani and Kumacheva [4] discuss the nuances between using a mobile robot arm, a stationary robot arm, and fluidic sample transfer, each with varying levels of human-likeness and difficulty. Here, we define hardware-centric design as:

> Leveraging existing hardware and using clever design choices to carry out experiments without pre-existing notions of mimicking human behavior

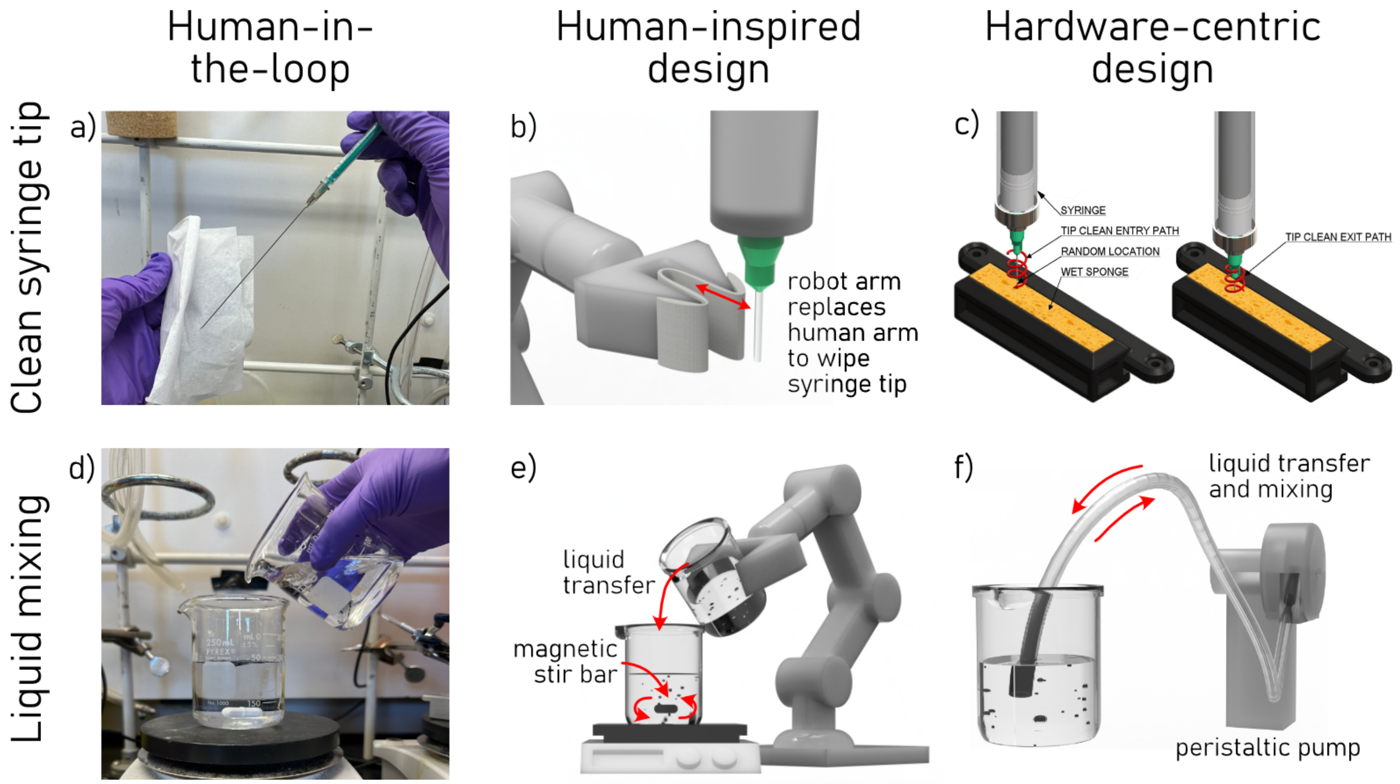


Figure 9: Examples of human-in-the-loop vs. human-inspired vs. hardware-centric design. (a) Wiping a needle by hand vs. (b) wiping a needle using a cloth attached to a robot arm vs. c) helical insertion into a sponge. Adapted from [17] under the Creative Commons license (CC-BY). Copyright © 2021, This is a U.S. government work and not under copyright protection in the U.S.; foreign copyright protection may apply. d) Mixing liquids together in a traditional lab setting using manual pouring vs. e) using a peristaltic with a digitally controlled stir plate vs. f) leveraging a bidirectional peristaltic pump to perform both liquid transfer and mixing.

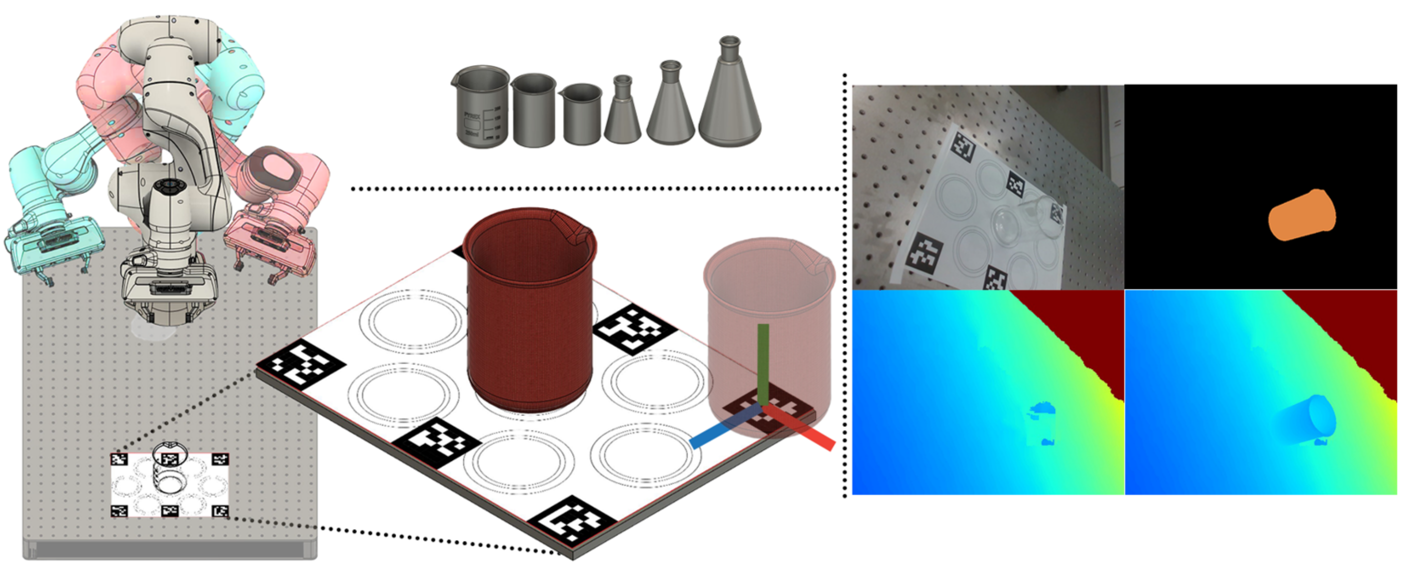


Figure 10: AprilTags, a type of fiducial marker, are affixed to a base plate to allow for accurate detection of its position and orientation (six degrees-of-freedom) relative to the camera. Reproduced from Xu, H.; Wang, Y. R.; Eppel, S.; Aspuru-Guzik, A.; Shkurti, F.; Garg, A. arXiv 2021. DOI: 10.48550/arXiv.2110.00087 ([103]) under

In terms of low-cost SDLs, Deneault et al. [17] provide a prudent example of leveraging the existing robotic setup (a 3-axis printer) and moving the syringe into and against a fixed sponge with a helical motion, to clean the external surface of the syringe (Figure 9c). When cleaning a syringe, a human might run it under water, wipe it with a cloth (Figure 9a), put it in an ultrasonic cleaner, or replace the tip entirely. A robotic arm with human-inspired design could be equipped with a cloth to wipe the syringe tip (Figure 9b), or remove the tip and place it in an ultrasonic cleaner. However, helical insertion into a sponge leverages existing equipment at a low cost. While it has limitations (e.g., how well is the syringe tip cleaned relative to more standard procedures; cross-contamination), it is an informative example of hardware-centric design. Another example is a peristaltic pump dual-purposed for both waste removal and mixing, where mixing occurs by cycles of forward and reverse pumping to agitate the solution (Figure 9f) instead of using a magnetic stir bar and stir plate (Figure 9d and Figure 9e). Likewise, rather than using an original equipment manufacturer (OEM) stir plate, Caramelli et al. [58] describes using a small electric fan in place of a stirring motor. For computer vision, which requires multi-angle capture for better object detection, using a robot arm with a mounted camera that moves to different positions instead of multiple cameras is more cost-efficient but also suffers from the lack of real-time processing, additional overall time, and lower precision [103].

A common thread in these examples is design from the standpoint of state variables such as temperature, pressure, and process functions such as heating, mixing, and irradiation. Each material state can be achieved without necessarily conforming to a particular piece of system. By designing equipment with desired material states and processing conditions in mind, we create hardware that is time- and cost-efficient for autonomous experimentation. Especially in low-cost settings, we should try to do as much hardware-centric design as possible. This will both lower cost and require less equipment.

4.2.3. Human-in-the-loop

However, it can be easy to over-automate, whether in hardware-centric or human-inspired design. Sometimes, we need humans to be “in the loop” for tasks where robots do not excel. We have evidence from Amazon, Tesla, Carnegie Mellon University cloud labs, and personal experience, where robots do not perform well on certain tasks. We define human-in-the-loop design as:

> Systems that require manual human intervention during an experiment

Here, we draw from the “Pareto principle”, described by Jana and Tiwari [108] as a commonplace case where “80% of the outcomes are controlled or decided by 20% of the activities or factors. For example, 80% of the total profit is generated by 20% of the product categories, or 80% of the maintenance expenses are incurred by 20% of the machines.” Applying the Pareto principle, the last 20% of automation may require 80% of the total effort towards bringing full autonomy to an experiment. A common example is sample transfer between automated experimental modules, especially of solid materials or sample containers. For example, samples often need to be moved between synthesis and characterization equipment, such as the transfer of well plates between an Opentrons robot and a plate reader in Vaddi et al. [109].

In the low-cost automation literature, there are many examples which incorporate automated modules while leaving experimental step(s) as human-in-the-loop because of high opportunity cost, time constraints, and tasks where humans are naturally better than robots. Xie et al. [60] automate the synthesis of metal-organic frameworks using a RepRap 3D printer and Bayesian optimization (BO) but leave humans to transfer the sample from the robot to the X-ray diffraction (XRD) instrument. Since many of these complex characterization techniques are costly and designed for humans, the time and cost of building another robot to perform sample transfer exceed the benefits gained from automating every single task in the workflow for greater efficiency. Rodriguez et al. [110] is an excellent example of automating the most effective process steps such as synthesis (with an OpenTrons liquid handling robot), melting point determination, and electrochemical characterization for discovering new deep eutectic solvent electrolytes. Rodriguez et al. [110] did not automate the processes of sample transfer or handling of existing equipment such as a dehydrator and vacuum oven because of the great opportunity cost.

In a similar vein, most of the experimentation from Salley et al. [85], Cao et al. [111], and Lachowski et al. [112] is automated except for ??haracterization, viscosity analysis, and UV-Vis spectroscopy, respectively. Conversely, Chen et al. [113] develop a new low-cost system, RAMSAY-2, for automating the burdensome task of sample preparation for mass spectroscopy. It involves two robot arms which aliquot the solutions, incubate the samples with the reagents, deliver the samples to the ion source of the mass spectrometer, and initiate data acquisition [113]. This significantly accelerates the characterization workflow but is a nontrivial solution that requires lots of time and effort. It is important to consider the opportunity cost of automating tasks that are trivial for humans but challenging for robots due to the consequential researcher time spent. Automation is most profoundly effective when researchers are freed from performing tedious, time-consuming, and repetitive tasks. Another opportunity cost is the amount of money required to acquire automated instruments. For example, an automated differential scanning calorimetry (DSC) instrument can be purchased for USD ∼50 000. [114]. However, Rodriguez et al. [115] automate DSC with a low-cost system of USD 1080, which can run samples in 15 minutes, with up to 96 samples at a time [115].

4.2.4. Role of frugal twins

While the implementation cost of robotic solutions can currently be prohibitive, the exploration of low-cost sample transfer, especially of solid materials and across modules remains important and robotic solutions remain a warranted goal. To push the agenda with a future-looking vision, we need to put low-cost frugal twins in the hands of the community.

Rather than polarizing the community between fully autonomous vs. human-in-the-loop generalist setups, we believe it is wiser to meet in the middle where individuals can pair the tool to the task. This type of experimentation and exploration, enabled by low-cost frugal twins, can form a rich test bed in classroom settings. For example, students could be tasked with a design problem and divided into three groups: human in the loop, human-inspired robotic design, and hardware-centric design. Students can present their experiences, learn from other groups, and discuss trade-offs between each approach: how many experiments could be performed within the first day for each group? Within the first week? This can be replicated for different experiments to solidify best practices related to autonomous system design and cross-pollinate seemingly disparate design approaches.

4.3. State-of-the-art software

Seifrid et al. [3] present challenges of setting up a SDL, such as the need for algorithms that can handle constraints and unexpected outcomes, and difficulties surrounding software control and integration (stemming from instrument manufacturers generally not designing with SDLs in mind). Here, we highlight key places where SDLs can benefit by leveraging and integrating frugal twins with SOTA software in terms of batch and asynchronous optimization (Section 4.3.1), multi-fidelity optimization (Section 4.3.2), workflow orchestration (Section 4.3.3, and cloud experimentation (Section 4.3.4).

4.3.1. Batch and asynchronous optimization

Fundamental to optimizing efficiency in the lab is the parallelization of experiments, which reduces the time to obtain results and allows more efficient experimental design. Using lower-cost hardware, even with an initial potential for loss of accuracy, facilitates parallelization of SDLs. This democratizes access to cutting-edge research tools, such that geographically-distant labs can build clones of the same low-cost SDL. These SDLs can then network to execute high-throughput and parallel materials discovery campaigns. Caramelli et al. [58] demonstrate the advantages of low-cost parallelization of SDLs with their network of identical autonomous research systems (Figure 11). The systems can evaluate the variability across different instances of the robot with four different experimental tasks in a financially-reasonable manner: the hardware components of their SDLs are low-cost ($\leq$ 500 USD). Similarly to adding more cores to a CPU, adding more instances of an SDL (which need not be in the same location or even operating on the same step at a given point in time) increases throughput for an optimization campaign at the cost of additional hardware. However, it is important to acknowledge the trade-off between parallelization and the total number of trials in an optimization campaign. There is an adaptivity gap between the parallel and the sequential approach for optimization models. In the parallel approach, the model is required to make decisions in advance of having all of the information. If time is not a limiting factor and/or cost is a limiting factor, it is ideal to prioritize the sequential approach. Conversely, if time is a limiting factor and/or cost is not a limiting factor, it is more efficient to prioritize the parallel approach. For additional discussion, see "Tradeoff between parallelism and total number of trials".

While the batch optimization described earlier implies that all experiments within the batch need to be completed before moving onto the next one, the complementary topic of asynchronous optimization uses resources as soon as they become available. This is important when experimental runtimes can vary depending on the input parameters: thereby, equipment downtime is reduced. Whether using batch or asynchronous optimization, care must be taken so that redundant or low-value experiments are not suggested by considering *either* completed or in-progress experiments. Examples of methods that factor in-progress experiments into the optimization scheme include Monte Carlo-based joint acquisition optimization and models where predictions for in-progress experiments are sequentially added as "fantasy datapoints" before suggesting the next experiment in the batch (see Appendix F2 of Balandat et al. [116]).

4.3.2. Multi-fidelity optimization

Another use of building low-cost SDLs is to have them work in tandem with high-cost SDLs on the same discovery campaign through multi-fidelity optimization. Multi-fidelity optimization refers to leveraging multiple information sources with varying accuracy and cost. In chemistry and materials science, many optimization problems involve finding the best set of parameters or conditions that maximize a certain objective function, such as the yield of a reaction or the strength of a material. However, obtaining accurate predictions for these systems often requires robust, reproducible, and expensive experimental setups. In the case for SDLs, multi-fidelity optimization seeks to balance the trade-off between accuracy and cost by using multiple SDLs of varying levels of fidelity, where fidelity refers to the degree to which a SDL accurately represents the true system. One approach is to start with a low-fidelity, low-cost SDL, to explore the parameter space and identify promising regions, and then employ a higher-fidelity SDL which is typically higher in costs to refine the optimization in those regions. This can reduce the overall cost of the optimization while still achieving high accuracy in the final result. Multi-fidelity optimization can also involve the incorporation of different types of data, including both simulations and experiments or multiple types of experiments. For example, in materials science, a high-fidelity simulation may accurately predict the properties of a material, but may not capture all of the complexities of its real-world entity. By combining this simulation data with experimental data from various sources, such as XRD or Raman spectroscopy, a more accurate and complete picture of the material can be obtained. An analogous example in chemistry is combining low-fidelity, relatively inexpensive density functional theory simulations with high-fidelity, costly experimental data to accurately predict new materials and optimize material properties [117, 118].

4.3.3. Workflow orchestration

When experiments contain multiple steps, workflow orchestration software should ideally be used. While custom code can be written to manage

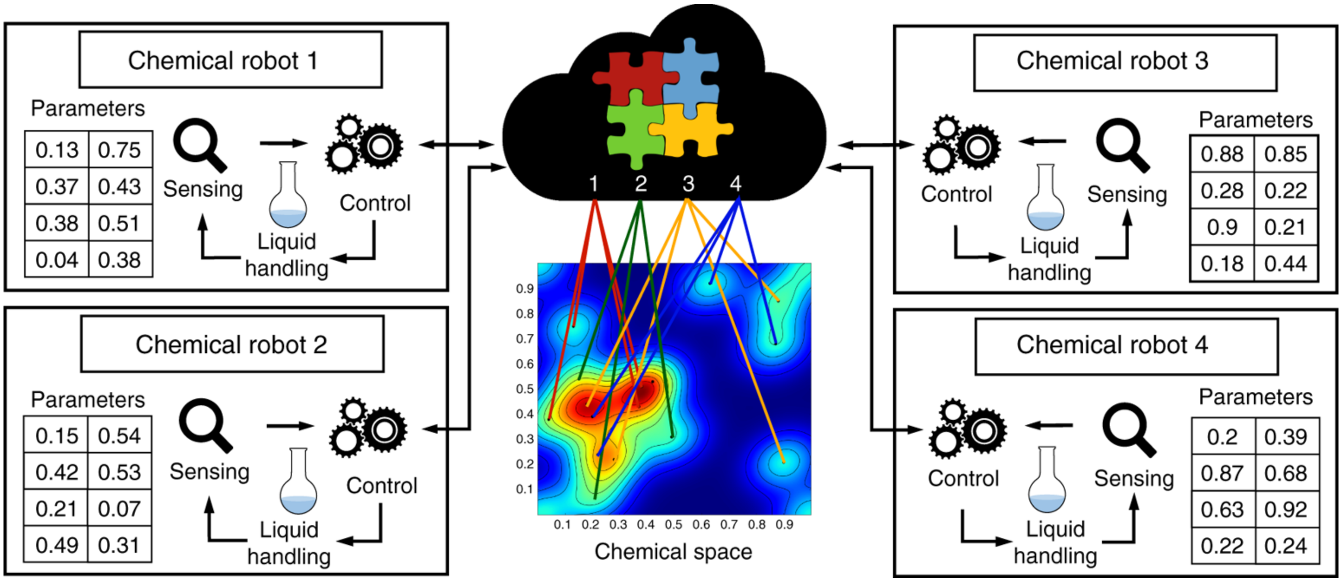


Figure 11: Illustration of a network of parallel chemical synthesis robots working towards a common optimization goal [58]. Reproduced from [58] with permission under the Creative Commons license (CC-BY). Copyright © 2018, Caramelli et al.

workflows, it is preferable to use existing packages that are fully-featured, modular (see software modularity in Section 4.1.2), and well-maintained to streamline orchestration efforts. Examples of workflow orchestration platforms include Covalent, BlueSky, alab-management, and HELAO. A curated list of workflow orchestration platforms applicable to SDLs is available in `https://github.com/AccelerationConsortium/awesome-self-driving-labs` under the "Workflow Orchestration" section.

4.3.4. Cloud experimentation

"Cloud experimentation" allows users to be geographically distant from experimental hardware, in analogy to cloud computing, where software programs can be executed remotely. One of the key benefits of removing geographic barriers is the decentralization of expertise [119]. For example, domain specialists, roboticists, and software developers can collaborate across continents on the same experiments.

Several examples of cloud-based SDLs exist, summarized in Table 3. Many commercial solutions focus on chemistry and biology applications such as the Emerald Cloud Lab and Lilly-Strateos cloud lab. On the other hand, solid-state materials science cloud laboratories are effectively non-existent except for some minor capabilities of biology- and chemistry-focused labs. While existing cloud labs have primarily targeted industry users, a noteworthy example beginning to target academic users is CMU Cloud Lab [120–125]. This is a partnership between Carnegie Mellon University (CMU) and Emerald Cloud Labs to build a subscription-based, 40 million-USD facility with over 200 types of scientific instruments. Unlike typical user research facilities, academic and industry users can conduct an end-to-end experimental workflow and acquire the results from anywhere around the world, 24/7, 365 days a year [120–125]. Typically, a research group needs to secure funding for the reagents, cost of the instrument, and upkeep costs to perform an experiment. Armer et al. [126] outline several systemic reasons for the lack of adoption of cloud-based science, such as the lack of cloud access to gain preliminary data for grant applications, the lack of cloud science grants in general, the lack of academic training, and the costs for a cloud lab subscription in addition to university facility expenses. To tackle some of these concerns, having an academic institution such as CMU build its own cloud labs will reduce some of the barriers of entry for academics to access SOTA scientific equipment [126].

In addition, CMU Cloud Lab promotes open science, a recent movement that aims to enhance the transparency, accessibility, inclusivity, and credibility of scientific knowledge [127], and in which problems and results can be shared easily.

Although CMU Cloud Lab aims to democratize and decentralize SOTA experimentation, it remains prohibitively expensive for educational settings and citizen science. A platform such as CMU Cloud Lab typically requires extensive capital and expertise to develop onboarding, security, access restriction, priority queuing, and workflow orchestration protocols. Likewise, it also typically relies on human-in-the-loop sample transfer between modules, necessitating full-time staff. This commercial infrastructure is not amenable for low-cost SDLs, which are typically not designed for commercialization. This means that low-cost SDLs will operate at a smaller scale, and the risks associated with data leakage and other malicious threats are lower. However, some free, open-source tools may be implemented into low-cost SDLs, such as Bluesky for workflow orchestration [128], secure, encrypted ?? style communication through platforms such as HiveMQ [72], and the Google Authentication API for security measures [128]. By leveraging the advantages of rapid, low-risk prototyping benefits of SDL frugal twins described in Section 2.2, we envision a low-cost SDL cloud lab that can act as a test bed for research-grade cloud experimentation ecosystems, but with dramatically lower operational costs. See Discussion #62 from Section 7.

5. Ethical benefits and risks

With any new technology, there are several ethical benefits and risks to consider, especially if low-cost SDLs can be put into the hands of many without regulation or guidelines, due to their low cost. In this section, we attempt to highlight why low-cost SDLs should overcome societal barriers to enable citizen science (Section 5.1), and address the concerns around democratizing this technology which is capable of discovering novel substances (Section 5.2).

5.1. Citizen science

Access to research facilities has historically been limited to universities, government, and industry laboratories, and their personnel. This limitation reduces access to non-professional, citizen scientists, many of whom could contribute greatly to the body of scientific understanding [135]. The lack of diversity, equity, and inclusion in science poses a hindrance to the advancement of citizen science. This challenge is especially pronounced for gender, racial, and ethnic minorities, as well as women and individuals from lower socio-economic backgrounds [136]. We hope that by making SDLs low-cost, accessible, and open source, it will be easier to build equity and inclusion into the educational system.

SDLs provide a great example of a research-based case study for citizen science, additive manufacturing or 3D printing since they are low-cost, easy to learn with the abundance of online resources, and adaptable to many different objectives. For example, Deneault et al. [17] developed an SDL known as AM ARES for optimizing the print parameters of several materials for additive manufacturing. It is a low-cost additive manufacturing SDL that uses a 300-USD commercial 3D printer with a custom syringe extruder, Raspberry Pi controllers and webcams, and software that will be released as open source (Figure 12). The authors use BO to guide the selection of 3D print parameters for latex caulk with silicone additives, attaining excellent extrusion properties after 100 iterations. In addition, AM ARES performed self-calibration for three different unknown source filaments, which resulted in better performance than default manufacturer specifications in an average of 15 experimental iterations. Although this system is robust, low-cost, and a stepping-stone for many to learn about SDLs, there is yet to be a widespread of adoption due to the lack of educational infrastructure such as open-source software, course materials, and a step-by-step build guide.

An extension of this project is the collaboration between the US Air Force Research Laboratory and Airship Consulting to create ATHENA, an affordable AM ARES system with open-source software (ARES OS 2.0) and off-the-shelf hardware. This initiative aims to make SDLs and autonomous ex-

Table 3: A summary of existing cloud experimentation solutions. For a continuing discussion, see Discussion #91 and Discussion #62.

Name or Group	Description	REF
RoboRXN	An AI-powered platform developed by Merck KGaA that accelerates chemical synthesis by predicting the outcomes of chemical reactions using ML algorithms	[129]
Emerald Cloud Lab	A cloud-based life sciences and chemistry experimentation platform	[130]
Strateos	A cloud-based life sciences and synthetic chemistry experimentation platform	[131]
Culture Biosciences	A cloud-based life sciences experimentation platform	[132]
Arctoris	A cloud-based life sciences experimentation platform	[133]
Kebotix	A cloud-based materials discovery platform	[134]
Cronin Group	An affordable, chemistry-capable robot with a standard set of hardware and software protocols that can be networked to coordinate multiple chemical experiments in real-time	[58]
AM ARES	A low-cost and accessible research robot that autonomously modulates print parameters using ml planners to optimize the materials discovery and development process for 3D printing	[17]
CLSLab	A series of low-cost teaching and prototyping demos that use a color-matching optimization task with light-, liquid-, and solid-based mixing of primary colors	[68]

perimentation systems widely accessible in grade schools, trade schools, and universities. ARES OS 2.0 is a platform-agnostic, web-facing software framework for autonomous experimentation/SDLs which takes much of the software development burden from the researcher. The goal is to provide a library of open-source modules for all to use and contribute back to the growing community, with the intent that "Anyone Can Download An Autonomous 'Research Robot'" [137]. ATHENA is an example of the movement towards low-cost Autonomous Experimentation Systems/SDLs to improve access to citizen scientists and especially under-served communities through open-source software and low-cost systems.

5.2. Risks

As with any technology, there are risks for people or organizations to engage in "actions that are harmful, illegal, or morally wrong" [138]. This is a polarizing topic. On one hand, there will always be some people with malicious intent; people will figure out a way. For example, the widespread adoption of low-cost 3D printers resulted in an increase in 3D-printed guns. Updated legislation regarding firearm manufacturing and use plays a key role in regulating this increase. However, incidents involving so-called "ghost guns" are typically Likewise, explosives can be created from commonly obtained materials, and safeguards have been put in place, such as limiting purchase amounts or requiring licenses, permits, and certifications. Naturally, regulations are also location-dependent.

Recently, concerns have been raised about the potential for large language models and autonomous platforms (e.g., SOTA cloud laboratories) to be used for nefarious purposes such as the synthesis of illicit drugs or chemical weapons Boiko et al. [119], Future of Life Institute [139], Bran et al. [140], Sohn [141], Falletti and Gallese [142]. One of the beauties of SDLs is that materials, therapeutics, and more can be autonomously discovered and created. However, it can be a double-edged sword where this technology creates dangerous substances whether it is by design or by accident.

We don't have *the* solution for safeguarding SDLs, but there are ways of making it harder for ill-intentioned people or organizations to engage in harmful behavior and making it easier for researchers to implement preventive strategies against the (accidental) synthesis of harmful substances. The key is to address this problem early, quickly and judiciously through governance, regulations, standards, education, awareness, and self-adherence to ethical use.

There are valuable open source practices that can be learned and adapted to low-cost SDLs because there are potential risks associated with open sourcing, such as open access to hazardous information or datasets and the potential misuse of research tools. To mitigate these risks, the cultural shift towards OS involves open methodology and open review, which helps regulate the dissemination of malicious code, data, or materials [143]. Open methodology and open review are tools that should also be adapted to the dissemination of low-cost SDLs. Furthermore, as low-cost creators SDLs, it is essential that we develop the tools and knowledge necessary to mitigate misuse risks, such as a failsafe device that will not endanger lives or property when SDL fails. For example, incorporating steps to assess the toxicity of autonomously generated substances can prevent the release of unknown toxic chemicals into the environment [144].

6. Future work

In this section, we describe ideas for new frugal twins (Section 6.1), suggested course content (Section 6.2, and classifying levels of autonomy (Section 6.3).

6.1. Ideas for new frugal twins

Fortunately, with the decrease in electronic component costs and the increase in additive manufacturing, many frugal twins can be realized for state-of-the-art SDLs. Although frugal twins are as necessary as Digital Twins for research and educational purposes, there are a scarce number of published examples of frugal twins to date. [58, 59, 69–71] We hypothesize that one of the main barriers to designing and building frugal twins is that researchers will prioritize working on the state-of-the-art counterparts rather than building a low-cost,

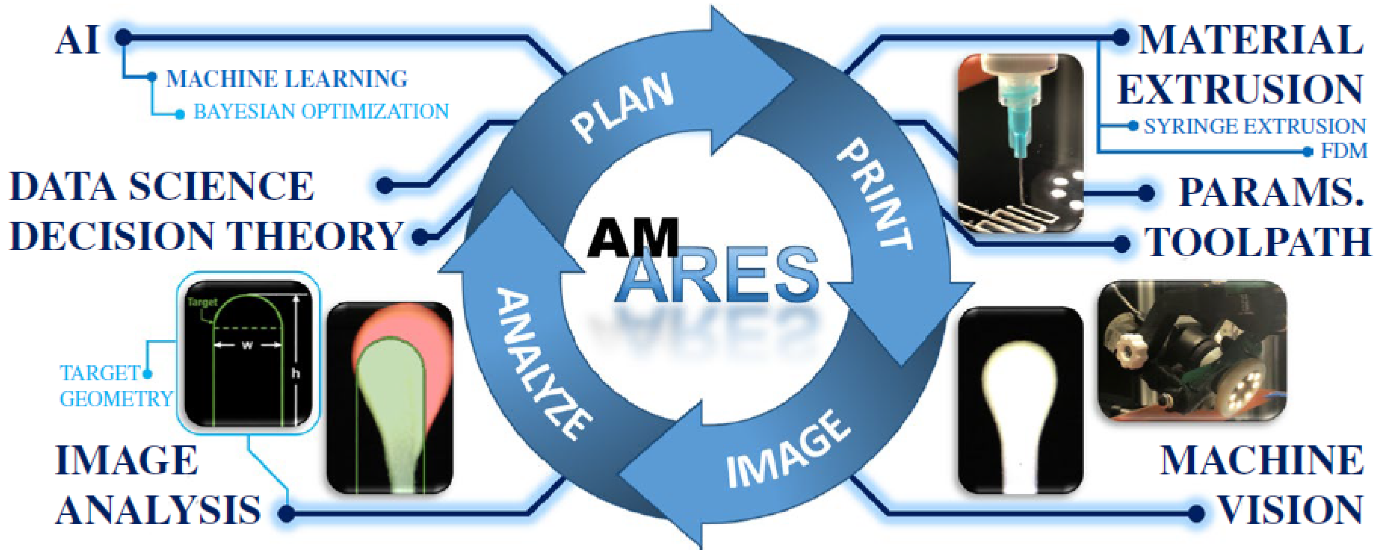


Figure 12

Figure 13: A simplified closed-loop workflow of the AM ARES platform. Reproduced from [17] with permission under the Creative Commons license (CC-BY). Copyright © 2021, This is a U.S. government work and not under copyright protection in the U.S.; foreign copyright protection may apply.

redundant version. For future work, we want to layout the blueprint for building the corresponding frugal twin of a state-of-the-art SDL to lower the barriers of entry to building the frugal twin.

As mentioned in Section 3.1.2 there are several examples of low-cost SDLs involving liquid handling; however, low-cost SDLs involving the transfer and processing of solid matter are practically non-existent. This largely stems from the relative ease of transferring liquids using e.g., diaphragm or peristaltic pumps and tubes compared with solids using e.g., powder feeders and robotic arms (see Discussion #92). For perspective, autonomous powder dispensers such as Trajan's CHRONECT cost significantly more (100k+ USD) than liquid handlers of similar resolution. While some issues with liquid transfer need to be considered such as viscosity, density, and surface tension, these are largely solved problems. With powder handling, variable particle sizes, consistencies, and electrostatic interactions make it difficult to robustly dispense powders of different types using the same type of equipment. One workaround to transferring solids is to dissolve or disperse them in liquids (e.g., slurries); however, this is not feasible for many materials science scenarios where suitable solvents are unavailable or unwanted chemical reactions may occur. To complicate matters further, matter phase changes and extreme processing conditions (temperatures and pressures) typically require substrates or sample holders.

To address the lack of solid-state materials science SDL demos, we propose a solid-based color-matching demo extension (Closed-loop Spectroscopy Lab: Solid-mixing (CLSLab:Solid)) that uses a low-cost mobile robot arm, mixtures of granulated colored wax powders (Figure 14), and a halogen lamp. Similar to moving from a light-mixing to a liquid-mixing demo (Section 3.1.2), the solid-mixing demo requires hardware and workflow changes. At the start of the experiment, a robotic arm will pick and place one tealight candle holder from a stacked array of holders in a storage array onto a motorized turntable. The turntable will then move the candle holder to a position beneath a funnel connected to red, yellow, and blue wax powder dispensers. The candle holder will then be positioned beneath a heat source (e.g., halogen lamp) to melt the wax, followed by color sensing using the same sensor as CLSLab:Light and CLSLab:Liquid. When the candle holder returns to its original position on the turntable, the robotic arm will pick it

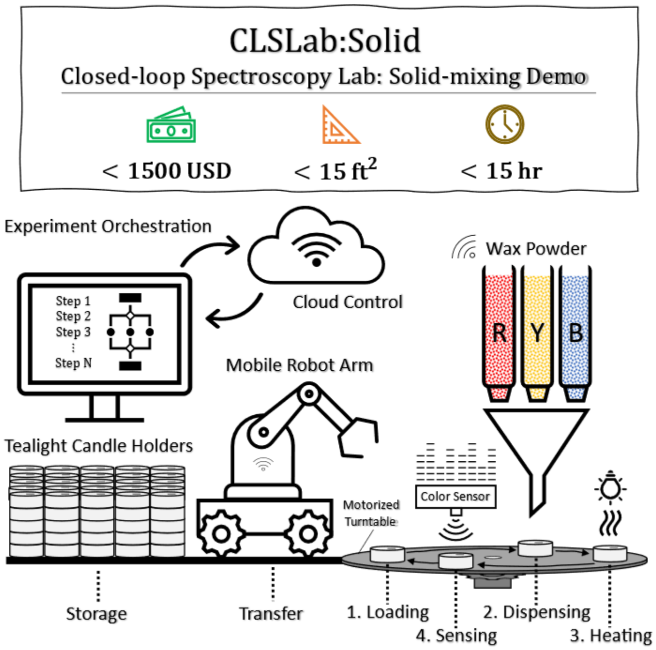


Figure 14: A summary schematic of the CLSLab:Solid demo [47].

up and place it into a separate storage/waste area.

Moving one step further is the idea of a "robot chocolatier." Chocolate captures key materials science principles such as liquid phase transformations, bulk materials characterization (as opposed to thin-film), and processing-structure-property relationships. This robot chocolatier (RoboChocolatier) will reuse many components from CLSLab:Solid and add a do-it-yourself tensile tester and a chocolate 3D printer. Both CLSLab:Solid and RoboChocolatier act as toy examples for the more industry-relevant materials discovery task of additively manufactured metal alloys for aerospace and automotive applications. Again, as a recurring theme, they can serve as proofs-of-concept that can be used during prototyping and the preparation of grant proposals (Section 2). For a continuing discussion of solid-state materials science SDL demos, see Discussion #153.

Other topics that the community may consider exploring in the context of SDL frugal twins include other types of inorganic synthesis, battery formulations, batch chemical synthesis, semiconductor fabrication, polymer synthesis, artificial organ compatibility, mobile and fixed robotic arms, microfluidic devices, and closed-loop microscopy.

6.2. Suggested course outcomes

Educators are wondering how to incorporate SDL concepts into existing and new curricula. To streamline efforts to democratize SDLs, it is important to define course structures and outcomes that can be tailored to meet the individual needs and disciplines of each student.

Abolhasani et al. [26] state:

> The workforce needed to effectively develop and maintain SDLs is inherently multidisciplinary and needs to include training spanning programming, automation, and core science disciplines. Educational opportunities and outreach efforts need to be developed to meet this workforce need including educational SDL kits from middle/high school to college.

Here, we present suggestions for possible educational outcomes for hands-on experience, learning best practices, and using algorithms (Table 4). Hands-on hardware and software development experience, brainstorming designs, and expertise with applying optimization algorithms are emphasized. We encourage the community to weigh in on and converge to a set of desired outcomes and skills necessary for successful SDL implementations. In future work, we plan to flesh out the details for creating a syllabus, course outline, and course content along with practical examples for teaching SDLs to students. Eventually, as the ecosystem matures, we envision higher education programs and degrees specific to SDL for chemistry and materials science.

6.3. Classifying levels of autonomy

In this work, we have focused on fully autonomous low-cost examples, but also pointed out a number of partially autonomous examples that are equally important in accelerating the discovery of new materials and teaching the next generation of data-driven scientists. However, there are no established standards to define the levels of autonomy for SDLs. To better categorize levels of automated chemical design, Goldman et al. [31] proposed a set of definitions in the context of ideation (finding non-obvious trends) and decision making, similar to what has been done for self-driving vehicles

Table 4: Suggested learning outcomes of a course covering SDL topics. For a continuing discussion, see Discussion #186.

Topic	Potential Learning Outcome
Experience	• Familiarize the concept of SDLs (hardware, algorithms, orchestration) • Acquire hands-on and software development experience by setting up a toy demo • Propose a design for a research-oriented SDL via a white paper
Best Practices	• Identify SDL best practices (e.g., modularity, reproducibility, safety, documentation) • Identify best practices for "cloud experimentation" (e.g., data transfer, storage) • Identify best practices for ML (e.g., validation, prevention of data leakage)
Algorithms	• Compare and contrast three forms of experiment planning algorithms • Test the complexity/efficiency trade-offs for advanced optimization • Identify methods for incorporating domain knowledge

[145, 146]. They define the highest level of autonomy (level 5) as systems where both ideation and decision-making are handled without human intervention over multiple iterations. Although its focus was primarily on artificial intelligence, in the case of SDLs, automation of synthesis, characterization, and sample transfer hardware and procedures are equally important aspects. The SDLs community will benefit from collectively determining a set of classifications or standards. One possibility is to classify autonomy levels on a per-category basis: *Synthesis*, *Characterization*, *Sample Transfer*, and *Experiment Planning*.

To make these categories conceptually and visually easy to understand, emoji can be used to represent whether a process is fully autonomous vs. one that requires manual intervention (Figure 15). This type of classification is utilized in `https://github.com/AccelerationConsortium/awesome-self-driving-labs` as of 2022-08-08. For a discussion centered on these representations, see `https://github.com/AccelerationConsortium/awesome-self-driving-labs/discussions/15`. Autonomy levels could also include failure rate/-tolerance, number of iterations without manual intervention, or use of physics-based simulations to supplement experiments.

7. A continuing discussion

While a review article represents a fixed snapshot, there is a benefit to allowing a continuing discussion of these important topics in a less rigid environment [147] that is amenable to the fast-paced evolution of SDLs. While this can also take on many forms such as social media (e.g., Twitter, LinkedIn) and informal communication (e.g., email, in-person), we provide a public, organized, and persistent set of public, ongoing discussions hosted on GitHub, as summarized in Table 5. Anyone can access up-to-date dialogue relevant to low-cost SDLs, and SDLs in general. GitHub accounts are free, and users may contribute to existing threads or open entirely new discussions. We hope that the content in this article spurs further dialogue in the community around democratizing SDLs, defining best practices, and gaining hands-on experience with advanced ML algorithms.

8. Conclusion

SDLs "frugal twins" can equip the next generation with necessary skills, provide a low-risk environment for prototyping and hands-on learning, and help to create a more equitable, global ecosystem through decentralized equipment, software, and expertise. SDL frugal twins are being used for both education and research, and there is a large room for improvement. Modularity for both hardware and software is an effective design principle for reducing re-design and maintenance costs, and care must be taken when considering human-inspired vs. hardware-centric vs. and human-in-the-loop design approaches. The true value of these

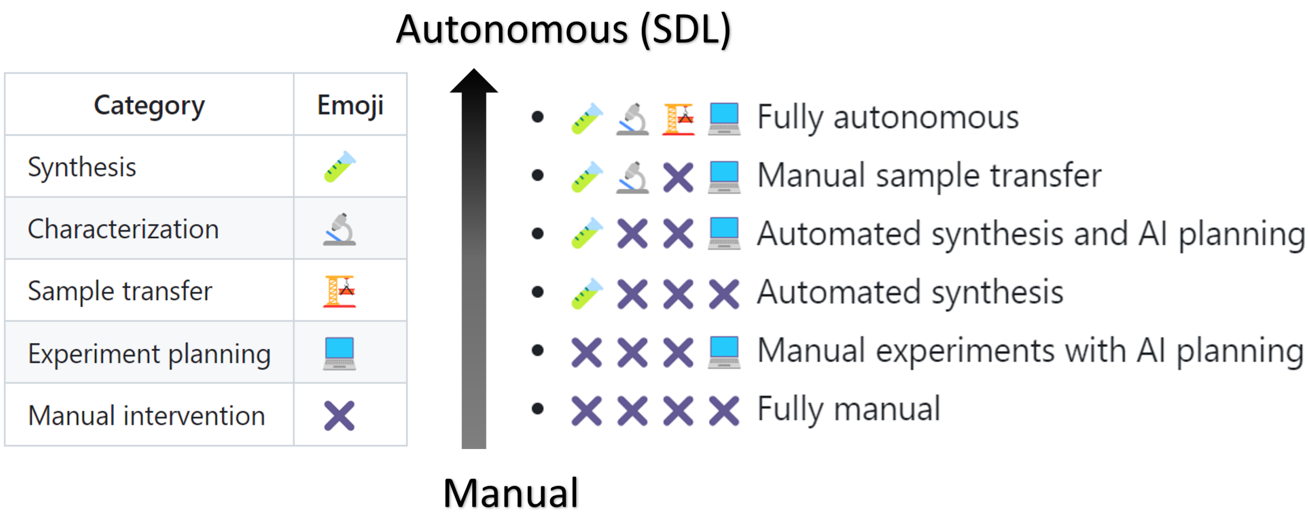


Figure 15: Classifying levels of autonomy in SDLs through multi-emoji classification. Emoji names and Unicode values are given. Synthesis ("test tube" - `U+1F9EA`). Characterization ("Microscope" - `U+1F52C`). Sample transfer ("Building Construction" - `U+1F3D7`). Experiment planning ("Personal Computer" - `U+1F4BB`). Manual intervention ("Heavy Multiplication X" - `U+2716`). Alternatively, these may be copy-pasted directly from https://github.com/AccelerationConsortium/awesome-self-driving-labs/blob/main/contributing.md.

Table 5: `self-driving-lab-demo` GitHub discussions and `awesome-self-driving-labs` GitHub discussions for various topics related to SDLs.

Topic	Repository	Link
All discussions	self-driving-lab-demo	All discussions
Data and access management	self-driving-lab-demo	Category
Demo extensions and design	self-driving-lab-demo	Category
Examples and tutorials	self-driving-lab-demo	Category
Scaling up SDLs	self-driving-lab-demo	Category
Packaging open-source hardware as commercial kits	self-driving-lab-demo	Discussion #124
Experimental orchestration software	self-driving-lab-demo	Discussion #64
Educational outcomes and homework problems	self-driving-lab-demo	Discussion #186
Solid-state materials science demo	self-driving-lab-demo	Discussion #153
Low-cost powder handling	self-driving-lab-demo	Discussion #153
Roadmap for demo extensions	self-driving-lab-demo	Discussion #77
A network of cloud-based experiments	self-driving-lab-demo	Discussion #62
Classifying level of autonomy	self-driving-lab-demo	Discussion #15
What is a self-driving lab?	awesome-self-driving-labs	Discussion #32

low-cost systems can be realized as state-of-the-art software implementations such as batch and multi-fidelity optimization, workflow orchestration, and cloud experimentation are combined with SDL frugal twins across the spectrum. With the right ethical and responsible use of this technology, frugal twins are poised to accelerate the discovery of society-benefiting materials within the SDL community.

Glossary

AM ARES Additive Manufacturing Autonomous Research System 22, 23, 25

BO Bayesian optimization 18, 22

CLSLab:Light Closed-loop Spectroscopy Lab: Light-mixing 10, 11, 25

CLSLab:Liquid Closed-loop Spectroscopy Lab: Liquid-mixing 10, 11, 25

CLSLab:Solid Closed-loop Spectroscopy Lab: Solid-mixing 25, 26

CMU Carnegie Mellon University 21

DSC differential scanning calorimetry 19

HPLC-MS high-performance liquid chromatography coupled with mass spectrometry 3, 7

MAP materials acceleration platform 2, 3

MASS materials acceleration for societal solutions 2, 3

ML machine learning 8, 14, 23, 27

NMR nuclear magnetic resonance spectroscopy 3

POM polyoxometalate 13, 14

SDL self-driving laboratory 1–3, 6–8, 10, 13–16, 18–22, 24–30

SOTA state-of-the-art 2, 3, 7, 8, 15, 19, 21, 22, 24

XRD X-ray diffraction 18, 20

Conflicts of Interest

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CRediT Statement

CRediT statement to be generated via Google Form results processed by credit-statement.nb immediately prior to submission to preprint server.

Data Availability

There is no raw data associated with this study. More information and resources can be found at `https://github.com/sparks-baird/self-driving-lab-demo/discussions` and `https://github.com/AccelerationConsortium/awesome-self-driving-labs`.

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