Title: Autonomous Experimentation Systems for Materials Development: A Community Perspective

Authors:
Eric Stach,[1,2] Brian DeCost,[3] A. Gilad Kusne,[3] Jason Hattrick-Simpers,[3] Keith A. Brown,[4] Kristofer G. Reyes,[5] Joshua Schrier,[6] Simon Billinge,[7,8] Tonio Buonassisi,[9] Ian Foster,[10,11,12] Carla P. Gomes,[13] John M. Gregoire,[14] Apurva Mehta,[15] Joseph Montoya,[16] Elsa Olivetti,[17] Chiwoo Park,[18] Eli Rotenberg,[19] Semion K. Saikin,[20] Sylvia Smullin,[21] Valentin Stanev,[22]
Benji Maruyama[23]*

1. Department of Materials Science and Engineering, University of Pennsylvania, Philadelphia, PA 19104, USA
2. Laboratory for Research on the Structure of Matter, University of Pennsylvania, Philadelphia, PA 19104, USA
3. National Institute of Standards and Technology, Gaithersburg, MD 20899, USA
4. Department of Mechanical Engineering, Boston University, Boston, MA 02215, USA
5. Department of Materials Design and Innovation, University of Buffalo, Buffalo, NY 14260, USA
6. Department of Chemistry, Fordham University, The Bronx, NY 10458, USA
7. Department of Applied Physics and Applied Mathematics, Columbia University, New York, NY 10027, USA
8. Condensed Matter Physics and Materials Science Department, Brookhaven National Laboratory, Upton, NY 11973, USA
9. Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA
10. Joint Center for Energy Storage Research (JCESR), Argonne National Laboratory, Lemont, IL 60439, USA
11. Data Science and Learning Division, Argonne National Laboratory, Lemont, IL 60439, USA
12. Department of Computer Science, University of Chicago, Chicago, IL 60637, USA
13. Department of Computer Science, Cornell University, Ithaca, NY 14850, USA
14. Joint Center for Artificial Photosynthesis, California Institute of Technology, Pasadena, CA 91125, USA
15. Stanford Synchrotron Radiation Lightsource, SLAC National Accelerator Laboratory, Menlo Park, CA 94025, USA
16. Toyota Research Institute, Los Altos, CA 94022, USA
17. Department of Materials Science and Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA
18. Department of Industrial and Manufacturing Engineering, Florida State University, Tallahassee, FL 32306, United States
19. Advanced Light Source, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA
20. Kebotix, Inc., Cambridge, MA 02139, USA
21. X, The Moonshot Factory, Mountain View, CA 94043 USA
22. Department of Materials Science and Engineering, University of Maryland, College Park, MD 20742, USA

23. *Air Force Research Laboratory, Materials and Manufacturing Directorate, Air Force Research Laboratory, Wright–Patterson Air Force Base, OH 45433, USA*
* Corresponding Author: benji.maruyama@us.af.mil

Progress and Potential

As human researchers, we are trained to reduce the number of variables to make experiments manageable. This limits the depth and kinds of phenomena we can study. High-dimensional iterative search empowers us to investigate richer, more complex materials phenomena.

Importantly we envisage network effects for the globally integrated autonomous experimentation systems, where beyond the tipping point, the size and degree of interconnectedness greatly multiply the impact of each research robot's contribution to the network.

However, to truly exploit the potential of autonomous research, we must build substantial programmatic investments to develop a workforce comfortable working with artificial intelligence.

Summary

Solutions to many of the world's problems depend upon materials research and development. However, advanced materials can take decades to discover and decades more to fully deploy. Humans and robots have begun to partner to advance science and technology orders-of-magnitude faster than humans do today through the development and exploitation of closed-loop, autonomous experimentation systems. This review discusses the specific challenges and opportunities related to materials discovery and development that will emerge from this new paradigm. Our perspective incorporates input from stakeholders in academia, industry, government laboratories, and funding agencies. We outline the current status, barriers, and needed investments, culminating with a vision for the path forward. We intend the article to spark interest in this emerging research area and to motivate potential practitioners by illustrating early successes. We also aspire to encourage a creative reimagining of the next generation of materials science infrastructure. To this end, we frame future investments in materials science and technology, hardware and software infrastructure, artificial intelligence and autonomy methods, and critical workforce development for autonomous research.

Keywords: autonomy, artificial intelligence, machine learning, algorithmic development, research methods, human–machine teaming, workforce development, materials discovery, carbon nanotubes, additive manufacturing

1. INTRODUCTION

Materials science and technology are at the core of society, and the development of new materials defines our history. Indeed, specific materials technologies give appellation to the Stone, Bronze, and Iron Ages, to the Industrial Revolution (steel), and to our modern Information Age (silicon).[1] Future advances in quantum computation[2] and synthetic biology[3] will similarly arise from advancements in materials research. However, while the pace of technological advancement is ever increasing, the rate of materials development remains slow, with decades typically needed to transition a new material from discovery to commercial use.[4, 5] This slow development directly impedes humanity's ability to solve existential problems such as climate change, and to generate new technologies that fuel economic growth.[6] Indeed, the futurist Hiroaki Kitano has said, "Scientific discovery is at pre-industry revolution level."[7] The importance of artificial intelligence (AI) in augmenting research and autonomous experimentation (AE) is becoming recognized as a solution to these needs. Former US Secretary of Defense M. Esper recently remarked, "…AI is advancing automated chemistry… These advances free up time for our scientists and researchers to focus on next-generation innovation, rather than countless tests and experiments."[8]

Materials AE uses advanced decision algorithms to plan and execute a series of materials experiments iteratively towards human-directed research outcomes.[6, 9-19] More precisely, an iterative research loop of *planning*, *experiment*, and *analysis* is carried out autonomously (see Figure 1). Once human researchers have provided the necessary information (e.g., campaign objectives; constraints; relevant data from previous experiments, and in general, prior knowledge), the AE campaign is initialized, and the AE system *plans* the first group of experiments. These *experiments*—which are broadly defined to encompass physical tests, modeling/simulation, or data mining—are conducted via automation without human intervention to generate experimental outputs from supplied inputs. Next, the results are *analyzed* automatically and incorporated into an updated understanding of the series of experiments in the framework of a knowledge representation.[20] Finally, a decision algorithm employing AI once again *plans* the next experiment phase and generates a new set of experimental inputs by considering the research campaign objectives and the value of a particular next experiment towards furthering the objective. The system autonomously advances through the iterations of planning, experiment, and analysis. Iterations continue until the campaign objective is achieved or other exit criteria are met, concluding the AE campaign. The hundreds or perhaps thousands of iterations that may comprise an experimental campaign form the powerful core of AE systems.

As many of the terms have multiple interpretations, note that we will use *automation* to refer to a system that can execute experimental actions without human intervention. An example is using robotics to mix chemicals and measure results. In contrast, *autonomy* is distinguished by the independence of action, integration of delegated decision-making, and complexity of operations. The AE (*autonomous* experimentation) system described above uses automation to execute experiments, and it critically has the additional capability to incorporate new knowledge derived from these experiments and to reason over and make decisions on subsequent iterations. AE systems can incorporate new knowledge and design appropriate experiments towards the

research objective using AI and machine learning (ML). While AI and ML are often used interchangeably, we will use the broader term AI to emphasize algorithms used for decision-making in experiments; ML will refer to a subset of methods that include interpolation, classification, and statistical inference.

Previous efforts to speed research include high-throughput and combinatorial (HT/Combi) approaches,[21] integrated computational materials engineering (ICME),[22] and the use of AI and ML methods to mine existing databases to identify potential compounds and processes.[23-26] While these efforts are powerful for exploring materials parameter spaces and producing and analyzing large amounts of data, they have low iteration rates (related to the "Analysis Bottleneck"[27]), where interpreting results and planning further iterations are the rate-limiting factor. In contrast, AE systems can execute tens or hundreds of iterations without human intervention, making exceptional speed and high fidelity in research results possible. Indeed, the value proposition of AE lies in the advantages of the autonomous iterative loop; when properly designed, the loop can advance research progress much faster than current methods, make better use of human researcher time and effort, allow for novel unanticipated findings, and enable a better understanding of a system—all while expending fewer resources. Highly autonomous systems also facilitate experiments to be performed remotely,[28] making AE highly accessible to the broad community.

The intent of this review is to inform the broad materials community about the current status and future directions of materials AE from researchers active in the area. After presenting some concepts to help the general readership appreciate AE campaigns, we will briefly look at previous attempts to speed research. We will then illustrate the state of the art of AE systems for materials using select examples, describe how AI technologies are being applied to materials AE, and consider the impact of AE on materials research. Lastly, we will set out a future vision for how to expand and exploit AE.

2. MORE ABOUT AUTONOMOUS EXPERIMENTATION

For those less familiar with autonomy research, we will explain additional concepts to complement the AE campaign described in the Introduction and Figure 1; further background theory can be found in the literature.[11, 19, 25, 29] We will also look at how AE can enhance the efforts of human researchers.

2.1 Campaign Objective

The campaign objective is the goal of the iterative search process, which comprises a series of experiments termed an experimental campaign. The campaign objective is designed by human researchers in the first step of developing an AE system. In its most basic form, the objective can be the optimization of a property,[30] testing a hypothesis,[31] or the prediction of a result (e.g., in an early campaign, an AE system was tasked with closely predicting the growth rate of carbon nanotubes using prior experiments).[10]

2.2 Analysis and Understanding (Knowledge Representation)

In our AE schema, the initial results and raw data from experiments are analyzed, or processed into information that can be exploited for decision-making. This could be, for example, translating force–displacement data to a material stiffness. During analysis, AI and other statistical methods may be used to identify trends or anomalies in data, categorize regions where experiments are prone to fail, detect fundamentally different system responses, or build beliefs into hyperparameters for models. The results of the analyses are captured into a knowledge representation, which is a machine-interpretable model of the information gained from past experiments, including the mapping from inputs to outputs.[20, 32] As the campaign advances, the internal knowledge representation, capturing understanding of the system under study, evolves to include newly observed data. The term "knowledge representation" is used for both the model of understanding and for how new data is captured by the model. The difference between the experimental results and the expected results based on the knowledge-representation model of the previous loop can be thought of as a feedback signal, and it can be used as the basis for training subsequent models.[29, 33]

2.3 Design of the Planning Algorithms

The design of the planning algorithms requires careful consideration of the design policy, which is directly related to the field of optimal experimental design.[29, 34, 35] Throughout the execution of a campaign, the task of achieving the research objective (such as minimizing a response) is often in tension with resolving the uncertainties inherent in the AE system's knowledge representation. This tension, also known as the exploration–exploitation dilemma in the AI community,[25, 36-39] fundamentally arises from the limited and uncertain knowledge the autonomous system has about the physical system under study. The system may choose to perform experiments that are more tailored to reducing overall uncertainties and to searching for new minima (exploration), or it may choose to perform experiments near minima predicted based on current knowledge, uncertainties in that knowledge not withstanding (exploitation). A balance between these two modes, in which the response function is learned globally prior to optimization, is often more efficient than the decoupled alternative.[30]

For an AE system to be autonomous, the planning algorithms should be able to function at a certain depth of intelligence; while a simple home thermostat can act on its own, its degree of intelligence is limited. Profound AI for AE can include logical reasoning, independent hypothesis generation and testing, understanding by analogy, the ability to extrapolate concepts, and the ability to design experiments to discern complex relationships efficiently and effectively, among myriad possible outcomes. Because of this versatility, decision authority can be delegated to the AI planner, making the iterative research loop possible. Additionally, the planning and analysis algorithms should be able to integrate contextual information and experimental uncertainties, e.g., intrinsic variability in the materials phenomena themselves, noise from the feedback characterization tools, or the influence of exogenous parameters we do not control/measure.

2.4 Human–Machine Teaming and Deciding on the Decision-Maker

Prior to designing an AE campaign, it is worth considering if AE is the best route for a particular research campaign and how human researchers and the system's algorithms will cooperate, also known as human–machine teaming. Among the many aspects of human–machine teaming, the division of labor is one that should be determined early. By considering the differing strengths and abilities of human and robot researchers, automation and AE can be used to enhance human efforts. Robots excel at performing repetitive work with precision, so manual labor can be done by research robots (automation) more quickly, reproducibly, and cost-effectively. Research robots can also analyze data in high-dimensional parameter space in ways that are beyond the capabilities of human researchers; they can make decisions that are more disciplined, and potentially more effective, towards a set of research goals and without human confirmation bias.[40] Meanwhile, human researchers provide insight, intuition, creativity, and a deep understanding of the context and overall goals of the research project, all of which are abilities that cannot be completely replaced by AI.

These factors are also relevant in determining if decision authority can be delegated to planning algorithms or remain with human researchers. Cognitive labor is better and more easily done by machine, when decisions require: (i) a faster pace than that of human cognitive and/or manual ability; (ii) holistic and detailed understanding of every preceding experiment; and (iii) interpolation/extrapolation in multi-dimensional spaces, with requisite tracking uncertainties, variances, and covariances; and lastly, (iv) when decisions are easy but numerous, and tedious such that they will tire or bore a human, potentially leading to errors. In such cases, a fully autonomous route is suitable.

In contrast, decision authority is best left to human researchers when (i) new insights or inferences beyond the supplied physical rules are required to understand a phenomenon, (ii) difficult-to-define objective functions are involved, and (iii) information beyond the context of what has been supplied to the AE system becomes relevant. When there are clear issues of safety and/or ethics involved in the next experiment, humans should oversee AI experiments to ensure relevant safety and ethical practices are observed, e.g., that dangerous reactions are avoided. This is an active area of study for autonomous systems in general,[41, 42] much of which is appropriate to materials AE systems.

Another aspect of human–machine teaming relevant to the design of AE campaigns is the collaborative interaction between the AE system and the human researcher.[43] As with any collaboration, good communication and trust are necessary for success, and all parties should be able to understand and use the results. Trust in the context of autonomous systems is an active area of study[44] and is broadly characterized by predictable behavior and the expectation of two-way communication of well-defined and achievable objectives.

3. FOUNDATIONS OF AUTONOMOUS RESEARCH AND THEIR CONTRIBUTIONS TO AE

The development of AE builds upon prior investments in technologies created to accelerate the research process, and AE integrates them in new ways. These technologies include: (i) HT/Combi experimentation as a method to increase the rate at which new experiments are

performed; (ii) modeling and simulation as a substitute for slow and costly experiments; and (iii) data science methods to extract information from simulation and experimental data. The groundwork for these developments was laid in part by the Materials Genome Initiative (MGI),[4, 45, 46] as well as by similar initiatives worldwide.[47, 48] We will briefly review the state of each of these technology areas to clarify their contribution to AE.

3.1 From HT/Combi Experimentation to AE

Traditional HT/Combi experiments expedite materials science discovery by parallelizing materials synthesis, processing, and characterization.[49] A typical HT/Combi experiment starts with the automated synthesis of a set of 10^1–10^2 samples, in which some combination of composition, microstructure, and processing have been systematically varied to cover the entire parameter space of interest. This library of samples is then screened either in parallel or serially using a set of automated measurement tools. HT/Combi experimental campaigns are typically limited to one or a few iterations of libraries. Some representative recent examples[50, 51] of this for materials are reviewed by Green et al.[49]

Historically, HT experimentation (HTE) hardware development has focused on increasing the number of experimental results per unit time and decreasing the cost per experiment. This makes sense in a *non*-autonomous ("open-loop") scenario, where the goal is either to obtain the composition–processing–structure–property linkages by an exhaustive experimental search or to generate a sufficiently large dataset that can be used *post hoc* to determine these linkages and provide information on regions of optimal performance for subsequent study. The shift towards autonomous approaches may eliminate the need for many experiments and instead favor faster turnaround for smaller batches of targeted experiments, as new results can be incorporated into the experiment planning. In a non-iterative ("open loop") system, AI can be used to intelligently guide an automated characterization tool to subsample a pre-deposited compositional spread library, realizing a 2× to 10× decrease in the number of samples required to extract information from the system.[49] Some relevant examples of the trend towards lower-throughput, low-latency, small-batch laboratory automation include 3D-printed carousels for performing iterative syntheses of gold nanoparticles to obtain a desired spectrum,[16] dexterous, free-roaming robot chemists that synthesize and characterize small batches of photocatalysts,[52] one-at-a-time synthesis and optoelectronic characterization of perovskite thin films,[14] and the iterative synthesis of perovskite nanocrystals.[53] Microfluidic flow chemistry targeting nanocrystalline materials are especially amenable to this type of approach, as the products can be observed in iteratively changed conditions.[54-56] While AE has certainly built upon the techniques used in traditional combinatorial experiments, AE campaigns can be designed to adapt the experimental sampling as needed; replicates can be made where uncertainties are high, while redundant information can be minimized.

3.2 From Modeling and Simulation to AE

Physics-based modeling is a mature field, and it is now widely accepted that simulations can identify possible materials of interest.[57] This is exemplified in national efforts, such as the MGI,[4, 45, 46] as well as by large-scale computational materials database/repositories,[58] such as the

Materials Project,[46] AflowLib,[59] Open Quantum Materials Database,[60] the Harvard Clean Energy Project (for solar materials),[61] and the NOMAD repository.[62] Rich toolsets have been developed for facilitating large-scale computation and data archiving, such as ChemML[63] and Atomate.[64] Whereas past efforts have focused on making predictions that are subsequently tested in the laboratory, autonomy enables the incorporation of this information into the ongoing experimental process. That is, simulations are used to select better experiments, and simultaneously incoming experimental data are used to select more informative simulations, in a closed-loop process. A notable recent example of this idea is in the use of density functional theory (DFT) alloy thermodynamics as a probabilistic constraint in the (experimental) Bayesian optimization (BO) of perovskite alloys for structure and stability.[65] More examples of these techniques in the context of AE campaigns will be presented in *Current and Related AI Technologies for Materials AE*.

3.3 From Data Science Methodologies to AE

The use of ML and AI methods for materials applications is now well established and is the topic of recent reviews.[24, 40, 66-70] Their use in accelerating tasks in materials research can be broadly classified as learning to "see" (e.g., spectral interpretation), learning to "estimate" (e.g., surrogate models for predicting outcomes), and learning to "search" (e.g., optimization).[71] Many ML predictions of new materials and properties have been confirmed experimentally.[72, 73] In addition to the use of these methods on simulation and experimental data, they have been used to process other sources of information, such as the natural language text descriptions of synthesis conditions and properties in published papers[65] and structured data showing the relationships between known materials.[74] In addition to mere prediction, ML approaches can play a role in facilitating human understanding. Relevant examples include the use of machine-learned natural language models to provide automated summarization of material properties,[75] collaborative human–algorithm optimization approaches,[43] and explainable AI (XAI) methods.[76, 77] ML and AI methods provide a necessary foundation for the planning and analysis algorithms of AE systems.

4. STATE OF THE ART THROUGH A SELECTION OF AE EXAMPLES

AE for materials is a quickly developing field with new systems coming online with increasing frequency. In order to separate the abstract capabilities of the continually evolving robotic systems from the discrete achievements, we will view this progress through the lens of a selection of completed AE research campaigns (see Table 1). One overarching theme to note is that reports of fully autonomous systems are often closely preceded by related advances in hardware automation, in ML-driven experimental planning, or in both, but without full autonomy. These related non-autonomous advances along with certain efforts towards AE will also be included to better illustrate the current state of materials AE development.

4.1 The First Reported AE System for Materials Development, ARES

Soon after realizing an automated system to map reaction conditions for carbon nanotube (CNT) growth,[78] Nikolaev et al. reported the first AE system for materials development (see Table 1, Study A).[10] Using *in-situ* Raman spectroscopy to monitor CNT growth,[79] their Autonomous

Research System, ARES, was able to learn to grow CNTs at controlled rates over a six-dimensional processing parameter space, ultimately delivering an improved understanding of CNT growth phenomena. The complete iterative research loop of its AE campaign is illustrated in Figure 2. After approximately 600 autonomous iterations, ARES was able to supply the input growth conditions that achieved the targeted growth rate. Starting from no prior knowledge of nanotube growth physics, ARES taught itself to grow CNTs at controlled rates via iterative sampling of a complex six-dimensional parameter space that was much too large to sample using grid-based[80] or open-loop DOE (design of experiments)[81] methods. As a straw-man, a full factorial span of 6 parameters with only 10 conditions per parameter yields 60,466,176 experiments. Not only is this orders-of-magnitude more experiments, but the sampling fidelity is much coarser than the iterative approach of ARES. Designs of further campaigns using ARES are underway; the more recent inclusion of scanning probe lithography to introduce compositional variations for screening CNT catalysts[82] highlights one path of future development.

4.2 AE for Solution Chemistry

One of the main focal points for the development of automation has been platforms for studying solution-phase chemistry in a broad sense. For instance, Bédard et al. developed a plug-and-play continuous-flow AE system for performing synthesis and analysis in an automated fashion (Table 1, study B);[83] user-specified reactions were automatically optimized through the exploration of three discrete reactions using a black-box optimization tool known as SNOBFIT.[84] Building on this platform, Coley et al.[85] integrated both a robotic system to dynamically reconfigure the flow chemistry platform and a pipeline to search the literature and predict synthetic pathways. This highly versatile system was used to discover the optimal synthetic pathways for six sample drug substances; however, the process did not comprise experimental feedback nor optimization of reaction conditions due to the complexity inherent to multi-step reaction chemistry.

An alternate approach to general chemistry has recently been shown by Burger et al., wherein a mobile robot can move around a room to access a variety of distinct stand-alone, commercial instruments, reducing the need for instrument customization. This AE system was used to optimize the hydrogen evolution reaction (Table 1, study G).[52]

4.3 AE for Emulsions: Algorithmic versus Random Sampling

Following the initial demonstrations of AE systems, an important trend started in the literature with systems explicitly testing the acceleration inherent to the confluence of automation and algorithmic planning. Specifically, DropFactory was constructed as an automated system to dispense reagents to form oil-in-water droplets, which exhibit a wide range of behaviors from locomotion to self-dividing.[86] Incorporating it into an AE campaign, Grizou et al. explored the behavioral range resulting from a four-dimensional parameter space (Table 1, study C). One important contribution from this work was the comparison of experimental campaigns run by random sampling versus those in which each subsequent experiment was chosen algorithmically. When given a budget of 1000 experiments, the algorithmically driven system explored 73% of

the parameter space while random sampling only explored 22%. Perhaps more importantly, the algorithmic sampling achieved the same performance in 128 experiments as the random sampling achieved in 1000.

4.4 AE for Additive Manufacturing: Bayesian Optimization versus Grid-Based Exploration

Building on the trend of introducing new categories of experiments in an autonomous context while benchmarking against traditional techniques, Gongora et al.[30] developed BEAR, a robotic manufacturing and testing system to autonomously optimize the toughness of additively manufactured components (BEAR = Bayesian Experimental Autonomous Researcher; see Figure 3 and Table 1, Study D). As part of the initial demonstration to study components defined by four geometric parameters, the authors included an explicit comparison between experimental campaigns guided by BO and those guided by grid-based exploration, revealing the time- and cost-efficiency of AE. What the grid-based system achieved in about a month, the Bayesian system accomplished in just 12 h; after 24 h, the Bayesian method produced a higher toughness performance than that achieved by the month-long grid-based search. They have now extended their work to include finite-element modeling of the physical response, successfully increasing the toughness by another 30% (see Figure 3, Conclude panel).[87]

4.5 AE for Thin Films

There has been a sustained effort by multiple research groups to develop AE to synthesize and study functional thin films for energy applications. Once again, examples in automation and HTE came first. In 2019, Sun et al. developed a HT process that allowed the synthesis and characterization of 75 unique compositions of perovskite-inspired inorganic films over a span of two months.[88] Following these results, Langner et al. developed a robotic system to synthesize polymer blends for organic photovoltaics and to study degradation in a totally automated fashion, at ~300 samples per day. The resulting large dataset in a four-dimensional parameter space of compositional blends was used to simulate autonomous campaigns, which suggested that a self-driving laboratory could achieve equivalent performance in this space with 32 times fewer experiments.[89] A fully autonomous realization of functional films was published shortly thereafter by MacLeod et al., in which they reported a robotic system moving between synthesis, processing, and multiple characterization stations (Table 1, Study E). By guiding this system with BO through two 35-sample experimental campaigns, they optimized the hole mobility of an organic semiconductor film. Significantly, they also identified a region that exhibits a previously unknown local maximum in mobility.[14]

4.6 AE for Quantum Dots

In addition to films, quantum dots (QDs) have been the subject of advances in both automation and, recently, autonomy. As far back as 2010, HT synthesis had been applied to map the synthetic parameter space corresponding to QDs.[90] Efforts to screen QDs continue with recent reports on metal–halide QDs.[91] Recently, the concept of automated QD synthesis was combined with a ML-guided experimental planner to realize an artificial chemist for optimizing QD synthesis (Table 1, Study F).[55] This system utilized flow reactors to study a variety of decision-

making policies in a BO framework. Further, the study showed that learning can be accelerated by at least two-fold when the knowledge of one set of precursors was transferred to a different set of precursors.

4.7 Developments in Characterization and Analytical Methods in Efforts towards AE

In some cases, efforts towards autonomy in the study of complex properties involve innovative approaches to assess properties. Kirman et al. employed optical observation of crystallization to identify novel perovskites.[92] HT experiments were made possible by using instrumentation developed for protein crystallography studies. ML was applied to both optically analyze samples to evaluate crystallization and to build a predictive model of whether samples would crystallize. Independently, Li et al. also combined robotic synthesis with ML-based experimental selection for perovskite synthetic studies.[93] While their analysis involved a number of manual steps including visual inspection, their experimental selection leveraged a previously developed experimental planner termed ESCALATE (Experiment Specification, Capture And Laboratory Automation Technology).[94]

Efforts towards materials AE need not originate from a synthetic viewpoint; the active guidance of analytical systems can itself accelerate the characterization process. For instance, Noack et al. demonstrated how a kriging-based approach could accelerate X-ray scattering experiments by selecting the parameters of subsequent experiments.[95] This approach was experimentally validated through a set of campaigns, each with 600 experiments, on a sample composed of nanoparticles; a reduction in error was observed when the system was guided by active learning (AL), where the ML model's uncertainty and expected value are used to select new data points. This study highlights a challenge inherent to benchmarking experimental-learning-based studies; comparisons can only be made to previously reported experiments. More recently, real-time control over X-ray measurements was combined with synthetic capabilities by Rakita et al. to dynamically adjust the redox state of compounds in solution.[96] While this approach only featured a single dimension of control (the presence of reducing or oxidizing agents), it is a promising example of how synthesis and characterization can be combined in an autonomous fashion.

4.8 AE and Materials Discovery

Efforts towards AE in materials science has also led to the discovery of new materials. Combining HTE and ML, Ren et al. discovered a new metallic glass using an iterative approach and an ML model for experimental selection.[97] Many important materials properties are intimately tied to the structure. As such, learning the relationship between the structure of a material and how it is formed—i.e., phase map—can serve as a blueprint for guiding materials discovery and optimization. Kusne et al.[12] developed CAMEO (Closed-loop, Autonomous system for Materials Exploration and Optimization), an AE system that maximizes overall knowledge of the composition–structure relationship (Table 1, Study H). By controlling synchrotron X-ray diffraction measurements and exploiting phase-map knowledge, they identified a novel phase-change material, which has recently attracted attention in the electronics industry.[98] Further, recent reports of AE systems using first-principles simulation provide more evidence that this approach is amenable to the rapid discovery of novel materials formulations.[18]

4.9 Materials AE as a Collaboration between AI and Materials Science

Although it is obvious that successful AE requires knowledge from both the AI and materials science communities, well-funded collaborations with experts in both fields may allow for tackling even larger problems. For example, a consortium of computer scientists and materials scientists are developing SARA (Scientific Autonomous Reasoning Agent)[99] to use combinatorial samples with laser spike annealing to generate time–temperature–transformation (TTT) diagrams for novel functional oxides. SARA will use AL strategies with the distinguishing feature that complex reasoning is required to guide experiment selection. For example, one operational mode for SARA is the identification of all unique synthesis routes for a given structure, requiring AI algorithms that are deeply aware of phase diagrams and the properties of all known phases, among other issues. Realizing this breadth of expertise in an AI system requires learning-and-reasoning-based algorithms well beyond the purview of ML algorithms demonstrated in materials research to date. The need for materials-aware AI combined with the substantial complexity of the composition–processing–structure instrumentation makes the SARA project emblematic of the grand challenges in materials AE.

5. CURRENT AND RELATED AI TECHNOLOGIES FOR MATERIALS AE

AE systems offer a unique opportunity to the AI community as platforms for the development and testing of their models and algorithms. The value proposition of materials AE to the AI community is the iterative nature of the platform over unknown search spaces, that nonetheless have a ground truth in materials phenomena because they originate from fundamental chemistry and physics. There is no direct mechanistic analogue in social media response or static voluminous databases, where advanced AI methods are often applied. On the other hand, materials AE depends on AI technologies for planning algorithms and knowledge-representation models; the distinguishing component of closed-loop AE systems from merely automated experimentation are the iterative decisions made by an AI/ML planner.

At this nascent stage, many of the existing AE systems offer proof-of-concept demonstrations, opting to use previously developed ML and AI methods. While these generic methods are attractive for their broad and perhaps immediate applicability, they do not necessarily capture aspects of the material system, experimental apparatus, and campaign constraints. To build more robust, intelligent platforms with greater autonomy, these factors should be included. In this section, we highlight a few examples of such problem-specific features and consider how—if at all—current state-of-the-art methods address them. We also present some new features materials science has brought to AI technologies: the trend towards models based on physical and chemical phenomena and new considerations required for planning algorithms.

5.1 Bayesian Optimization (BO) and Gaussian Process (GP) Models

Many general methodologies—such as BO,[100] AL,[101] and statistical DOE[102, 103]—suggest a model of the relevant quantities-of-interest to learn sequentially as well as the decision-making policies that can select a set of experimental actions to execute towards a research objective,

making them useful to closed-loop techniques. For example, in BEAR (Figure 3 and Table 1, Study D),[30, 87] the mechanical performance of a manufactured structure is viewed as an experimental response function over such structures and is modeled as a random function using a Gaussian process (GP) model.[32] Used with the expected improvement (EI) policy, in which sampling is pursued at the point most likely to maximize improvement of a value, this GP model is used to select the next structure to test.[104] GP models with the EI policy or similar modeling and policy choices are attractive because of the modeling and computational ease. The GP model allows the specification of the assumed structure, such as smoothness, of the response function without being overly restrictive. However, in many materials systems, such assumptions are not globally accurate. The archetypal example of this are critical phenomena. Critical regions of experiment space (e.g., delineating regimes of pressure or temperature) result in responses that change rapidly or discontinuously, which cannot be properly modeled using off-the-shelf GP models. This is not isolated to the use of GP models in BO. Many AL and DOE methods ultimately rely on similar types of generic models. For example, uncertainty-based methods[105-107] often rely on GP or linear models to model responses.

Another feature not immediately captured with off-the-shelf methods is the fact that experiments often yield several types of responses, e.g., various characterizations, experiment failure, experimental time or cost, or an uncontrolled factor, such as laboratory humidity. More complex models are needed to properly capture the relationships between the different responses, as well as the uncertainties between these relationships. A joint description capturing a variety of measurable responses and phenomena may not be easy to work with. An alternative direction is to utilize an ensemble of more traditional models, each offering simple estimates of the functions of interest; however, the lack of formalism makes inference and predictions more difficult. For example, Powell and Reyes and co-workers[108, 109] describe methods for using an ensemble of physics-based kinetic models to represent beliefs on experimental responses. Other models such as ensembles of neural networks[55] can directly offer multi-variate predictions for several types of responses, in which correlations between outputs are emergent rather than having to explicitly couple them statistically. Such networks have already been used in experimental science and control settings.[110] In a broader context, ensemble-based methods could allow us to use a variety of different types of models in a single decision-making framework. Here, methods such as Bayesian hypothesis testing,[111] model averaging,[112] multi-fidelity modeling,[113, 114] strategies for multi-fidelity optimization with variable dimensional hierarchical models,[113, 115] and multi-information source optimization (MISO),[116] offer potential avenues for more robust modeling and decision-making.

5.2 Reinforcement Learning (RL)

Closely related to closed-loop techniques, such as BO, are reinforcement learning (RL)[29] and optimal control.[35] Markov decision processes (MDPs), a core RL framework, models generic states of a closed-loop campaign, stochastic transitions between states upon taking experimental actions, and rewards or costs incurred when making such transitions,[117] offering a more fluent way of modeling many aspects of materials research. Through RL, MDPs allow an agent to make more operational considerations. RL decisions are obtained by estimating expected future cumulative rewards incurred when pursuing a particular branch of an experimental campaign.

Many such techniques do so by approximating a value function (i.e., a measure of how "good" states are) or a policy function (i.e., the expected best action we can take to transition to high-value states). As with BO, learning such functions can be done with generic black-box models or with more problem-specific models that use probabilistic beliefs on response functions, experimental failure, costs, or rewards obtained.

5.3 Deep Learning (DL)

Regardless of the type of modeling, approximating the functions needed to execute decision-making in RL generally requires a significant computational investment. The coupling of deep learning (DL)[118] with RL—so-called deep reinforcement learning (DRL),[119]—to calculate DL-model surrogates of value or policy functions may prove useful here. DL models are trained against a large number of states/value pairs. This can be done offline, by considering a large number of potential states a campaign can be in and assuming that a representative set of potential states can be simulated. While this methodology proved successful in the case of AlphaGo[120] and other cases,[121] it remains to be seen whether something similar can be applied in the context of AE.

In general, DL methods are also proving useful outside the context of predicting value or policy functions. They work well by self-discovering latent and predictive features from raw, often high-dimensional data.[122] Despite impressive results in many problems, the direct use of DL in materials AE is limited due to the high data requirements needed to train models. Requiring large sets of representative data is somewhat antithetical to the intelligent and nuanced exploration of experiment space discussed above. There are, however, opportunities for this powerful technique to be used inside the closed loop when simulations and physical models are used to generate synthetic data for offline pre-training of the DL model. DL can also be used to autonomously analyze rich characterization data, such as microscopy or tomography data, and possibly map such data into signals that the autonomous agent can use to close the loop. Current examples of this use in non-autonomous settings include DL for optimal microscopy,[123] cryo-electron microscopy,[124] and atom probe tomography.[125]

5.4 Transfer Learning (TL)

The lack of data is frequently encountered in autonomous research and generally prohibits the use of larger DL outright. To mitigate this, transfer learning (TL) can be used to leverage existing data of previously studied, related materials systems. One way to do this is with deep transfer learning (DTL).[126] Above, we discussed pre-training a DL model in a way similar to what would be encountered during the online execution of the closed loop. In DTL, a DL model is trained using data obtained from a separate task, often in an unsupervised manner, resulting in a learned latent representation of some material in general. Then, within the closed loop, the model is trained from latent representation features to a material property of interest. Pre-training the mapping from material to latent features reduces the data requirements needed to learn the mapping to the property of interest. Alternatively, one can use adjacent data to build more informative priors for BO models used in closed-loop design. This is the perspective taken by Roy and Kaelbling[127] and applied, for example, to building Bayesian priors for the tribological

properties in two-dimensional TMD (transition metal dichalcogenide) materials using adjacent materials descriptors.[128]

5.5 Towards Physics-Based Models

The iterative nature of AE can be used to explicitly test physics-based models,[65] as opposed to black-box statistical models comprising raw experimental parameters. A campaign may also be designed to search over multiple potentially operative physical and chemical models, known in the AI community as model selection. These approaches are particularly appealing because they incorporate physics-based phenomena, e.g., Arrhenius behavior, into their knowledge representations rather than being naïve or purely statistical representations.[108] King et al.[31] built one of the earliest robot scientists called "ADAM," which produced yeast enzymes by generating hypotheses of biological synthesis routes that it evaluated in a closed loop.[129] Similar to the symbolic regression work of Schmidt and Lipson,[130] we envisage AE campaigns where the objective is to select and parameterize from a broad range of materials phenomena (in place of mathematical symbols) using iterative experimental search strategies that are designed to regress quickly to the operative physics. With appropriately chosen models, AE output as physical models is often superior to output as naïve or black-box statistical models—which, while they may be predictive, are scientifically uninformative. Additionally, while statistical techniques, such as ML, are appropriate for interpolation, they do not excel at extrapolation, which is possible with physics-based models.

The design of planning algorithms to test the physics-based models is currently the subject of intense research, including both established approaches (e.g., BO, RL)[31, 99, 108] and more exploratory advanced AI/ML methods.[12, 131-133] The integration of ML with AI reasoning in the context of scientific knowledge may be used emulate how humans would interpret data; AI reasoning comprises the ability to infer new facts via the consideration of various information sources, complementing statistical ML. This coupling of AI-reasoning and ML is a pillar of the so-called third wave of AI,[134-136] and the phenomenological nature of the physical sciences makes it particularly well-suited for the development and demonstration of such AI/ML systems.

5.6 Challenges in the Design of Planning Algorithms for Materials AE

Materials AE campaigns often have real-life operational considerations or constraints (e.g., time, cost, available inventories) that may need to be incorporated into the planning algorithm. Decisions may require a "cost–benefit" analysis that utilizes multiple information sources,[116, 137] which may include a mix of experiments that exploit various characterization techniques and *in-silico* simulations of multiple levels of fidelity. Frequently, advanced materials development involves expensive methods and instrumentation (e.g., electron microscopy or molecular beam epitaxy) or limited-access, highly competitive facilities (e.g., synchrotron X-ray or neutron sources), making the ability to reliably select the right experiment especially impactful. New algorithms should be developed for the efficient exploration of high-dimensional parameter space in a time-constrained environment, thus reducing the number of required experiments. This was realized in the recent AE campaign of CAMEO (Table 1, Study H);[12] a combinatorial library with an effectively infinite number of compositions to characterize was generated during limited synchrotron beam time. Exploiting the phase map autonomously, they discovered an optimal

phase-change memory material using only one-tenth the number of measurements required by the standard (non-autonomous) grid-based approach.

While autonomous systems promise to more reliably perform optimal experiments towards an objective, some have expressed concern that robots will ignore results that are outside the objective but are nonetheless interesting and that they will miss serendipitous and synergistic unanticipated results that a human would naturally recognize.[138] In the future, serendipity-awareness may be incorporated into autonomous research algorithms.[86]

6. POTENTIAL IMPACT OF AE ON MATERIALS SCIENCE RESEARCH

6.1 Increased Speed and Decreased Cost

AE promises to disrupt the current research enterprise and investment structure by increasing returns on capital and skilled labor. While it is difficult to quantify the rate of research progress, it is a function of iteration time, number of iterations needed to find a solution, and the unit cost per iteration, all of which are expected to improve as experimental hardware is automated and as closed-loop iterative algorithms are implemented and improved. Early demonstrations of AE, such as the ARES,[10] BEAR,[30] and CAMEO[12] AE systems discussed above, have already demonstrated orders-of-magnitude reductions in iteration time and number of iterations needed to discover and characterize novel functional materials.[12] AE can also achieve better research outcomes than current processes in terms of parameters, such as materials performance or fidelity of characterization.[12, 30]

The exponential increase in research-progress speed enabled by AE will make research more affordable. Labor dominates the cost of research, and AE can effectively multiply the productivity of an individual researcher; hundreds of experimental iterations can be done in the time and labor it previously took to do one, reducing the marginal cost of subsequent experiments and allowing us to consider the economics of the AE process. In principle, AE-enabled research equipment need not be more expensive than traditional equipment; in practice, any additional capital costs are a fixed cost, and the amortized marginal cost is small because of the increased duty cycle. As research becomes more affordable, we expect it to become more accessible, just as computing power became more accessible with low-cost processors.

6.2 Future Directions: Globally Integrated AE Systems and a Rise in Citizen Science

With the increasing speed of research (per researcher), we predict the trend depicted in Figure 4; it assumes each researcher will have access to research robots, which will increase the number of researchers. We expect three phases of AE development stemming from their degree of interconnectedness. Current AE systems are stand-alone and self-contained. In 3–5 years, we anticipate a transition to locally connected systems, where multiple robots can perform mutually dependent research. In 15–20 years, we expect a network of AE systems to be globally integrated, much like the internet is today. Importantly, we envisage network effects for the globally integrated AE systems, where beyond the tipping point, the size and degree of interconnectedness greatly multiply the impact of each new research robot's contribution to the

network. We can thus expect solutions to currently intractable problems, as a result of leveraging network effects from data sharing and interpretation and a community-driven approach to scientific investigation.

Currently, only those with access to large, well-resourced laboratories are able to participate in materials research at the highest level. As a result of the decreased cost and increased accessibility of research, a potential outcome is a rise in citizen science where—as in the astronomy and high-energy physics communities—contributions to the field can be made by enthusiasts with access to data or instruments. In the future, greater access to AE will provide more people the opportunity to access research robots and be able to do meaningful research. This may take the form of remote-access "cloud labs" (e.g., Emerald Cloud Lab, Strateos); low-cost, relatively self-contained networkable benchtop equipment analogous to 3D printers (e.g., modular automated organic synthesizers,[139] ChemPuters[140]); or open-access challenges where participants can propose new experiments based on collected datasets (e.g., the DARPA SD2 Perovskites Synthesis challenge, performed on the RAPID system).[93] With the expected increase in accessibility, AE can help address the lack of diversity in science at the earliest stages. Studies have shown that while children may lose confidence in their potential to be scientists, they do not lose their ability to do science; this was especially evident in underrepresented groups.[141] As AE progresses, it can help make scientific research more accessible and appealing to everyone, especially those at risk.

6.3 Changes in Research Strategies

As AE is applied to more types of materials systems, we must also consider the implications of AE on the design of campaign objectives and search strategies. Human researchers design experimental campaigns to balance the likelihood of success, potential benefits of success, and explainability of outcomes. Often this takes the form of starting from known experiments[142] and making modifications one variable at a time.[143] This strategy can be effective for local optimizations, but it has difficulty in multiparameter problems and results in biased datasets.[144] The speed and reduced human effort of AE enable a greater diversity of experiments, and since AI/ML algorithms excel at high-dimensional search problems, they are holistic rather than reductionist. AE also increases the risk appetite per experiment. The failure of one or even several experiments does not doom a campaign. In fact, "failed experiments" can serve to inform where experiments do not work and further improve the ML model.[145] Using AE, previously intractable problems become more likely to succeed, and we can pursue more challenging, high-dimensional problems.

7. INVESTMENTS FOR MATERIALS AE

In order to fully benefit from AE, the community must overcome significant challenges by investing in ways that make experimental hardware, software, and data sharing more suited to AE. Investments in fundamental research typically focus on addressing specific foundational questions. However, investments in AE will establish an infrastructure that will broadly enable faster research towards *many* scientific questions as well as industry-relevant results.

7.1 Investments in Experimental Hardware

We encourage non-proprietary interfaces to enable facile sample exchange across multiple commercial experimental tools for synthesis and characterization. Although it is possible to design mobile robotic systems that can work in existing human-centric laboratories,[52] this is not an ideal long-term solution compared to standardized sample exchange interfaces, which will reduce complexity and design or robot-path planning time. The redesign of microscopes, synchrotron beamlines, and other sophisticated instrumentation to be compatible with robotic sample handling—akin to the multi-plate-handling robots in the bio-community—is an essential area of investment. It will also be necessary to integrate *in-situ*/inline and real-time metrologies with automated data processing pipelines for various material data formats.[52] For example, *in-situ* microscopes could generate a massive amount of image frames at microsecond frame rates,[146] and to exploit them, inline image analysis carried out as fast as the frame rate is crucial for accelerating their experimental campaigns.[147]

Innovative new technologies for on-demand sample fabrication and *in-situ* characterization are also needed to translate these early wins to the full spectrum of materials science applications. With many material properties and desired functionalities emergent from multiple phenomena, detailed characterization of samples would improve the rate and degree of convergence towards campaign goals. However, it is not generally tractable to measure every spot of a heterogeneous sample with every tool. Optimizing the information obtained by multiple techniques requires a judicious subsampling of this measurement space to uncover the relevant descriptors.[148]

7.2 Investments in Data Management and Sharing

By their very nature, AE systems will generate much larger data sets than current laboratory practice, and these data are "born digital," making them inherently easy to incorporate into digital workflows, and avoiding the bottleneck of human data-entry. This creates an opportunity to encourage the organized collection, sharing, and reuse of data at much larger scales than at present. Such accumulated and well-curated databases can be reused by a distributed network of AE systems (see Figure 4). This in turn provides a dataset from which prior knowledge of related scientific domains[97, 149, 150] can be extracted and then used to supplement RL[151] and TL,[128, 152, 153] algorithms. As highlighted in efforts, such as the MGI,[45] more attention needs to be paid to the collection of data from failed experiments[145] and to the automated labeling of data as they are collected, which should consider the FAIR data principles of findability, accessibility, interoperability, and reusability.[154]

Despite efforts to make data more widely available (e.g., Materials Data Facility[155]), most data are kept proprietary and are not used fully even by the team that produced them. We encourage open sharing of data and AE algorithms to maximize exploitation of AE campaigns. We also encourage increased investment into open-source/open-standards data file formats and application programming interfaces (APIs) to lower the barrier to access, and discourage proprietary software and data formats for experimental hardware. Investments will be needed for the large-scale structured repositories of both data (e.g., Materials Data Facility,[156] Materials Project,[46] PRISMS[157]) and trained AI/ML models (e.g., DLHub[158])—designed for use by

machines and people—as well as the automated tools for constructing and curating these databases.[46] Additionally, efforts to develop uniform metadata descriptions, such as tracking material sources and workflow methodologies will be needed to improve knowledge representation.

7.3 Investments in Software Infrastructure

To build automated or AE systems that can incorporate multiple commercial systems for synthesis and characterization, more open-source software, data standards, and APIs are needed. Irrespective of whether a system is fully automated, the algorithms used to direct experimental decision-making need to be both robust and flexible enough to be used on a variety of different experimental platforms. Investment is needed in the software infrastructure for materials AE. Atinary (formerly ChemOS),[159] ESCALATE,[94] LabMate.ML,[160] MAOS,[161] BlueSky,[162] and ARES™ OS[28] are examples of such efforts. However, the broader range of materials, modeling software, and experimental hardware will require further investment into software. Commercial hardware often uses proprietary software and data formats that are difficult to access or modify for incorporation into AE systems.

7.4 Collaborations as the Foundation to Future Cooperative Networks

AE requires its collaborative network to expand to reach its full potential. As the AE infrastructure becomes more accessible with hardware, data-storage, and software investments, efforts should also be made to encourage key stakeholders in research—industry, academia, and government—to work together and take advantage of the increased accessibility. Current collaborations and partnerships will lay the foundations for the network of AE systems we anticipate in the future. Many materials and chemical corporations have HT/Combi research units that collaborate with academic researchers. Academic research teams are also directly commercializing technologies of AE materials discovery, e.g., ML tools for materials data analysis (Citrine Informatics). The main barrier to effective partnerships between academic and industrial teams is in the ownership of the co-developed intellectual property. With laboratory capabilities distributed across different entities and open-sourced ML algorithms trained with proprietary data, the questions about product ownership and the contributions of involved parties will be a persistent concern, requiring much legal effort to predefine the conditions of each partnership. Programs to standardize these partnerships would be helpful.

Government-funded scientific user facilities (SUFs) can play a critical role in encouraging the transition from small-team independent research to cooperative scientific networks. The centralized nature of these facilities offers an opportunity to establish common data formats, data sharing policies, and new access paradigms such as multi-facility proposals. The national laboratory-scale engineering resources can be leveraged to enhance automation, develop hardware and software standards around which large community-scale AE programs can nucleate.

In addition to encouraging collaborations between academic, government, and industrial partners, investments for improving the collaborative interaction between human researchers and

the AI algorithms of AE systems are necessary. Designing effective human–machine teaming is an emerging area in autonomy and user-experience research.[163] With good teaming, humans and chess-playing computers working together outperform either humans alone or computers alone.[164] In the 2005 Freestyle Chess Tournament, a team of chess masters and a supercomputer were defeated by a team of amateur humans and desktop computers with superior teaming. There are on-going efforts to incorporate human expertise, judgement, and prior knowledge into search and decision-making algorithms.[165] With respect to materials, only nascent efforts at teaming humans with AI exist for inorganic materials.[43]

7.5 Educating the Materials–AI Workforce

We have recommended a variety of investments to help establish a new infrastructure for AE to accelerate research progress. This new infrastructure will make possible the globally integrated AE systems we expect in 15–20 years (Figure 4). The systems will be linked together over networks, where experimental, simulation, and information processing nodes combine with human direction to form autonomous "collaboratories,"[166] generating scientific knowledge at rates barely imaginable today. Changes in the workforce behind AE will be required to support this future infrastructure.

The current lack of AI and autonomy expertise is a barrier to AE progress. Most individuals in our existing workforce do not have the skillset to do both materials and autonomy research, and universities are just beginning to develop curricula to address computer science and AI for materials research. With autonomous vehicles and huge demands for AI professionals, the AE community will need substantial programmatic investments to develop a workforce of "AI natives" that are comfortable doing closed-loop AE as they are doing materials research, as well as value propositions to attract autonomy and AI experts to materials problems.[167]

Workforce development and curricular innovation is needed at all levels,[167] but one particularly pressing need is for technicians that can manage the hybrid mechanical–electrical–chemical systems. Because of similarities to workforce needs in advanced manufacturing, there may be opportunities to extend the existing efforts of community colleges.[168]

8. CONCLUSION

We hope that this paper informs, sparks interest, and potentially inspires the larger community for AE systems. The first research robots are already making an impact in materials research and development. From optimizing the growth of CNTs to accelerating the understanding of composition–structure–property maps, they are revolutionizing the way scientific research is conducted. Disrupting conventional research methods, AE has demonstrated an increased rate of knowledge generation by orders of magnitude and has resulted in the discovery of new compounds. Broad deployment of AE will require substantial investment in hardware, software, and data infrastructure, as well as in education to overcome technological and workforce challenges. Integrated, online AE systems need to be made cheaper and exponentially more accessible. Upon the demonstration of a sufficient number of AE platforms, funding of large-

scale multi-institutional "collaboratories" will enable researchers to attack civilization's most pressing topics.

The extensive collaboration of the fields of materials science and autonomy research have and will continue to benefit both sides. Novel materials have been identified and syntheses optimized, while a unique platform with complex real-world problems is available to develop and test advanced AI and autonomy approaches. With the potential to revolutionize research, an opportunity exists for the autonomous materials and AI communities to pursue the Nobel–Turing Challenge.[169]

Overcoming the challenges identified in the paper has the potential to reshape science and particularly the roles of human researchers, freeing us to engage with science more meaningfully and interactively. This will lower the barrier to entry for asking and answering scientific questions, generating a new breed of scientists who focus on insight and creativity and lowering the barrier to entry for citizen scientists. These tools will bring together artificial and human intelligence in efficient and effective efforts to accelerate technological and fundamental scientific progress transforming the world around us.

Acknowledgements:
The authors gratefully acknowledge the contributions of the participants of the Autonomous Systems for Materials Development Workshop, held at the University of Pennsylvania Singh Center for Nanotechnology, 4–6 September, 2019, with
support from the University of Pennsylvania, the Air Force Research Laboratory, Materials & Manufacturing Directorate, ACS Combinatorial Science, and the NSF through the University of Pennsylvania Materials Research Science and Engineering Center (MRSEC) (DMR-1720530). We also gratefully acknowledge John Russell of the Singh Center for his assistance in organizing this workshop. This research used resources of the Advanced Light Source, which is a DOE Office of Science User Facility under contract no. DE-AC02-05CH11231. Support from the Air Force Research Laboratory Air Force Office of Scientific Research (AFOSR) LRIR no. 19RXCOR322 is gratefully acknowledged. K.A.B. acknowledges support from NSF CMMI-1661412. J.S. acknowledges support from the National Science Foundation (grant no. DMR-1928882), the Defense Advanced Research Projects Agency (contract no. HR001118C0036), and the Camille and Henry Dreyfus Foundation (TH-14-010). S.J.L.B. was supported by the U.S. National Science Foundation through grant DMREF-1922234. J.M.G. and C.P.G. acknowledge support from U.S. Department of Energy Office of Basic Energy Sciences under award DE-SC0020383. C.P. ac- knowledges support from AFOSR grant FA9550-18-1-0144. The authors acknowledge Lianne M.C. Beltran for professional editing.

REFERENCES

1. Sass, S.L. (1998). The substance of civilization: Materials and human history from the stone age to the age of silicon (Arcade Publishing).
2. USDOE Office of Science (SC)(United States). (2017). Basic Energy Sciences Roundtable: Opportunities for Quantum Computing in Chemical and Materials Sciences (USDOE Office of Science (SC)(United States)).
3. Ball, P. (2018). Synthetic biology—Engineering nature to make materials. MRS Bulletin *43*, 477-484.
4. Holdren, J. (2014). National Science and Technology Council, Committee on Technology, Subcommittee on the Materials Genome Initiative, Materials Genome Initiative Strategic Plan.
5. Gordon, R.J. (2016). Perspectives on the rise and fall of American growth. American Economic Review *106*, 72-76.
6. Tabor, D.P., Roch, L.M., Saikin, S.K., Kreisbeck, C., Sheberla, D., Montoya, J.H., Dwaraknath, S., Aykol, M., Ortiz, C., Tribukait, H.*, et al.* (2018). Accelerating the discovery of materials for clean energy in the era of smart automation. Nature Reviews Materials *3*, 5-20. 10.1038/s41578-018-0005-z.
7. Kitano, H. Nobel-Turing Challenge. http://www.oecd.org/going-digital/ai-intelligent-machines-smart-policies/conference-agenda/ai-intelligent-machines-smart-policies-kitano.pdf.
8. Esper, M. (2020). Secretary of Defense Remarks for DOD Artificial Intelligence Symposium and Exposition.
9. Sparkes, A., Aubrey, W., Byrne, E., Clare, A., Khan, M.N., Liakata, M., Markham, M., Rowland, J., Soldatova, L.N., and Whelan, K.E. (2010). Towards Robot Scientists for autonomous scientific discovery. Automated Experimentation *2*, 1.
10. Nikolaev, P., Hooper, D., Webber, F., Rao, R., Decker, K., Krein, M., Poleski, J., Barto, R., and Maruyama, B. (2016). Autonomy in materials research: a case study in carbon nanotube growth. npj Computational Materials *2*, 16031.
11. Häse, F., Roch, L.M., and Aspuru-Guzik, A. (2019). Next-generation experimentation with self-driving laboratories. Trends in Chemistry *1*, 282-291.
12. Kusne, A.G., Yu, H., Wu, C., Zhang, H., Hattrick-Simpers, J., DeCost, B., Sarker, S., Oses, C., Toher, C., Curtarolo, S.*, et al.* (2020). On-the-fly closed-loop materials discovery via Bayesian active learning. Nature Communications *11*, 5966. 10.1038/s41467-020-19597-w.
13. Flores-Leonar, M.M., Mejía-Mendoza, L.M., Aguilar-Granda, A., Sanchez-Lengeling, B., Tribukait, H., Amador-Bedolla, C., and Aspuru-Guzik, A. (2020). Materials Acceleration Platforms: on the way to autonomous experimentation. Current Opinion in Green and Sustainable Chemistry, 100370.
14. MacLeod, B.P., Parlane, F.G., Morrissey, T.D., Häse, F., Roch, L.M., Dettelbach, K.E., Moreira, R., Yunker, L.P., Rooney, M.B., and Deeth, J.R. (2020). Self-driving laboratory for accelerated discovery of thin-film materials. Science Advances *6*, eaaz8867.
15. Correa-Baena, J.-P., Hippalgaonkar, K., van Duren, J., Jaffer, S., Chandrasekhar, V.R., Stevanovic, V., Wadia, C., Guha, S., and Buonassisi, T. (2018). Accelerating materials development via automation, machine learning, and high-performance computing. Joule *2*, 1410-1420.

16. Salley, D., Keenan, G., Grizou, J., Sharma, A., Martín, S., and Cronin, L. (2020). A nanomaterials discovery robot for the Darwinian evolution of shape programmable gold nanoparticles. Nature Communications *11*, 1-7.
17. Chang, J., Nikolaev, P., Carpena-Núñez, J., Rao, R., Decker, K., Islam, A.E., Kim, J., Pitt, M.A., Myung, J.I., and Maruyama, B. (2020). Efficient Closed-loop Maximization of Carbon Nanotube Growth Rate using Bayesian Optimization. Scientific Reports *10*, 1-9.
18. Montoya, J.H., Winther, K.T., Flores, R.A., Bligaard, T., Hummelshøj, J.S., and Aykol, M. (2020). Autonomous intelligent agents for accelerated materials discovery. Chemical Science *11*, 8517-8532. 10.1039/D0SC01101K.
19. Stein, H.S., and Gregoire, J.M. (2019). Progress and prospects for accelerating materials science with automated and autonomous workflows. Chemical Science *10*, 9640-9649.
20. Davis, R., Shrobe, H., and Szolovits, P. (1993). What is a knowledge representation? AI magazine *14*, 17-17.
21. Green, M.L., Takeuchi, I., and Hattrick-Simpers, J.R. (2013). Applications of high throughput (combinatorial) methodologies to electronic, magnetic, optical, and energy-related materials. Journal of Applied Physics *113*, 9_1.
22. Allison, J., Backman, D., and Christodoulou, L. (2006). Integrated computational materials engineering: a new paradigm for the global materials profession. Jom *58*, 25-27.
23. Butler, K.T., Davies, D.W., Cartwright, H., Isayev, O., and Walsh, A. (2018). Machine learning for molecular and materials science. Nature *559*, 547-555.
24. Schmidt, J., Marques, M.R.G., Botti, S., and Marques, M.A.L. (2019). Recent advances and applications of machine learning in solid-state materials science. npj Computational Materials *5*, 83. 10.1038/s41524-019-0221-0.
25. Ramprasad, R., Batra, R., Pilania, G., Mannodi-Kanakkithodi, A., and Kim, C. (2017). Machine learning in materials informatics: recent applications and prospects. npj Computational Materials *3*, 1-13.
26. Wang, A.Y.-T., Murdock, R.J., Kauwe, S.K., Oliynyk, A.O., Gurlo, A., Brgoch, J., Persson, K.A., and Sparks, T.D. (2020). Machine Learning for Materials Scientists: An introductory guide towards best practices. Chemistry of Materials.
27. Bessa, M., Bostanabad, R., Liu, Z., Hu, A., Apley, D.W., Brinson, C., Chen, W., and Liu, W.K. (2017). A framework for data-driven analysis of materials under uncertainty: Countering the curse of dimensionality. Computer Methods in Applied Mechanics and Engineering *320*, 633-667.
28. Deneault, J.R., Chang, J., Myung, J., Hooper, D., Amstrong, A., Pitt, M., and Mauryama, B. (2021). Toward Autonomous Additive Manufacturing: Bayesian Optimization on a 3D Printer. MRS Bulletin. 10.1557/s43577-021-00051-1.
29. Sutton, R.S., and Barto, A.G. (2018). Reinforcement learning: An introduction (MIT press).
30. Gongora, A.E., Xu, B., Perry, W., Okoye, C., Riley, P., Reyes, K.G., Morgan, E.F., and Brown, K.A. (2020). A Bayesian experimental autonomous researcher for mechanical design. Science Advances *6*, eaaz1708. 10.1126/sciadv.aaz1708.
31. King, R.D., Rowland, J., Oliver, S.G., Young, M., Aubrey, W., Byrne, E., Liakata, M., Markham, M., Pir, P., and Soldatova, L.N. (2009). The automation of science. Science *324*, 85-89.
32. Williams, C.K., and Rasmussen, C.E. (2006). Gaussian processes for machine learning, Vol 2 (MIT press Cambridge, MA).

33. Gelman, A., Carlin, J.B., Stern, H.S., Dunson, D.B., Vehtari, A., and Rubin, D.B. (2014). Bayesian Data Analysis, 3rd edn (United Kingdom: Taylor & Francis).
34. Box, G.E. (1982). Choice of response surface design and alphabetic optimality. Paper presented at: Proceedings of the Conference on the Design of Experiments in Army Research, Development and Testing (US Army Research Office).
35. Bertsekas, D.P. (1995). Dynamic programming and optimal control, Vol 1 (Athena scientific Belmont, MA).
36. Lookman, T., Balachandran, P.V., Xue, D., Hogden, J., and Theiler, J. (2017). Statistical inference and adaptive design for materials discovery. Current Opinion in Solid State and Materials Science *21*, 121-128.
37. Powell, W.B., and Ryzhov, I.O. (2012). Optimal learning, Vol 841 (John Wiley & Sons).
38. Lin, F.-R., and Shaw, M.J. Active training of backpropagation neural networks using the learning by experimentation methodology.
39. Wang, Y., Reyes, K.G., Brown, K.A., Mirkin, C.A., and Powell, W.B. Nested-Batch-Mode Learning and Stochastic Optimization with An Application to Sequential MultiStage Testing in Materials Science. SIAM J Sci Comput *37*, B361-B381. 10.1137/140971117.
40. DeCost, B., Hattrick-Simpers, J.R., Trautt, Z., Kusne, A.G., Campo, E., and Green, M.L. (2020). Scientific AI in materials science: a path to a sustainable and scalable paradigm. Machine Learning: Science and Technology.
41. Winfield, A.F., Michael, K., Pitt, J., and Evers, V. (2019). Machine Ethics: The Design and Governance of Ethical AI and Autonomous Systems [Scanning the Issue]. Proceedings of the IEEE *107*, 509-517. 10.1109/JPROC.2019.2900622.
42. Shahriari, K., and Shahriari, M. (2017). IEEE standard review — Ethically aligned design: A vision for prioritizing human wellbeing with artificial intelligence and autonomous systems. Paper presented at: 2017 IEEE Canada International Humanitarian Technology Conference (IHTC). 10.1109/IHTC.2017.8058187.
43. Duros, V., Grizou, J., Sharma, A., Mehr, S.H.M., Bubliauskas, A., Frei, P., Miras, H.N., and Cronin, L. (2019). Intuition-enabled machine learning beats the competition when joint human-robot teams perform inorganic chemical experiments. Journal of chemical information and modeling *59*, 2664-2671.
44. Ososky, S., Schuster, D., Phillips, E., and Jentsch, F.G. (2013). Building appropriate trust in human-robot teams. Paper presented at: 2013 AAAI spring symposium series.
45. Materials Genome Initiative. https://www.mgi.gov/.
46. Jain, A., Ong, S.P., Hautier, G., Chen, W., Richards, W.D., Dacek, S., Cholia, S., Gunter, D., Skinner, D., and Ceder, G. (2013). Commentary: The Materials Project: A materials genome approach to accelerating materials innovation. Apl Materials *1*, 011002.
47. de Pablo, J.J., Jones, B., Kovacs, C.L., Ozolins, V., and Ramirez, A.P. (2014). The materials genome initiative, the interplay of experiment, theory and computation. Current Opinion in Solid State and Materials Science *18*, 99-117.
48. de Pablo, J.J., Jackson, N.E., Webb, M.A., Chen, L.-Q., Moore, J.E., Morgan, D., Jacobs, R., Pollock, T., Schlom, D.G., and Toberer, E.S. (2019). New frontiers for the materials genome initiative. npj Computational Materials *5*, 41.
49. Green, M.L., Choi, C., Hattrick-Simpers, J., Joshi, A., Takeuchi, I., Barron, S., Campo, E., Chiang, T., Empedocles, S., and Gregoire, J. (2017). Fulfilling the promise of the materials genome initiative with high-throughput experimental methodologies. Applied Physics Reviews *4*, 011105.

50. Cui, J., Chu, Y.S., Famodu, O.O., Furuya, Y., Hattrick-Simpers, J., James, R.D., Ludwig, A., Thienhaus, S., Wuttig, M., and Zhang, Z. (2006). Combinatorial search of thermoelastic shape-memory alloys with extremely small hysteresis width. Nature materials *5*, 286-290.
51. Fujino, S., Murakami, M., Anbusathaiah, V., Lim, S.-H., Nagarajan, V., Fennie, C., Wuttig, M., Salamanca-Riba, L., and Takeuchi, I. (2008). Combinatorial discovery of a lead-free morphotropic phase boundary in a thin-film piezoelectric perovskite. Applied Physics Letters *92*, 202904.
52. Burger, B., Maffettone, P.M., Gusev, V.V., Aitchison, C.M., Bai, Y., Wang, X., Li, X., Alston, B.M., Li, B., Clowes, R.*, et al.* (2020). A mobile robotic chemist. Nature *583*, 237-241. 10.1038/s41586-020-2442-2.
53. Li, J., Lu, Y., Xu, Y., Liu, C., Tu, Y., Ye, S., Liu, H., Xie, Y., Qian, H., and Zhu, X. (2018). AIR-Chem: Authentic intelligent robotics for chemistry. The Journal of Physical Chemistry A *122*, 9142-9148.
54. Lignos, I., Morad, V., Shynkarenko, Y., Bernasconi, C., Maceiczyk, R.M., Protesescu, L., Bertolotti, F., Kumar, S., Ochsenbein, S.T., and Masciocchi, N. (2018). Exploration of near-infrared-emissive colloidal multinary lead halide perovskite nanocrystals using an automated microfluidic platform. ACS nano *12*, 5504-5517.
55. Epps, R.W., Bowen, M.S., Volk, A.A., Abdel-Latif, K., Han, S., Reyes, K.G., Amassian, A., and Abolhasani, M. (2020). Artificial Chemist: An Autonomous Quantum Dot Synthesis Bot. Advanced Materials, 2001626.
56. Mekki-Berrada, F., Ren, Z., Huang, T., Wong, W.K., Zheng, F., Xie, J., Tian, I.P.S., Jayavelu, S., Mahfoud, Z., and Bash, D. (2020). Two-Step Machine Learning Enables Optimized Nanoparticle Synthesis.
57. Curtarolo, S., Hart, G.L., Nardelli, M.B., Mingo, N., Sanvito, S., and Levy, O. (2013). The high-throughput highway to computational materials design. Nature materials *12*, 191-201.
58. Thygesen, K.S., and Jacobsen, K.W. (2016). Making the most of materials computations. Science *354*, 180-181.
59. Curtarolo, S., Setyawan, W., Wang, S., Xue, J., Yang, K., Taylor, R.H., Nelson, L.J., Hart, G.L., Sanvito, S., and Buongiorno-Nardelli, M. (2012). AFLOWLIB. ORG: A distributed materials properties repository from high-throughput ab initio calculations. Computational Materials Science *58*, 227-235.
60. Choudhary, K., Garrity, K.F., Reid, A.C., DeCost, B., Biacchi, A.J., Walker, A.R.H., Trautt, Z., Hattrick-Simpers, J., Kusne, A.G., and Centrone, A. (2020). The joint automated repository for various integrated simulations (JARVIS) for data-driven materials design. npj Computational Materials *6*, 1-13.
61. Hachmann, J., Olivares-Amaya, R., Atahan-Evrenk, S., Amador-Bedolla, C., Sánchez-Carrera, R.S., Gold-Parker, A., Vogt, L., Brockway, A.M., and Aspuru-Guzik, A. (2011). The Harvard clean energy project: large-scale computational screening and design of organic photovoltaics on the world community grid. The Journal of Physical Chemistry Letters *2*, 2241-2251.
62. Draxl, C., and Scheffler, M. (2019). The NOMAD laboratory: from data sharing to artificial intelligence. Journal of Physics: Materials *2*, 036001.
63. Haghighatlari, M., Vishwakarma, G., Altarawy, D., Subramanian, R., Kota, B.U., Sonpal, A., Setlur, S., and Hachmann, J. (2019). Chemml: A machine learning and informatics program package for the analysis, mining, and modeling of chemical and materials data. Wiley Interdisciplinary Reviews: Computational Molecular Science, e1458.

64. Mathew, K., Montoya, J.H., Faghaninia, A., Dwarakanath, S., Aykol, M., Tang, H., Chu, I.-h., Smidt, T., Bocklund, B., and Horton, M. (2017). Atomate: A high-level interface to generate, execute, and analyze computational materials science workflows. Computational Materials Science *139*, 140-152.
65. Sun, S., Tiihonen, A., Oviedo, F., Liu, Z., Thapa, J., Zhao, Y., Hartono, N.T.P., Goyal, A., Heumueller, T., Batali, C.*, et al.* (2021). A data fusion approach to optimize compositional stability of halide perovskites. Matter *4*, 1305-1322. https://doi.org/10.1016/j.matt.2021.01.008.
66. Morgan, D., and Jacobs, R. (2020). Opportunities and challenges for machine learning in materials science. Annual Review of Materials Research *50*.
67. Schleder, G.R., Padilha, A.C., Acosta, C.M., Costa, M., and Fazzio, A. (2019). From DFT to machine learning: recent approaches to materials science–a review. Journal of Physics: Materials *2*, 032001.
68. Vasudevan, R.K., Choudhary, K., Mehta, A., Smith, R., Kusne, G., Tavazza, F., Vlcek, L., Ziatdinov, M., Kalinin, S.V., and Hattrick-Simpers, J. (2019). Materials science in the artificial intelligence age: high-throughput library generation, machine learning, and a pathway from correlations to the underpinning physics. MRS Communications *9*, 821-838.
69. Hong, Y., Hou, B., Jiang, H., and Zhang, J. (2020). Machine learning and artificial neural network accelerated computational discoveries in materials science. Wiley Interdisciplinary Reviews: Computational Molecular Science *10*, e1450.
70. Chibani, S., and Coudert, F.-X. (2020). Machine learning approaches for the prediction of materials properties. APL Materials *8*, 080701.
71. Suh, C., Fare, C., Warren, J.A., and Pyzer-Knapp, E.O. (2020). Evolving the Materials Genome: How Machine Learning Is Fueling the Next Generation of Materials Discovery. Annual Review of Materials Research *50*.
72. Saal, J.E., Oliynyk, A.O., and Meredig, B. (2020). Machine Learning in Materials Discovery: Confirmed Predictions and Their Underlying Approaches. Annual Review of Materials Research *50*.
73. Sparks, T.D., Kauwe, S.K., Parry, M.E., Tehrani, A.M., and Brgoch, J. (2020). Machine Learning for Structural Materials. Annual Review of Materials Research *50*.
74. Hegde, V.I., Aykol, M., Kirklin, S., and Wolverton, C. (2020). The phase stability network of all inorganic materials. Science Advances *6*, eaay5606.
75. Ganose, A.M., and Jain, A. (2019). Robocrystallographer: automated crystal structure text descriptions and analysis. MRS Communications *9*, 874-881.
76. Yeung, C., Tsai, J.-M., King, B., Kawagoe, Y., Ho, D., Knight, M.W., and Raman, A.P. (2020). Elucidating the Behavior of Nanophotonic Structures through Explainable Machine Learning Algorithms. ACS Photonics *7*, 2309-2318.
77. Feng, J., Lansford, J.L., Katsoulakis, M.A., and Vlachos, D.G. (2020). Explainable and trustworthy artificial intelligence for correctable modeling in chemical sciences. Science advances *6*, eabc3204.
78. Nikolaev, P., Hooper, D., Perea-López, N., Terrones, M., and Maruyama, B. (2014). Discovery of Wall-Selective Carbon Nanotube Growth Conditions via Automated Experimentation. ACS Nano *8*, 10214-10222. 10.1021/nn503347a.
79. Rao, R., Liptak, D., Cherukuri, T., Yakobson, B.I., and Maruyama, B. (2012). In situ evidence for chirality-dependent growth rates of individual carbon nanotubes. Nature materials *11*, 213-216.

80. Tanoto, A., and Rückert, U. (2012). Local navigation strategies for multi-robot exploration: from simulation to experimentation with mini-robots. Procedia Engineering *41*, 1197-1203.
81. Kuehl, R.O., and Kuehl, R. (2000). Design of experiments: statistical principles of research design and analysis.
82. Kluender, E.J., Hedrick, J.L., Brown, K.A., Rao, R., Meckes, B., Du, J., Moreau, L., Maruyama, B., and Mirkin, C.A. (2019). Catalyst discovery through megalibraries of nanomaterials. Proceedings of the National Academy of Sciences of the United States of America *116* 40-45.
83. Bédard, A.-C., Adamo, A., Aroh, K.C., Russell, M.G., Bedermann, A.A., Torosian, J., Yue, B., Jensen, K.F., and Jamison, T.F. (2018). Reconfigurable system for automated optimization of diverse chemical reactions. Science *361*, 1220-1225.
84. Huyer, W., and Neumaier, A. (2008). SNOBFIT--stable noisy optimization by branch and fit. ACM Transactions on Mathematical Software (TOMS) *35*, 1-25.
85. Coley, C.W., Thomas, D.A., Lummiss, J.A., Jaworski, J.N., Breen, C.P., Schultz, V., Hart, T., Fishman, J.S., Rogers, L., and Gao, H. (2019). A robotic platform for flow synthesis of organic compounds informed by AI planning. Science *365*, eaax1566.
86. Grizou, J., Points, L.J., Sharma, A., and Cronin, L. (2020). A curious formulation robot enables the discovery of a novel protocell behavior. Science advances *6*, eaay4237.
87. Gongora, A.E., Snapp, K.L., Whiting, E., Riley, P., Reyes, K.G., Morgan, E.F., and Brown, K.A. (2021). Using Simulation to Accelerate Autonomous Experimentation (AE): A Case Study using Mechanics. iScience *24*. 10.1016/j.isci.2021.102262.
88. Sun, S., Hartono, N.T.P., Ren, Z.D., Oviedo, F., Buscemi, A.M., Layurova, M., Chen, D.X., Ogunfunmi, T., Thapa, J., Ramasamy, S.*, et al.* (2019). Accelerated Development of Perovskite-Inspired Materials via High-Throughput Synthesis and Machine-Learning Diagnosis. Joule *3*, 1437-1451. https://doi.org/10.1016/j.joule.2019.05.014.
89. Langner, S., Häse, F., Perea, J.D., Stubhan, T., Hauch, J., Roch, L.M., Heumueller, T., Aspuru-Guzik, A., and Brabec, C.J. (2020). Beyond Ternary OPV: High-Throughput Experimentation and Self-Driving Laboratories Optimize Multicomponent Systems. Advanced Materials *32*, 1907801.
90. Chan, E.M., Xu, C., Mao, A.W., Han, G., Owen, J.S., Cohen, B.E., and Milliron, D.J. (2010). Reproducible, high-throughput synthesis of colloidal nanocrystals for optimization in multidimensional parameter space. Nano letters *10*, 1874-1885.
91. Higgins, K., Valleti, S.M., Ziatdinov, M., Kalinin, S.V., and Ahmadi, M. (2020). Chemical Robotics Enabled Exploration of Stability in Multicomponent Lead Halide Perovskites via Machine Learning. ACS Energy Letters *5*, 3426-3436.
92. Kirman, J., Johnston, A., Kuntz, D.A., Askerka, M., Gao, Y., Todorović, P., Ma, D., Privé, G.G., and Sargent, E.H. (2020). Machine-Learning-Accelerated Perovskite Crystallization. Matter.
93. Li, Z., Najeeb, M.A., Alves, L., Sherman, A.Z., Shekar, V., Cruz Parrilla, P., Pendleton, I.M., Wang, W., Nega, P.W., Zeller, M.*, et al.* (2020). Robot-Accelerated Perovskite Investigation and Discovery. Chemistry of Materials *32*, 5650–5663.
94. Pendleton, I.M., Cattabriga, G., Li, Z., Najeeb, M.A., Friedler, S.A., Norquist, A.J., Chan, E.M., and Schrier, J. (2019). Experiment Specification, Capture and Laboratory Automation Technology (ESCALATE): a software pipeline for automated chemical experimentation and data management. MRS Communications *9*, 846-859.

95. Noack, M.M., Yager, K.G., Fukuto, M., Doerk, G.S., Li, R., and Sethian, J.A. (2019). A kriging-based approach to autonomous experimentation with applications to x-ray scattering. Scientific reports *9*, 1-19.
96. Rakita, Y., O'Nolan, D., McAuliffe, R.D., Veith, G.M., Chupas, P.J., Billinge, S.J., and Chapman, K.W. (2020). Active Reaction Control of Cu Redox State Based on Real-Time Feedback from In Situ Synchrotron Measurements. Journal of the American Chemical Society.
97. Ren, F., Ward, L., Williams, T., Laws, K.J., Wolverton, C., Hattrick-Simpers, J., and Mehta, A. (2018). Accelerated discovery of metallic glasses through iteration of machine learning and high-throughput experiments. Science advances *4*, eaaq1566.
98. Kusne, A.G. U.S. Provisional Patent Application No. 63/151,263.
99. Ament, S., Amsler, M., Sutherland, D.R., Chang, M.-C., Guevarra, D., Connolly, A.B., Gregoire, J.M., Thompson, M.O., Gomes, C.P., and van Dover, R.B. (2021). Autonomous synthesis of metastable materials. arXiv preprint arXiv:210107385.
100. Frazier, P.I., and Wang, J. (2016). Bayesian optimization for materials design. In Information Science for Materials Discovery and Design (Springer), pp. 45-75.
101. University of Wisconsin-Madison Department of Computer Sciences. (2009). Active learning literature survey (University of Wisconsin-Madison Department of Computer Sciences).
102. Fisher, R.A. (1936). Design of experiments. Br Med J *1*, 554-554.
103. Montgomery, D.C. (2017). Design and analysis of experiments (John wiley & sons).
104. Bull, A.D. (2011). Convergence Rates of Efficient Global Optimization Algorithms. Journal of Machine Learning Research *12*.
105. Settles, B., Craven, M., and Ray, S. (2008). Multiple-instance active learning. Paper presented at: Advances in neural information processing systems.
106. Cohn, D.A., Ghahramani, Z., and Jordan, M.I. (1996). Active learning with statistical models. Journal of artificial intelligence research *4*, 129-145.
107. Cressie, N. (1990). The origins of kriging. Mathematical geology *22*, 239-252.
108. Chen, S., Reyes, K.-R.G., Gupta, M.K., McAlpine, M.C., and Powell, W.B. (2015). Optimal learning in experimental design using the knowledge gradient policy with application to characterizing nanoemulsion stability. SIAM/ASA Journal on Uncertainty Quantification *3*, 320-345.
109. He, X., Reyes, K.G., and Powell, W.B. (2020). Optimal Learning with Local Nonlinear Parametric Models over Continuous Designs. SIAM Journal on Scientific Computing *42*, A2134-A2157.
110. Raza, S.E.A., Cheung, L., Epstein, D., Pelengaris, S., Khan, M., and Rajpoot, N.M. (2017). Mimo-net: A multi-input multi-output convolutional neural network for cell segmentation in fluorescence microscopy images. Paper presented at: 2017 IEEE 14th International Symposium on Biomedical Imaging (ISBI 2017) (IEEE).
111. Bernardo, J.M., and Rueda, R. (2002). Bayesian hypothesis testing: A reference approach. International Statistical Review *70*, 351-372.
112. Hoeting, J.A., Madigan, D., Raftery, A.E., and Volinsky, C.T. (1999). Bayesian model averaging: a tutorial. Statistical science, 382-401.
113. Robinson, T., Eldred, M., Willcox, K., and Haimes, R. (2006). Strategies for multifidelity optimization with variable dimensional hierarchical models. Paper presented at: 47th AIAA/ASME/ASCE/AHS/ASC Structures, Structural Dynamics, and Materials Conference 14th AIAA/ASME/AHS Adaptive Structures Conference 7th. 10.2514/6.2006-1819.

114. Pilania, G., Gubernatis, J.E., and Lookman, T. (2017). Multi-fidelity machine learning models for accurate bandgap predictions of solids. Computational Materials Science *129*, 156-163.
115. Sen, R., Kandasamy, K., and Shakkottai, S. (2018). Multi-Fidelity Black-Box Optimization with Hierarchical Partitions. Paper presented at: Proceedings of the 35th International Conference on Machine Learning (Proceedings of Machine Learning Research: PMLR).
116. Poloczek, M., Wang, J., and Frazier, P. (2017). Multi-information source optimization. Paper presented at: Advances in Neural Information Processing Systems.
117. Puterman, M.L. (2014). Markov decision processes: discrete stochastic dynamic programming (John Wiley & Sons).
118. Goodfellow, I., Bengio, Y., Courville, A., and Bengio, Y. (2016). Deep learning, Vol 1 (MIT press Cambridge).
119. Mnih, V., Badia, A.P., Mirza, M., Graves, A., Lillicrap, T., Harley, T., Silver, D., and Kavukcuoglu, K. (2016). Asynchronous methods for deep reinforcement learning. Paper presented at: International conference on machine learning.
120. Silver, D., Hubert, T., Schrittwieser, J., Antonoglou, I., Lai, M., Guez, A., Lanctot, M., Sifre, L., Kumaran, D., and Graepel, T. (2018). A general reinforcement learning algorithm that masters chess, shogi, and Go through self-play. Science *362*, 1140-1144.
121. Mnih, V., Kavukcuoglu, K., Silver, D., Graves, A., Antonoglou, I., Wierstra, D., and Riedmiller, M. (2013). Playing atari with deep reinforcement learning. arXiv preprint arXiv:13125602.
122. LeCun, Y., Bengio, Y., and Hinton, G. (2015). Deep learning. nature *521*, 436-444.
123. Rivenson, Y., Göröcs, Z., Günaydin, H., Zhang, Y., Wang, H., and Ozcan, A. (2017). Deep learning microscopy. Optica *4*, 1437-1443.
124. Zhu, Y., Ouyang, Q., and Mao, Y. (2017). A deep convolutional neural network approach to single-particle recognition in cryo-electron microscopy. BMC bioinformatics *18*, 1-10.
125. Madireddy, S., Chung, D.-W., Loeffler, T., Sankaranarayanan, S.K., Seidman, D.N., Balaprakash, P., and Heinonen, O. (2019). Phase Segmentation in Atom-Probe Tomography Using Deep Learning-Based Edge Detection. Scientific reports *9*, 1-10.
126. Tan, C., Sun, F., Kong, T., Zhang, W., Yang, C., and Liu, C. (2018). A survey on deep transfer learning. Paper presented at: International conference on artificial neural networks (Springer).
127. Roy, D.M., and Kaelbling, L.P. (2007). Efficient Bayesian Task-Level Transfer Learning. Paper presented at: IJCAI.
128. Sattari Baboukani, B., Ye, Z., G Reyes, K., and Nalam, P.C. (2020). Prediction of Nanoscale Friction for Two-Dimensional Materials Using a Machine Learning Approach. Tribology Letters *68*, 1-14.
129. Coutant, A., Roper, K., Trejo-Banos, D., Bouthinon, D., Carpenter, M., Grzebyta, J., Santini, G., Soldano, H., Elati, M., Ramon, J.*, et al.* (2019). Closed-loop cycles of experiment design, execution, and learning accelerate systems biology model development in yeast. Proceedings of the National Academy of Sciences *116*, 18142-18147. 10.1073/pnas.1900548116.
130. Schmidt, M., and Lipson, H. (2010). Symbolic regression of implicit equations. In Genetic Programming Theory and Practice VII (Springer), pp. 73-85.
131. Park, C., Rao, R., Nikolaev, P., and Maruyama, B. (2019). Gaussian process metamodeling for experiments with manipulating factors. arXiv preprint arXiv:191100955.

132. Segler, M.H.S., Preuss, M., and Waller, M.P. (2018). Planning chemical syntheses with deep neural networks and symbolic AI. Nature *555*, 604-610. 10.1038/nature25978.
133. Korovina, K., Xu, S., Kandasamy, K., Neiswanger, W., Poczos, B., Schneider, J., and Xing, E. (2020). Chembo: Bayesian optimization of small organic molecules with synthesizable recommendations. Paper presented at: International Conference on Artificial Intelligence and Statistics.
134. National Academies of Sciences, E., and Medicine (2018). Artificial Intelligence and Machine Learning to Accelerate Translational Research: Proceedings of a Workshop—in Brief.
135. Haenlein, M., and Kaplan, A. (2019). A brief history of artificial intelligence: On the past, present, and future of artificial intelligence. California management review *61*, 5-14.
136. Gomes, C.P., Selman, B., and Gregoire, J.M. (2019). Artificial intelligence for materials discovery. MRS Bulletin *44*, 538-544.
137. Reyes, K., Chen, S., Li, Y., and Powell, W.B. (2015). Quantifying experimental characterization choices in Optimal Learning and materials design. Paper presented at: TMS 2015 144th Annual Meeting & Exhibition (Springer).
138. Yaqub, O. (2018). Serendipity: Towards a taxonomy and a theory. Research Policy *47*, 169-179.
139. Li, J., Ballmer, S.G., Gillis, E.P., Fujii, S., Schmidt, M.J., Palazzolo, A.M., Lehmann, J.W., Morehouse, G.F., and Burke, M.D. (2015). Synthesis of many different types of organic small molecules using one automated process. Science *347*, 1221-1226.
140. Steiner, S., Wolf, J., Glatzel, S., Andreou, A., Granda, J.M., Keenan, G., Hinkley, T., Aragon-Camarasa, G., Kitson, P.J., Angelone, D.*, et al.* (2019). Organic synthesis in a modular robotic system driven by a chemical programming language. Science *363*, eaav2211. 10.1126/science.aav2211.
141. Lei, R.F., Green, E.R., Leslie, S.J., and Rhodes, M. (2019). Children lose confidence in their potential to "be scientists," but not in their capacity to "do science". Developmental science *22*, e12837.
142. Aykol, M., Hegde, V.I., Hung, L., Suram, S., Herring, P., Wolverton, C., and Hummelshøj, J.S. (2019). Network analysis of synthesizable materials discovery. Nature communications *10*, 1-7.
143. Cao, B., Adutwum, L.A., Oliynyk, A.O., Luber, E.J., Olsen, B.C., Mar, A., and Buriak, J.M. (2018). How to optimize materials and devices via design of experiments and machine learning: Demonstration using organic photovoltaics. ACS nano *12*, 7434-7444.
144. Javdekar, C., Watson, E., Kapilow, V., Bograd, M., Boyer, P., Zeid, I., and Duggan, C. (2016). Closing the advanced manufacturing talent gap. Procedia Manufacturing *5*, 1197-1207.
145. Raccuglia, P., Elbert, K.C., Adler, P.D., Falk, C., Wenny, M.B., Mollo, A., Zeller, M., Friedler, S.A., Schrier, J., and Norquist, A.J. (2016). Machine-learning-assisted materials discovery using failed experiments. Nature *533*, 73-76. 10.1038/nature17439.
146. Horwath, J.P., Zakharov, D.N., Mégret, R., and Stach, E.A. (2020). Understanding important features of deep learning models for segmentation of high-resolution transmission electron microscopy images. npj Computational Materials *6*, 1-9.
147. Park, C., and Ding, Y. (2019). Automating material image analysis for material discovery. MRS Communications *9*, 545-555.
148. Melton, C.N., Noack, M.M., Ohta, T., Beechem, T.E., Robinson, J., Xiaotian Zhang, Bostwick, A., Jozwiak, C., Koch, R., Zwart, P.H.*, et al.* (2020). K-Means-Driven Gaussian

Process Data Collection for Angle-Resolved Photoemission Spectroscopy Machine Learning Science and Technology *in review*.
149. Lake, B.M., Salakhutdinov, R., and Tenenbaum, J.B. (2015). Human-level concept learning through probabilistic program induction. Science *350*, 1332-1338.
150. Olson, M., Wyner, A., and Berk, R. (2018). Modern neural networks generalize on small data sets. Paper presented at: Advances in Neural Information Processing Systems.
151. Arulkumaran, K., Deisenroth, M.P., Brundage, M., and Bharath, A.A. (2017). A brief survey of deep reinforcement learning. arXiv preprint arXiv:170805866.
152. Weiss, K., Khoshgoftaar, T.M., and Wang, D. (2016). A survey of transfer learning. Journal of Big data *3*, 9.
153. Chen, D., Bai, Y., Zhao, W., Ament, S., Gregoire, J.M., and Gomes, C.P. Deep Reasoning Networks for Unsupervised Pattern De-mixing with Constraint Reasoning.
154. Wilkinson, M.D., Dumontier, M., Aalbersberg, I.J., Appleton, G., Axton, M., Baak, A., Blomberg, N., Boiten, J.-W., da Silva Santos, L.B., and Bourne, P.E. (2016). The FAIR Guiding Principles for scientific data management and stewardship. Scientific data *3*, 1-9.
155. Blaiszik, B., Ward, L., Schwarting, M., Gaff, J., Chard, R., Pike, D., Chard, K., and Foster, I. (2019). A data ecosystem to support machine learning in materials science. MRS Communications *9*, 1125-1133.
156. Blaiszik, B., Chard, K., Pruyne, J., Ananthakrishnan, R., Tuecke, S., and Foster, I. (2016). The Materials Data Facility: Data services to advance materials science research. JOM *68*, 2045-2052.
157. Aagesen, L., Adams, J., Allison, J., Andrews, W., Araullo-Peters, V., Berman, T., Chen, Z., Daly, S., Das, S., and DeWitt, S. (2018). Prisms: An integrated, open-source framework for accelerating predictive structural materials science. JOM *70*, 2298-2314.
158. Chard, R., Li, Z., Chard, K., Ward, L., Babuji, Y., Woodard, A., Tuecke, S., Blaiszik, B., Franklin, M., and Foster, I. (2019). DLHub: Model and data serving for science. Paper presented at: 2019 IEEE International Parallel and Distributed Processing Symposium (IPDPS) (IEEE).
159. Roch, L.M., Häse, F., Kreisbeck, C., Tamayo-Mendoza, T., Yunker, L.P., Hein, J.E., and Aspuru-Guzik, A. (2020). ChemOS: An orchestration software to democratize autonomous discovery. PLoS One *15*, e0229862.
160. Reker, D., Hoyt, E.A., Bernardes, G.J., and Rodrigues, T. (2020). Adaptive Optimization of Chemical Reactions with Minimal Experimental Information. Cell Reports Physical Science *1*, 100247.
161. Li, J., Tu, Y., Liu, R., Lu, Y., and Zhu, X. (2020). Toward "On-Demand" Materials Synthesis and Scientific Discovery through Intelligent Robots. Advanced Science *7*, 1901957.
162. Bluesky. https://blueskyproject.io
163. Amershi, S., Weld, D., Vorvoreanu, M., Fourney, A., Nushi, B., Collisson, P., Suh, J., Iqbal, S., Bennett, P.N., Inkpen, K.*, et al.* (2019). Guidelines for Human-AI Interaction. Paper presented at: Proceedings of the 2019 CHI Conference on Human Factors in Computing Systems (Glasgow, Scotland Uk: Association for Computing Machinery). 10.1145/3290605.3300233.
164. Carter, S., and Nielsen, M. (2017). Using Artificial Intelligence to Augment Human Intelligence. Distill.
165. Nikolaidis, S., and Shah, J. (2012). Human-robot teaming using shared mental models. ACM/IEEE HRI.
166. Wulf, W.A. (1993). The collaboratory opportunity. Science *261*, 854-856.

167. TMS. (2019). Creating the next-generation Materials Genome Initiative workforce (Pittsburgh, PA: TMS). DOI: 10.7449/mgiworkforce_1. www.tms.org/mgiworkforce.
168. Reynolds, E.B., and Uygun, Y. (2018). Strengthening advanced manufacturing innovation ecosystems: The case of Massachusetts. Technological Forecasting and Social Change *136*, 178-191.
169. Kitano, H. (2016). Artificial intelligence to win the nobel prize and beyond: Creating the engine for scientific discovery. AI magazine *37*, 39-49.

Figure Captions

Figure 1. Schematic showing the different parts of an autonomous experimentation (AE) campaign.
An AE campaign comprises an iterative research loop that is carried out autonomously towards a research objective. *Initialize*: Before the first research cycle, the AE system incorporates information provided by human researchers to initialize the campaign. *Plan:* In this first part of the research loop, the system considers the predefined campaign objective and the most recent knowledge base and plans the next experiments to be pursued. *Experiment*: The experiments—which are broadly defined to encompass physical tests, modeling/simulation, or data mining—are carried out without human intervention. *Analyze:* Finally, the AE system uses the output data of the experiments to update the knowledge base, which will then be used in the planning of the next loop. *Conclusion:* Once the campaign objective is reached or some other criteria is met, the system completes the AE campaign and discontinues the iterations of planning, experiment, and analysis. Further development of this new research process is expected to significantly increase the efficiency of scientific investigations and completely shift the way research is carried out.

Figure 2. Schematic showing the autonomous experimentation (AE) campaign of ARES (Autonomous Research System), the first reported AE system.[10]
Initialize: ARES was provided with a database to seed its AI planner algorithm of 140 input synthesis condition with resultant growth rates. *Plan:* ARES used the subsequent database to train a random-forest model, which it used to determine the reaction conditions of the first experimental phase, beginning the first cycle of planning, experiment, and analysis. *Experiment:* Using automated apparatus, carbon nanotubes (CNTs) were synthesized via chemical vapor deposition (CVD), and CNT growth was tracked via *in-situ* Raman spectroscopy. Left inset shows the experimental set-up: an array of pillars for experiments with a laser heating one pillar. Right inset shows the time series of spectra (waterfall plot), revealing CNT growth via the increasing intensity of the G peak with time. *Analyze*: The maximum growth rate, v_{max}, of each experiment was extracted as shown by plotting the G-band area versus time. Along with the results of previous experiments (input conditions and output results), the results were analyzed and used to update the random-forest knowledge representation. *Plan*: Considering the latest knowledge representation, the AI planner once again decides on new experimental input conditions to target growth rates using a genetic algorithm. *Conclude:* After hundreds of iterations, the system converged on the maximum growth rate, demonstrating that ARES taught itself to grow CNTs at controlled rates.

Figure 3. Schematic showing features of autonomous experimentation (AE) campaigns of BEAR (Bayesian Experimental Autonomous Researcher).[30, 87]
BEAR is an AE system for producing and mechanically testing additively manufactured components. *Initialize:* The diagrams define the strut thickness (t), strut radius (r), number of struts (n), and twist (θ) of the components. These four parameters were varied to optimize toughness, the campaign objective. Performance was measured during uniaxial compression in which the structure was compressed by displacement D. *Plan*: The plot is an example of how parameter selection in one of BEAR's AE campaigns progressed with campaign time. Planning involved Bayesian optimization (BO) in all AE campaigns; in a set of campaigns, finite-element

modeling of prior physical data was also included through transfer learning to evaluate the inclusion of this data into the AE campaign. *Experiment:* The image shows the automated experimental apparatus of BEAR, where components were manufactured and tested for toughness (*U*). *Analyze:* Plot showing how *U* was obtained by measuring the force (*F*) as *D* was varied, adding to the knowledge base. *Conclude*: BEAR was used to benchmark the performance of AE by exploring the mechanical toughness of components that were either chosen from a grid or by an active-learning algorithm. Plotted are the median performance of the grid-based exploration and the AE campaigns. Even after 60 experiments, AE (blue diamonds) outperformed the 1800 experiments chosen from a grid (black squares). Providing the system with prior information about physical response (orange triangles) led to a +30% improvement in median performance.

Figure 4. Schematic showing the expected exponential increase of the speed of research as autonomous experimentation (AE) is further developed. We see a progression from connected AE systems to locally integrated systems, and finally to globally integrated systems. At a critical (or tipping) point, integration will create network effects that multiply the contribution of individual research nodes, greatly increasing research speed. Global integration and reduced cost will exponentially impact the access of researchers to AE systems. By leveraging network effects from data sharing and interpretation, and from the community-driven approach to scientific investigation, we anticipate solutions to currently intractable problems.

Table

Table 1. Selected Autonomous Experimentation (AE) Campaigns for Materials Development. The breadth of materials classes, synthesis methods, and characterization methods reveals the versatility of AE, and the benchmarked examples show that AE has successfully accelerated the research process. (UV, vis, and NIR represent ultraviolet, visible, and near infrared, respectively.)

Study (including publication date)	Material class and synthesis method	Characterization method	Planning and learning algorithm	Experimental campaigns and objectives	Metric of acceleration and benchmarking
(A) Autonomy in materials research: a case study in carbon nanotube growth (Oct 2016)[10] *see Figure 2 and the ARES example in the text*	Chemical vapor deposition of nano-materials	*in-situ* Raman spectroscopy	Random-forest model	600 experiments to obtain a controlled growth rate	none
(B) Reconfigurable system for automated optimization of diverse chemical reactions (Sept 2018)[83]	Flow-based chemistry of soluble molecules	High-performance liquid chromatography	Blackbox optimization software (SNOBFIT)	112 experiments to optimize three chemical reactions	none
(C) A curious formulation robot enables the discovery of a novel protocell behavior (Jan 2020)[86]	Syringe-based liquid handling of oil-in-water emulsions	Optical imaging	Random goal exploration on a support vector regressor	1000 experiments to explore temperature response of emulsions	8× reduction in the number of experiments needed to match the performance of 1000 random experiments
(D) A Bayesian experimental autonomous researcher for mechanics (April 2020)[30] *see Figure 3 and the BEAR example in text*	Additive manufacturing of structural polymers	Mechanical uniaxial compression, weight measurement, optical imaging	Bayesian optimization	6 repetitions of 100 to maximize component toughness	55× reduction in number of experiments needed to match 1800 experiments on a grid
(E) Self-driving laboratory for accelerated discovery of thin-film materials (May 2020)[14]	Spin-coating of mixtures of photoactive chemicals	Dark-field photography, UV–vis–NIR spectroscopy, 4-point probe	Bayesian optimization	2 campaigns, each with 35 experiments to maximize hole mobility	none
(F) Artificial chemist: an autonomous quantum dot synthesis (June 2020)[55]	Solution-phase quantum-dot halide exchange reaction in flow	*in-situ* UV–vis absorption and photoluminescence spectroscopy	Neural network ensemble, Bayesian optimization	*X* campaigns of 25 experiments to obtain a target emission energy with maximized brightness	Comparison of decision-making policies and role of pre-training
(G) A mobile robotic chemist (July 2020)[52]	Vial-based solution chemistry	Gas chromatography	Batched, constrained, Bayesian optimization algorithm	688 experiments performed over 8 days	none
(H) On-the-fly closed-loop materials discovery via Bayesian active learning (November 2020)[12] *see CAMEO example in the text*	Solid-state materials	Synchrotron X-ray diffraction	Physics-informed graph-based Bayesian optimization	19 measurements to discover best-in-class material during limited synchrotron beam time	10× reduction in number of experiments relative to grid-based approach