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Review

Recent Progress in Autonomous Laboratories for Chemical Synthesis

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Abstract: The integration of artificial intelligence (AI) and robotics into chemical synthesis has given rise to autonomous laboratories, transformative systems designed to overcome limitations in traditional experimental approaches. This review synthesizes recent advancements in autonomous laboratory systems, highlighting their applications in chemical synthesis and the innovations driving their evolution. Autonomous laboratories combine automated hardware, intelligent software, and adaptive systems to optimize experimental workflows, reduce human intervention, and enhance efficiency in complex reaction environments. Key developments include AI-driven reaction pathway planning, closed-loop optimization frameworks, and robotic platforms capable of executing multi-step synthesis with minimal expert oversight. Leading research groups have demonstrated significant progress, such as AI-guided discovery of functional materials, automated photocatalytic reaction optimization, and self-learning microfluidic systems. This review provides a comprehensive analysis of current achievements and remaining gaps, offering insights for researchers and policymakers in advancing this transformative technology.

Key words: autonomous laboratory, chemical synthesis, artificial intelligence, machine learning.

1. Introduction

Global challenges in energy development, healthcare, and food safety have underscored the limitations of traditional chemical synthesis processes, particularly their slow experimental throughput, high trial-and-error costs, and poor adaptability to complex reactions [1]. To circumvent these hurdles, next-generation autonomous laboratories have arisen, synergizing automated robotic workstations with advanced artificial intelligence (AI) decision-making systems [2]. In these laboratories, experimental protocols are first designed by artificial intelligence, then implemented by robotic platforms, with data analysis performed concurrently. This closed-loop system achieves significant time reduction and efficiency gains [3], and empowers researchers to investigate more extensive and complicated experimental setups, transforming the creation and improvement of sophisticated experiments into attainable objectives [4].

Autonomous laboratory systems are built upon three fundamental elements: physical equipment, digital program, and integrated platform. The physical apparatus manages chemical transformations, carries out synthetic procedures, and performs material characterization. This component comprises dedicated synthesis and analysis tools for routine operations, versatile robotic manipulators capable of adaptive tasks, modular devices including additive manufacturing systems [5,6] and liquid handling workstations [7]. These tools reduce hardware procurement costs and enable autonomous device construction. The digital program concentrates on planning optimal experimental protocols and controlling robotic activities, merging: (1) device communication, (2) data management, (3) AI decision-making, and (4) experimental planning modules [8]. The modular architecture is further augmented through the integration of advanced probabilistic optimization frameworks and machine learning paradigms. Specifically, Gaussian process-based Bayesian Optimization (BO)

facilitates efficient exploration of high-dimensional experimental parameter spaces by constructing surrogate models that balance the exploitation of known optima with an exploration of uncertain regions [9]. Reinforcement learning (RL) algorithms, implemented through Markov decision processes, enable autonomous policy optimization by maximizing cumulative reward signals derived from experimental outcomes [10]. Deep neural network architectures, particularly attention-based transformer models, provide robust pattern recognition capabilities for multivariate experimental data analysis, enabling the prediction of complex structure-property relationships [11]. This synergistic integration of machine learning methodologies significantly enhances the system's capacity for autonomous experimental design and closed-loop optimization while maintaining rigorous statistical foundations. The integrated platform serves as the laboratory's "brain", physical sensors, executing algorithmic decisions, and delivering accurate operational commands. The platform simultaneously serves as a bidirectional communication interface, permitting investigators to conduct remote experiment supervision, access instantaneous measurement data, and execute necessary manual override [12].

To date, several research teams globally have effectively implemented self-operating laboratory systems in synthetic chemistry applications (Figure 1), demonstrating substantial advancements. Nevertheless, current automated research platforms continue to face considerable challenges, including underdeveloped algorithms for complex chemical processes, exorbitant costs of research and development as well as maintenance, and unavoidable human participation in select procedural stages [3]. These limitations impede the broad adoption and continued evolution of autonomous laboratories. Consequently, this review seeks to analyze state-of-the-art innovations in automated synthesis technologies, define their operational frameworks and characteristic features, and evaluate their successes and ongoing challenges, providing references for future research on autonomous laboratories.

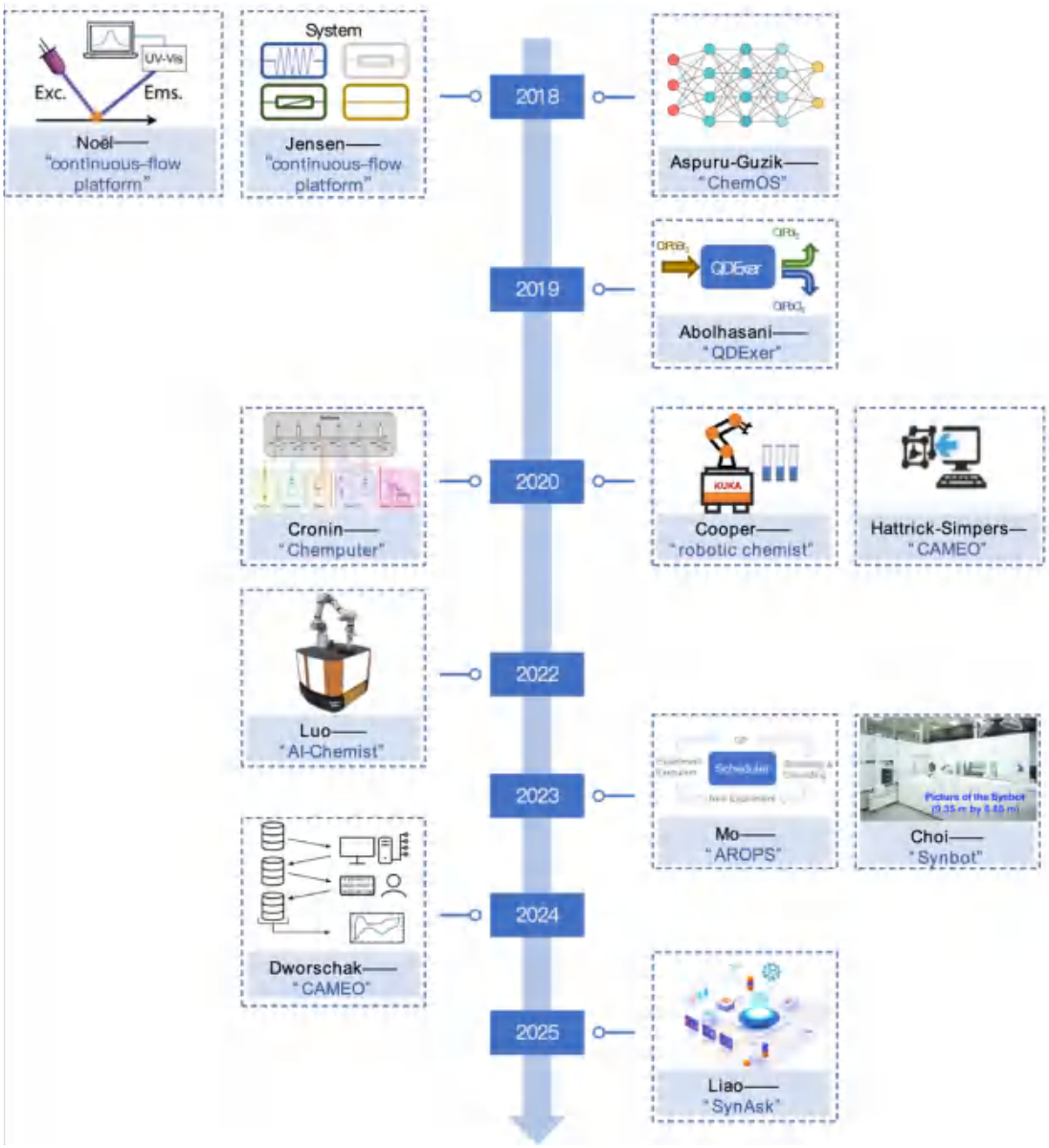

Figure 1. Timeline of the publication of the first key achievements by various research teams [13-24]. Panels reproduced/adapted with permission. Copyright: Refs 13,15,18 © AAAS; 14,17 © Wiley (CC-BY); 16 © Wiley-VCH; 19 © Nature Communications (CC-BY); 20 © National Science Review (CC-BY); 21 © ACS; 22 © Science (CC-BY); 23 © J. Mater. Chem. A (CC-BY); 24 © Chem. Sci. (CC-BY). Full license links in Supporting Information.

2. Research groups and their landmark achievements

2.1 Dr. Alán Aspuru-Guzik's group (University of Toronto)

To overcome the inefficiencies, manual-intensive processes, and extended durations inherent in conventional laboratory research, Aspuru-Guzik *et al.* developed ChemOS [13,25], an autonomous laboratory software platform. ChemOS employs closed-loop experimental design and AI-driven parameter adjustments, enabling applications in chemistry, materials science, and drug development (Figure 2) [25]. This platform features a central workflow manager and six constituent modules: an AI algorithm module for experimental planning, supporting Bayesian machine learning (ML) techniques (such as Phoenics [26], SMAC [27-29], Spearmint [30,31], and randomized search methods [32,33]); an automation and robotics module for executing experiments; an analytical interface module for result characterization; a database module for data management; a human-machine interaction module for researcher engagement; and a real-time analysis module for processing and visualizing results. This modular framework enables easier implementation, cost reduction, and flexible adaptation, making it compatible with diverse experimental scenarios and hardware platforms. Using ChemOS, Aspuru-Guzik *et al.* created "Ada", an autonomous laboratory for thin-film material discovery [34]. The system's self-learning capability has proven effective in improving hole transport properties in organic hole-transporting materials (HTMs) (Figure 3) [34]. Nevertheless, the platform's current architecture may face operational challenges when handling complex multilayer thin-film architectures or sophisticated experimental designs.

Building upon progress in robotic automation and ML technologies, Aspuru-Guzik *et al.* introduced ChemOS 2.0 [35] as an enhanced version of their original laboratory automation framework, better aligned with the requirements of modern self-driving laboratories. ChemOS 2.0 employs UNIX-compliant [36] to enhance modularity and interoperability. Its fog computing architecture optimizes workflow management, while rigorous state management improves reproducibility. The platform supports ab-initio simulations for materials discovery and enables device communication via middleware (such as SiLA2 [37]), simplifying lab automation integration. Its database design supports the table structures of general and specific equipment, enhancing the system's scalability and adaptability. The software platform is highly customizable, though its current interface may require some familiarity to navigate efficiently. Future iterations could benefit from a more user-friendly design to accommodate a broader range of users.

To further enhance the platform's explainability and autonomy, Aspuru-Guzik *et al.* developed the closed-loop transfer (CLT) method [38], integrating physics-informed feature selection with supervised learning in closed-loop experimentation to simultaneously optimize objective functions and extract chemical insights. The system employs a human-in-the-loop architecture that combines domain expertise in initial closed-loop stages and supports real-time monitoring through interpretable ML models. CLT's use of BO for molecule recommendation provides a valuable approach for hypothesis validation, this approach may require additional experimental iterations to achieve optimal results. Additionally, although CLT enables efficient hypothesis generation in data-limited scenarios, the potential emergence of spurious correlations underscores the importance of independent experimental validation

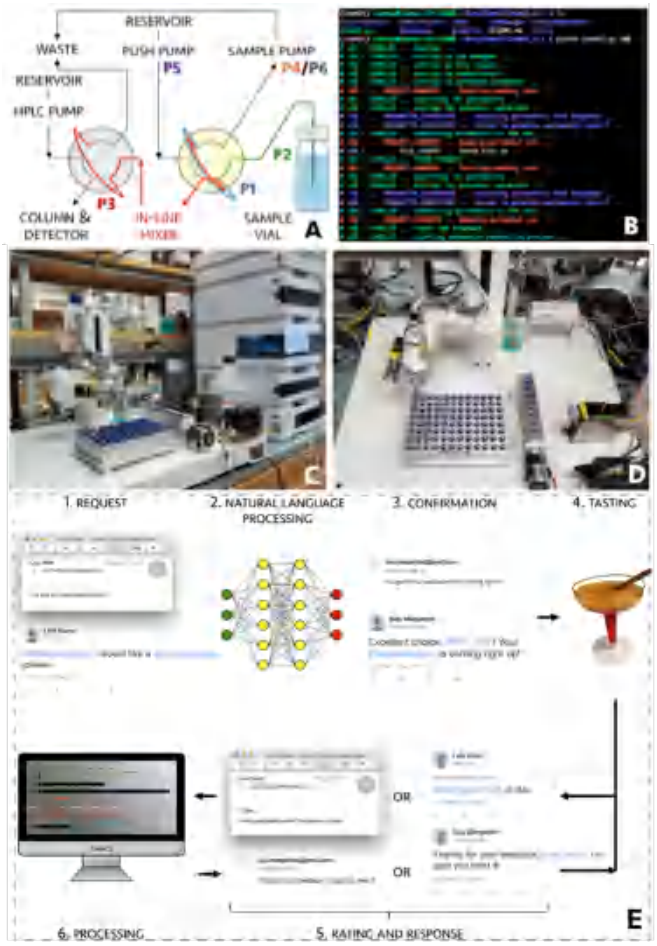

Figure 2. (A) Schematic of the flow path for the sampling sequence used with the N9 robotic platform. The six parameters (P1-P6) are color coded to illustrate the effect they have on the sampling sequence. The yellow shade highlights the arm valve, and the grey shade the HPLC valve. (B) Example of logging messages from ChemOS. (C) Side and (D) top view of the robotic hardware. Lower panels: Results from the autonomous calibration of an HPLC setup maximizing the magnitude of the response. (E) Representation of the ChemOS pipeline while screening the Tequila Sunrise space [25].

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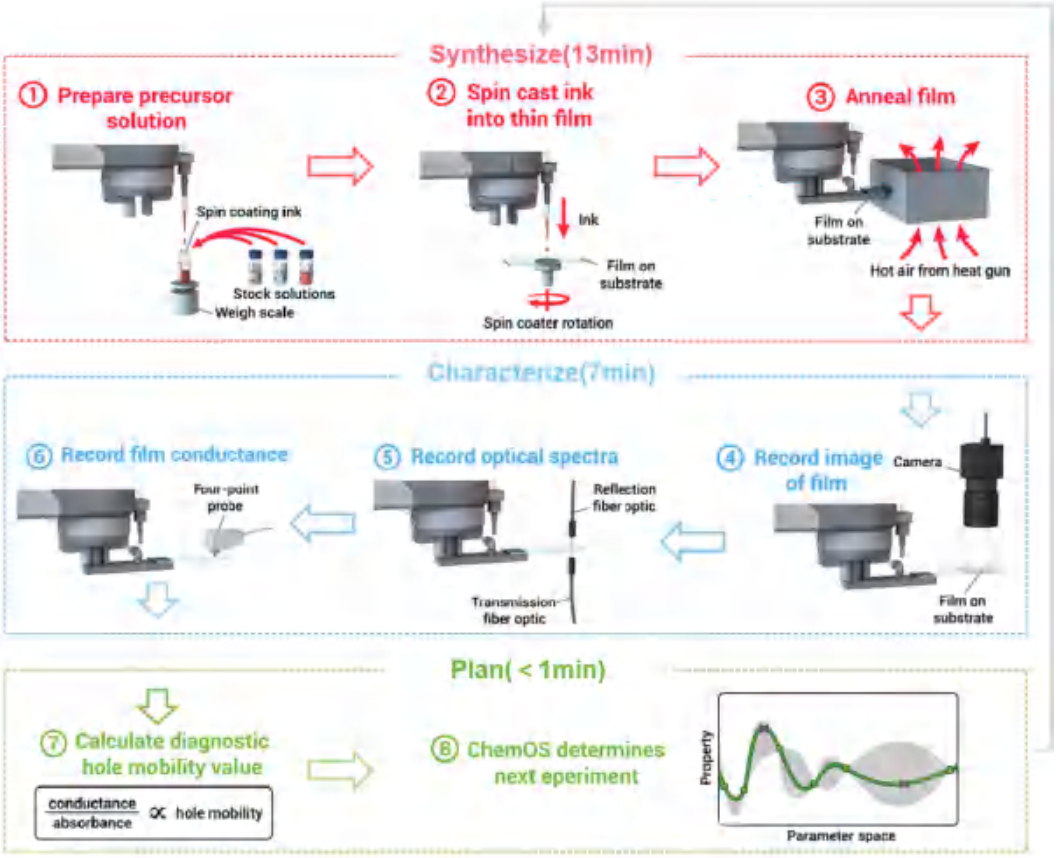

Figure 3. This automated workflow uses iterative experiments to find a thin-film composition with the highest pseudomobility. Each iteration includes mixing ink, spin coating, annealing, imaging, obtaining spectra, measuring I-V curves, calculating pseudomobility, and inputting results into software to optimize the next experiment [34]. Copyright 2020 The Authors, some rights reserved; exclusive licensee American Association for the Advancement of Science. No claim to original U.S. Government Works. Distributed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC), https://creativecommons.org/licenses/by-nc/4.0/.

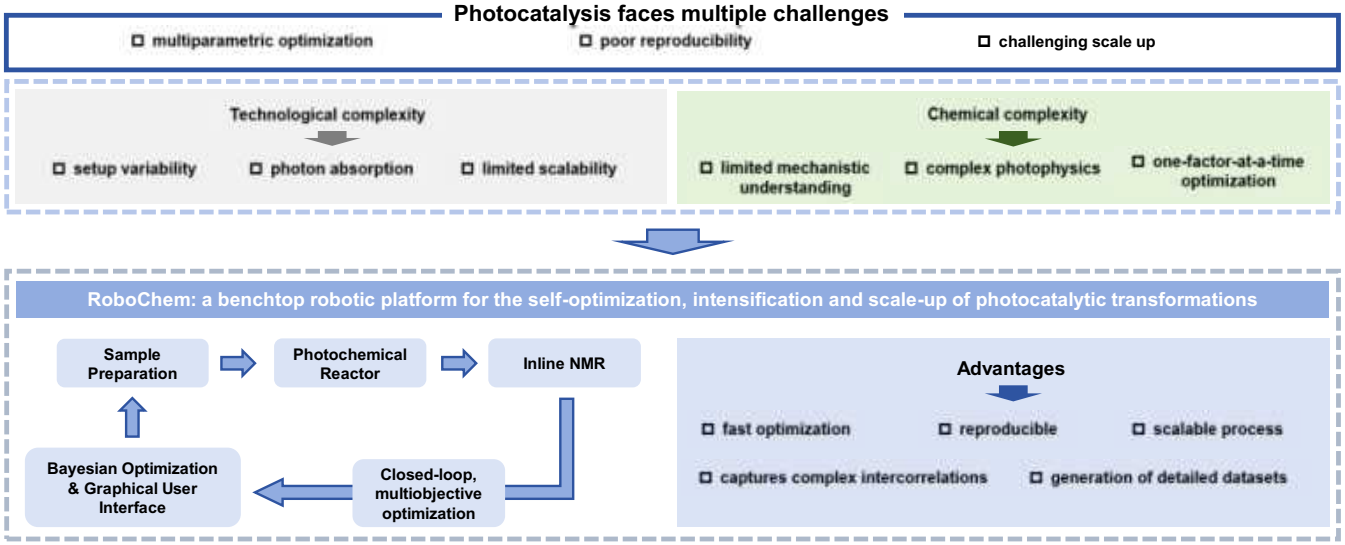

Figure 4. Overview and design idea of RoboChem [4].

2.2 Dr. Timothy Noël's group (University of Amsterdam)

Noël et al. developed an automated continuous-flow platform to accelerate mechanistic studies of photocatalytic reactions [14]. The system integrates fluorescence quenching measurements with Stern-Volmer analysis using a quartz flow cuvette, HPLC pump, tunable light source, and UV-Vis spectrometer [40]. The Python-based graphical user interface (GUI) facilitates straightforward parameter definition and execution, thereby diminishing the maintenance burden associated with the system. Datasets are automatically archived within an SQLite database, enabling expeditious real-time

queries. Moreover, the modular design readily accommodates diverse experimental requirements, while the seamless transition between automated screening and Stern - Volmer analysis modes further augments the system's versatility. Compared with conventional experimental approaches, this method not only enables rapid screening of a multitude of photocatalysts, thereby abbreviating optimization timelines and enhancing reaction yields but also permits more in-depth mechanistic investigations. However, considering the stringent conditions required for air-sensitive photocatalysts, further optimization of the platform's sealing mechanisms and inert atmosphere control is warranted.

Subsequently, Noël et al. created RoboChem - an automated robotic platform combining robotics, ML, and Bayesian optimization for photocatalytic reaction optimization [41]. The three-module system (control, planning, interface) initiates with user-defined reaction parameters through its GUI. Bayesian optimization algorithms guide experimental condition refinement, while inline NMR spectroscopy provides real-time analytical feedback (Figure 4) [41. This closed-loop system iteratively adjusts reaction parameters until achieving optimal conditions, demonstrating efficacy across hydrogen atom transfer and photoredox catalysis applications. The platform reduces expert dependency by automating workflow execution and leveraging ML-driven parameter relationships. While the current system performs well for most applications, substrates with particularly demanding reactivity control requirements present an opportunity for further refinement. Future iterations may benefit from incorporating expanded reactor configurations and advanced ML approaches to enhance optimization precision.

2.3 Dr. Timothy Noël's group (University of Amsterdam)

Jensen et al. developed a reconfigurable continuous flow platform to address experimental inefficiencies in conventional chemistry laboratories 15. The platform integrates modular fluidics and Integrated process analytical technology (PAT) instruments (HPLC, IR, Raman, MS) for autonomous optimization. Standardized reagent selection initiates molecular transformations, while a fluidic system delivers reactants to modular reactors. Real-time PAT data feeds SNOBFIT 42, a BO algorithm that iteratively refines parameters to convergence. This architecture facilitates automated optimization across a range of reaction types, from single-step transformations to multi-step sequences including C-C/N coupling and photocatalytic reactions. The unified graphical interface enables remote monitoring capabilities and supports machine-readable protocol exports. While the system has shown promising results in optimization accuracy and reproducibility, certain complex reaction systems involving specialized substrates may benefit from tailored hardware configurations to achieve optimal performance.

Building on this foundation, Jensen et al. developed a mixed-integer nonlinear programming (MINLP) method for simultaneous optimization of discrete and continuous variables in microfluidic reactions 43 Compared to conventional algorithms, MINLP achieved 37% faster convergence in Suzuki-Miyaura coupling optimizations (60 experiments vs. 95 previously). However, prediction inaccuracies persist for complex reactions with experimental noise sensitivity.

Furthermore, Jensen et al. created a BO-driven platform for multi-step synthesis route development 44. The workflow begins with computer-generated synthetic route validation using computer-aided synthesis planning (CASP) tools 45, 46, followed by BO-directed experimental campaigns with real-time FT-IR/LC-MS monitoring. This approach enabled high-yield optimizations through automated parameter adjustments and reactor reconfigurations (Figure 5) 44. While effectively reducing manual workloads, the system requires expert intervention for chemical compatibility challenges in complex sequences. For example, in the sonidegib synthesis case study, catalyst deactivation caused by byproducts from upstream reactions necessitated intermediate purification and reconfiguration of the reaction order, highlighting the ongoing need for human expertise in handling such issues.

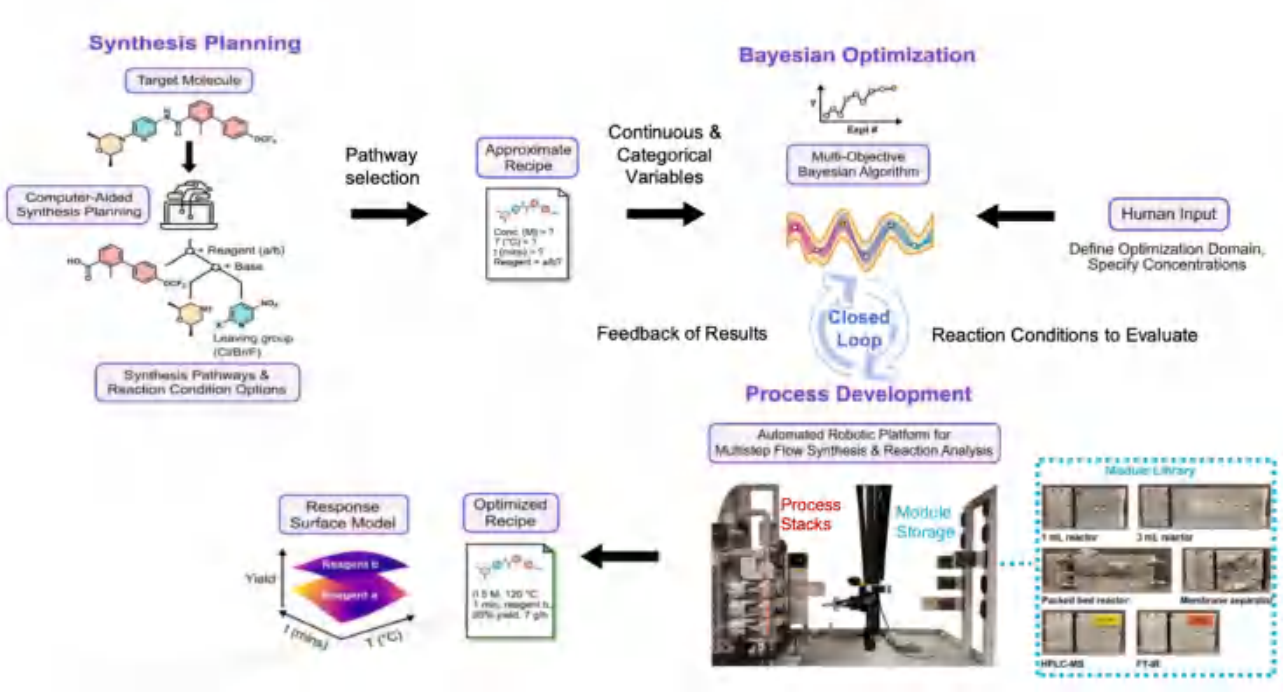

Figure 5. Comprehensive strategy for machine-assisted synthesis planning and process development (encompassing Synthesis Planning, Bayesian Optimization, and Process Development).

2.4 Dr. Milad Abolhasani's group (North Carolina State University)

Abolhasani *et al.* developed QDExer - a modular microfluidic platform for studying perovskite quantum dot (PQD) anion-exchange kinetics [16]. The system integrates Cetoni neMESYS syringe pumps with hydrodynamic focusing micromixers and a 76-port serpentine reaction channel, enabling precise temporal resolution (500 ms - 90 s) through radially distributed sampling. The integration of optical sensors and spectrometers enables real-time reaction monitoring, offering enhanced control and reproducibility relative to conventional batch synthesis methods. While the platform exhibits notable batch-to-batch reproducibility; however, its commercial feasibility for optoelectronic applications necessitates rigorous validation of scalable manufacturability and economic viability. Critical challenges encompass preserving performance homogeneity at industrial production scales through refined process parameter optimization, alongside guaranteeing long-term system stability and uninterrupted operational robustness for viable industrial implementation.

Building on QDExer, the team created an Artificial Chemist system combining neural networks and BO for autonomous PQD synthesis [47]. This self-learning platform optimized 11 quantum dot compositions within 30 hours using <210 mL reagents through real-time spectral analysis and parameter space exploration. The researchers further advanced this framework with an AI-guided system for lead halide perovskite (LHP) quantum dot synthesis [48]. Three key modules operate synergistically: 1) precision precursor formulation (10 reagent streams), 2) temperature-controlled microfluidic reactors, and 3) in-line optical monitoring. The system employs AI algorithms to autonomously explore over 20 million parameter combinations, while a three-phase flow process enables continuous bandgap tuning while eliminating intermediate washing steps. This approach has demonstrated a 90% reduction in material consumption, though broader laboratory adoption may benefit from further optimization of implementation costs. Future development efforts could prioritize cost efficiency and enhanced compatibility with downstream manufacturing workflows.

The culmination of these advances produced AlphaFlow - an RL-driven robotic microfluidic laboratory [49]. Four functional modules process microdroplets through formulation, synthesis, spectral monitoring, and phase separation (Figure 6) [49]. RL serves as the core decision-making framework, enabling the system to autonomously explore high-dimensional parameter spaces through iterative trial-and-error interactions with the chemical environment. By continuously balancing exploration of new reaction pathways and exploitation of known optimal conditions, RL maximizes long-term cumulative rewards across multi-step synthesis processes. This closed-loop system reduces reagent consumption by 65% while maintaining 98% process reproducibility.

Lately, the team engineered Fast-Cat for autonomous optimization of homogeneous catalysis [50]. The four-stage platform (preparation-initiation-operation-Pareto screening) combines deep neural networks (DNN) with BO to balance yield and selectivity. In 1-octene hydroformylation tests, Fast-Cat identified optimal ligand performance frontiers using 2 mmol ligands within one week - 90% faster than conventional methods. To ensure long-term reliability and scalability, the team undertook comprehensive hardware validation and benchmarking. They compared the performance of Fast-Cat with that of traditional batch reactors and meticulously fine-tuned the ML algorithms to produce high-quality experimental data.

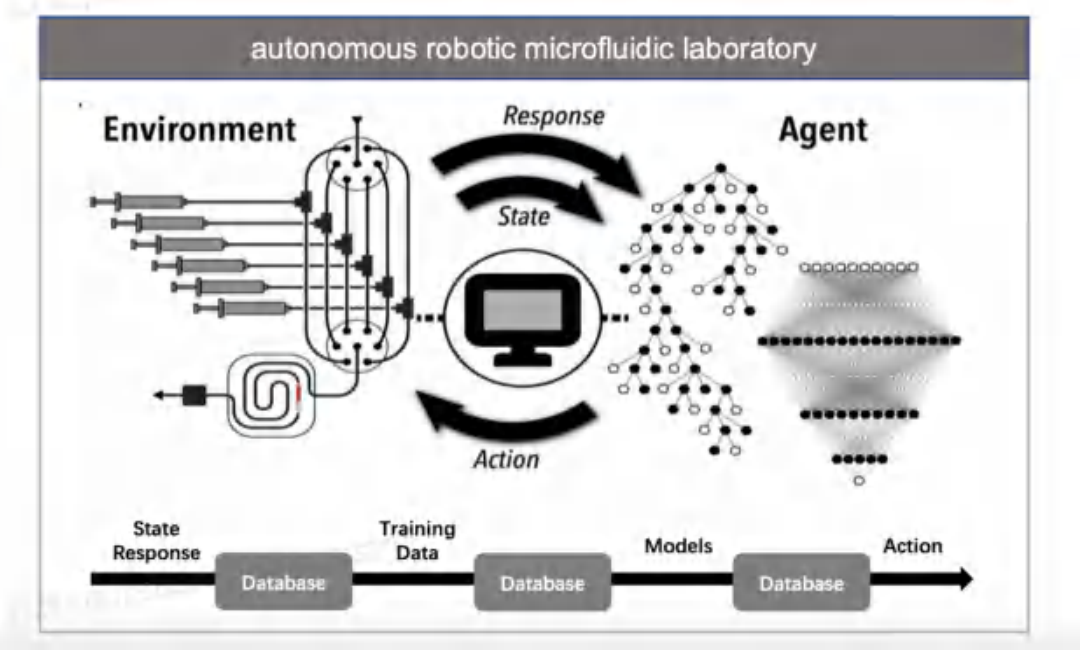

Figure 6. Overview of two kinds of autonomous laboratories a)autonomous robotic microfluidic laboratory called AlphaFlow; b)autonomous catalytic laboratory called Fast-Cat [49].

2.5 Dr. Leroy Cronin's group (University of Glasgow)

Cronin *et al.* developed the Chemputer - a universal automated synthesis platform addressing limitations in small-molecule production [17]. The modular system integrates plug-and-play components through standardized interfaces, enabling autonomous synthesis across multiple reaction classes including iterative cross-coupling and solid-phase peptide synthesis. Its workflow progresses through four phases: 1) automated data collection, 2) statistical

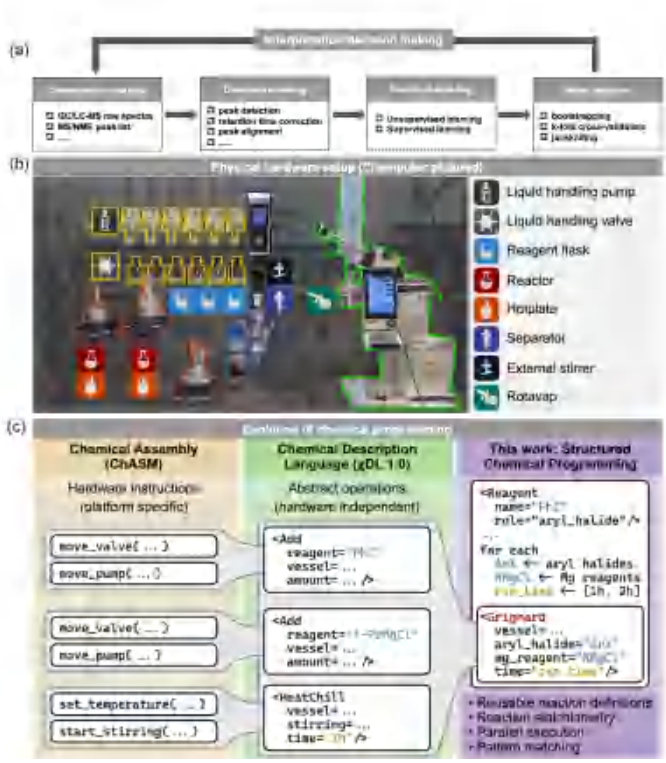

Figure 7. The basic workflow of the Chemputer; b) The hardware setup of the Chemputer; c) The evolution of chemical programming in the Chemputer.

preprocessing, 3) k-fold validated modeling, and 4) algorithmic decision-making (Figure 7a) [17]. This architecture enhances synthetic efficiency by 40% compared to manual methods while maintaining 95% operational reliability. Despite demonstrating multi-molecule synthesis capabilities, high implementation costs and technical complexity hinder cross-disciplinary adoption.

To enhance reaction optimization, the team integrated online NMR spectroscopy for real-time Grignard reaction monitoring [51], employing indirect hard modeling (IHM) [52] and ML to resolve spectral interference in particulate systems (85% parameter accuracy). Subsequent development of χDL - a chemical-specific programming language—enabled cross-platform synthesis standardization [53], validated across four laboratories for reductive amination, esterification, and amide coupling. Modular Schlenk line integration expanded air-sensitive reaction capabilities via tube-in-tube gas-liquid interfaces [54-56], albeit with increased maintenance complexity. Further analytical integration (UV/Vis-NMR) [57] extended mechanistic studies within the Chemputer framework.

Further enhancements to χDL introduced parallel execution and logical operation queues, improving experimental throughput by 300 % [58]. The enhanced system demonstrated successful synthesis of chiral diarylprolinol catalysts, achieving 85% recovery efficiency via automated recycling protocolsThe upgraded system synthesized chiral diarylprolinol catalysts with 85% recovery efficiency through automated reuse protocols (Figures 7b,c) [58]. While these results are promising, further development could focus on incorporating dynamic microenvironment simulation capabilities and real-time feedback mechanisms to better approximate biological system conditions.

2.6 Dr. Andrew I Cooper's group (University of Liverpool)

Cooper *et al.* developed a mobile robotic chemistry platform using BO to autonomously explore 10-dimensional parameter spaces, achieving six-fold higher photocatalytic hydrogen evolution activity than conventional systems [18]. The integrated system combines solid-phase dispensing, photolytic reactors, and gas chromatography (GC) with laser-triangulated spatial positioning and haptic feedback manipulators. This automated configuration achieves experimental

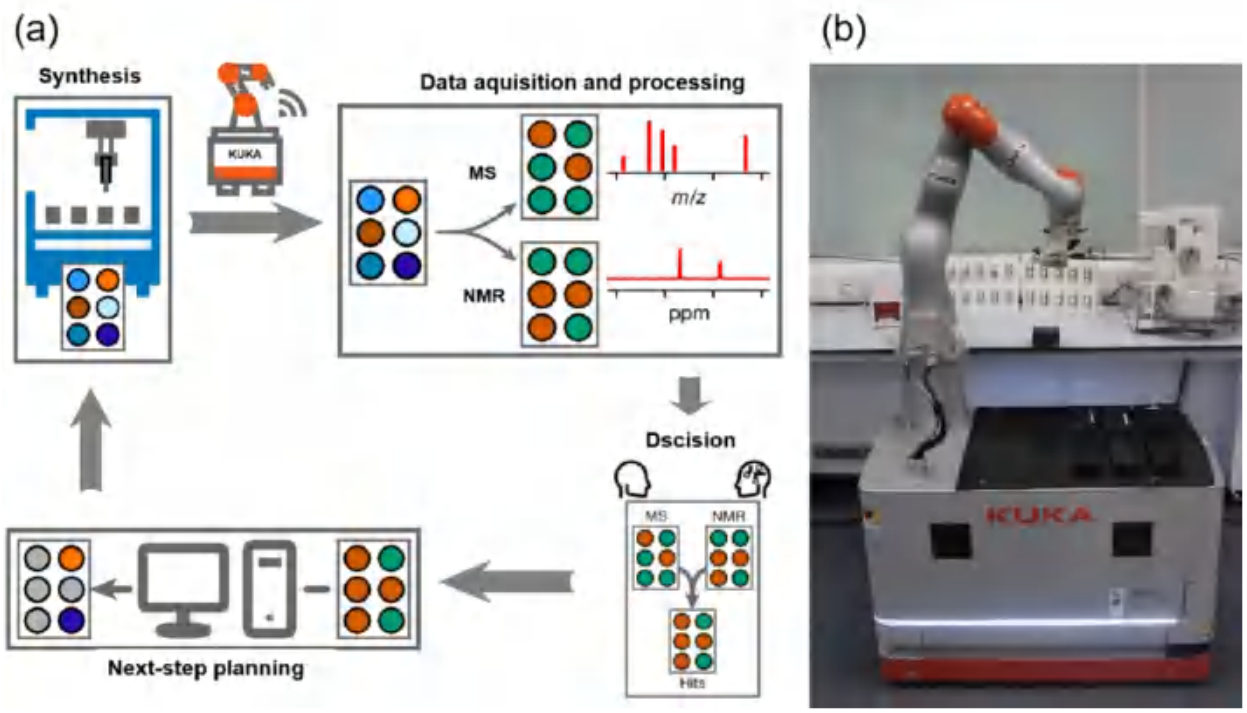

Figure 8. The Chemspeed ISynth workflow (NMR/MS test results: green for pass; orange for fail) [61]. Copyright 2024 Nature under Creative Commons CC-BY license, http://creativecommons.org/licenses/by/4.0/.

throughput approximately 1000 times faster than manual approaches while minimizing subjective human bias. The modular design supports diverse applications from biohazard screening to auditable synthesis processes, while demonstrating remarkable/extensive scalability. Future improvements may include developing chemically informed priors for the BO algorithm and streamlining the GC analysis to maximize the platform's acceleration capabilities.

To enhance platform flexibility, the team created ARChemist - a robotic integration framework using domain-specific language for experimental protocols [59]. Subsequent implementation of a fully automated solid-state chemistry workflow achieved autonomous powder X-ray diffraction (PXRD) characterization through coordinated robotics [60]. The system integrates three specialized units that collectively perform: 1) liquid handling for crystallization phases, 2) automated sample transport and analysis, and 3) specimen preparation, achieving 98% data consistency across characterization cycles. While continuous operation has shown productivity improvements of approximately 80%, further enhancing subsystem reliability could help maximize operational uptime.

Addressing previous systems' decision-making limitations, Cooper *et al.* engineered the Chemspeed ISynth platform for end-to-end automated synthesis [61]. Modular units enable complex multistep reactions with mobile robots (± 0.12 mm positioning accuracy) transferring samples to analytical instruments (Figure 8) [61]. Wireless data transmission to a central database supports real-time decision-making, achieving 99% process automation and 95% data fidelity. The platform's modularity is enhanced by standardized communication protocols and customizable Python scripts, allowing adaptation to diverse workflows without hardware overhauls. A robust data management strategy systematically stores raw analytical data and decision logs, streamlining troubleshooting and future upgrades. While dramatically speeding discovery workflows, the system strategically preserves human involvement for supramolecular characterization tasks and performance tuning, areas where future automation could provide additional benefits. 2.7 Dr. Jason Hattrick-Simpers's group (Autonomous Discovery of Alloys)

Hattrick-Simpers *et al.* developed CAMEO - a Bayesian optimization-driven autonomous system for accelerated materials discovery [19]. The closed-loop platform integrates three core components: 1) physics-informed machine learning for structure-property analysis, 2) active learning for optimal experiment selection, and 3) synchrotron-integrated high-throughput X-ray diffraction (XRD) characterization (Figure 9) [19]. This framework achieves 85% phase diagram mapping accuracy through iterative human-AI collaboration, reducing discovery timelines by 70% compared to conventional methods. While demonstrating improved interpretability via expert knowledge integration, the system's autonomy decreases by 40% when requiring manual validation. To advance the field, expanding materials databases and enhancing the integration of machine learning with fundamental physical principles could significantly improve the predictive accuracy and performance optimization of multicomponent systems. Given the requirement for long-term stable operation during iterative experimentation, additional refinements in system architecture and hardware robustness will be essential to ensure sustained reliability and experimental reproducibility.

This team also developed a high-throughput scanning droplet cell platform [62]. The platform combines scanning droplet cells with GP modeling to optimize coating performance through 200-cycle experiments. This Bayesian active learning system represents a significant advance in efficient parameter exploration, delivering 90% information gain across competing optimization targets. The methodology establishes a strong basis for future development, where enhanced incorporation of physical principles may both deepen mechanistic understanding and optimize the training dataset size needed for reliable generalization. However, the non-modular architecture of the platform presents significant challenges for functional scalability and system extensibility.

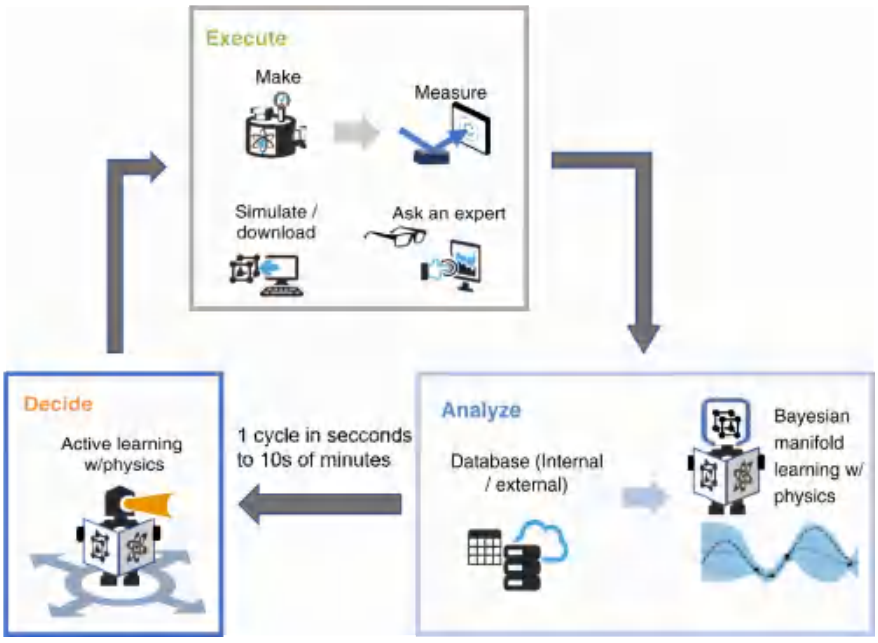

Figure 9. The scientific research process from experiment execution to data analysis, and then to active learning and decision-making based on physics with CAMEO [19]. Copyright 2020 Nature Communications under Creative Commons CC-BY license, http://creativecommons.org/licenses/by/4.0/.

2.8 Dr. Yi Luo's group (University of Science and Technology of China)

While existing AI systems and robots exhibit specialized chemical capabilities, holistic scientific research remains challenging. Luo *et al.* introduced the AI-Chemist [20], an autonomous system capable of executing core chemical research tasks. The system integrates a service platform, mobile robots, intelligent workstations, and a computational core to establish an autonomous theory-experiment-optimization loop. Multimodal knowledge extraction (ML/cloud database access/hypothesis generation) drives automated protocol generation, executes experimental protocols through robotic synthesis and high-throughput testing, and iteratively refines hypotheses via BO and ML-driven simulations, enabling autonomous self-optimization in chemical discovery (Figure 10) [20]. Validation studies demonstrated its ability to identify optimal concentrations of biocompatible aggregation-induced emission (AIE) molecules [63-65], optimize hydrogen doping ratios for metal oxide photocatalysts, and discover high-performance non-precious metal oxygen evolution reaction (OER) electrocatalysts [66-69]. These achievements highlight its potential for accelerating scientific discovery. This AI-driven platform demonstrates significant potential for chemical discovery. Future development requires workstation scalability enhancements, computational architecture upgrades, and deeper domain knowledge integration to address evolving research challenges.

Figure 10. The workflow of AI-Chemist and related laboratory equipment. From the formulation of a scientific question to its processing by a service platform, followed by the execution of experimental operations by a mobile robot, and finally the analysis and theoretical simulation of data by a computational brain [20].

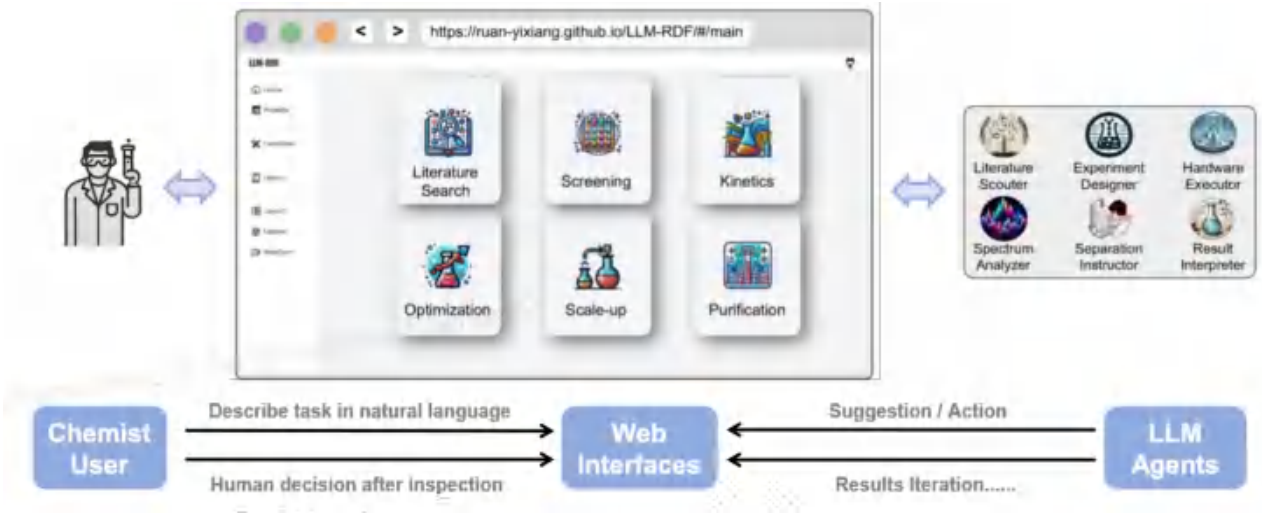

Figure 11. The interaction between Chemist User and LLM Agents is achieved through the Web interface [73].

The AI-Chemist's capabilities extend beyond these demonstrations. Luo *et al.* deployed AI-Chemist to autonomously synthesize OER catalysts from Martian meteorite analogs [70]. Integrating ML with first-principles calculations and experimental validation, the system efficiently identified optimal catalyst compositions from over 3×10^6 candidates. Compared to traditional trial-and-error methods, AI-Chemist accelerated the discovery process by several orders of magnitude, reducing the time and resources required for

optimization. The fully autonomous workflow spanned meteorite processing, catalyst synthesis, characterization, and performance testing, demonstrating high throughput with intelligent automation. However, additional validation under combined Martian stressors remains essential for practical implementation.

The AI-Chemist was further applied to accelerate the discovery of high-entropy alloy (HEA) nanozymes through integrated computational-experimental workflows [71]. By integrating BO with GPT-4 [72], the research team successfully identified high-entropy-alloy nanozymes with significantly enhanced catalytic efficiency in just 12 optimization steps. These nanozymes achieved a catalytic efficiency (Vmax/KM) of 2.97 × 10^{-3} s^{-1}, which is one order of magnitude higher than that of the natural enzyme horseradish peroxidase (HRP) with a catalytic efficiency of 2.9 × 10^{-4} s^{-1}. Additionally, the research team introduced redundant designs in key components and modules, effectively enhancing the reliability of the system. The remarkable compositional diversity of HEAs and their complex catalytic mechanisms present exciting opportunities for further refinement of theoretical models.

2.9 Dr. Yiming Mo's group (Zhejiang University)

Mo *et al.* developed a framework termed AROPS for chemical reaction optimization, enabling parallelized experimental task allocation across multiple reactors/analyzers [21]. Users define reaction condition design spaces and prepare reagents. The system initializes via Latin hypercube sampling. The optimization cycle includes reaction execution, HPLC analysis, GP model updating, and experiment pruning based on probability of improvement (PI) criteria. Parallel scheduling proposes new candidates filtered by Euclidean distance and PI scores, iterating until the PI stopping criteria are met to yield optimized conditions. The integration of BO with adaptive parallel scheduling achieves high equipment utilization efficiency. While the current PI mechanism performs well for continuous and mixed-variable spaces, its effectiveness for purely categorical design spaces could be further enhanced by improving GP model accuracy. Future work to develop advanced molecular descriptors or alternative modeling frameworks may help extend the system's predictive capabilities to broader variable types.

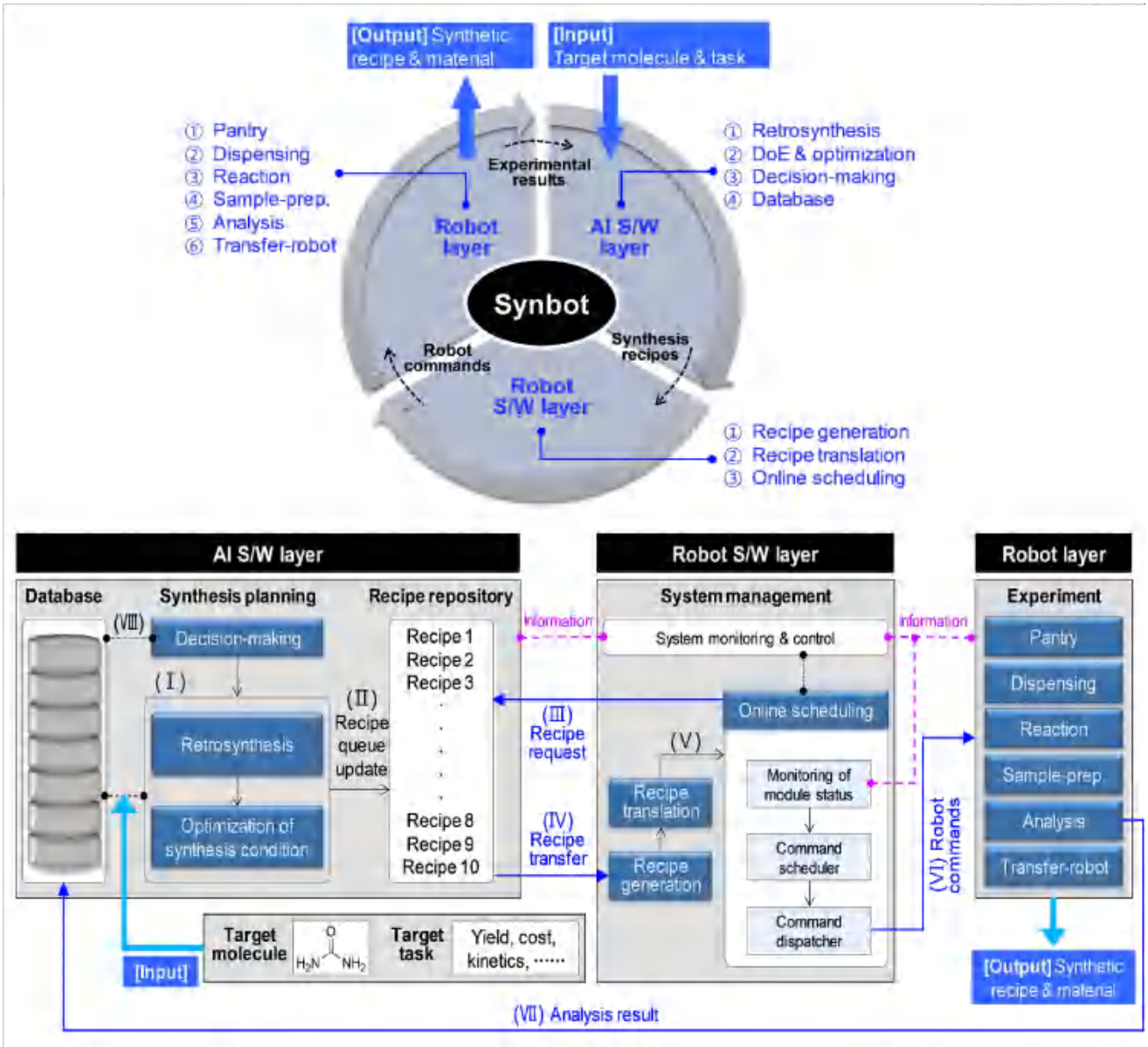

Figure 12. Synbot structure and working principle (including AI S/W layer, Robot S/W layer, and Robot layer) [22]. Copyright 2023 Science under Creative Commons CC-BY license, http://creativecommons.org/licenses/by/4.0/.

Building on AI advancements, Mo *et al.* further developed LLM-RDF [73], an automated chemical synthesis platform leveraging LLMs. Built on GPT-4 [72], LLM-RDF integrates six specialized agents: Literature Scouter, Experiment Designer, Hardware Executor, Spectrum Analyzer, Separation Instructor, and Result Interpreter, to orchestrate end-to-end synthesis workflows from literature search to product purification (Figure 11) [73]. This design lowers the barrier to automation applications by eliminating conventional programming requirements. For instance, in the optimization of aerobic alcohol oxidation conditions, LLM-RDF achieved a product yield of 94.5%, significantly higher than the approximately 70% yield obtained through traditional methods. Additionally, the platform reduced the number of experiments required for optimization from over 50 to just 26, thereby accelerating the reaction optimization process. However, its reliance on proprietary large language models (LLMs) raises concerns regarding reproducibility, transparency, and data security.

2.10 Dr. Youn-Suk Choi's group (Samsung Advanced Institute of Technology)

Research on conventional functional organic materials has long relied on laborious and inefficient empirical approaches. To address this limitation, Choi *et al*. developed "Synbot" - an intelligent robotic platform for comprehensive organic synthesis automation [22]. This system adopts a tripartite architecture consisting of cognitive computing modules, robotic control systems, and automated instrumentation, enabling seamless integration of synthetic route design and experimental implementation (Figure 12) [71]. The modular architecture of the Synbot system markedly enhances its scalability, while automated operations effectively minimize human error. Moreover, the precise control of reaction conditions significantly improves reaction yields. For instance, in the case of Suzuki coupling reactions (M1), the Synbot achieved a conversion yield of 100% in its first trial within a search space of 2722 cases, which is notably higher than the reference yield of 86.5% reported in the literature. For Buchwald amination reactions (M2), the Synbot achieved a 100% conversion yield in the 36th and 37th trials, compared to the reference yield of only 15.0% reported in the literature. Similarly, for the synthesis of another Buchwald amination reaction (M3), the Synbot achieved a target conversion yield of 80% in the 42nd trial, which is a substantial improvement over the reference yield of 50.9% reported in the literature. These results collectively demonstrate that the Synbot system is capable of achieving significantly higher yields and substantially reduced reaction optimization times compared to traditional methods. However, despite its modular architecture, the hardware cost remains a significant factor when scaling up, and the system's substantial footprint (9.35 m × 6.65 m) poses challenges for its application in many standard laboratories.

2.11 Dr. Dominik Dworschak's group (Helmholtz Institute Erlangen-Nuremberg)

To address nonstandard data management and restricted sharing in materials research, Dworschak *et al.* developed an integrated data management system utilizing structured query language (SQL) databases [23]. This system implements comprehensive lifecycle management of experimental data, encompassing acquisition, analytical processing, visualization, and dissemination, thereby significantly advancing research reproducibility and efficiency. In electrochemical synthesis processes, systematic optimization of current density increased product yield from 70% to 90%. Similarly, in electrodeposition studies, the system identified optimal parameters within merely three days, substantially reducing experimental duration. To ensure long-term reliability, the system employs a robust backup strategy with daily full backups and regular incremental backups stored across multiple geographic locations. It also features a modular design that allows for easy addition of new functionalities. Ongoing work aims to develop more researcher-friendly implementations that maintain these advantages while broadening accessibility.

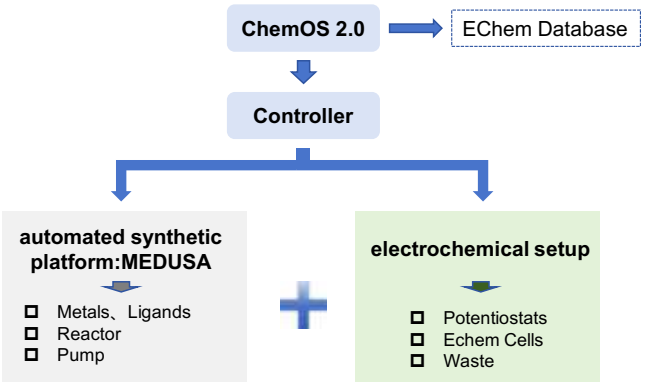

Figure 13. Composition of the automated platform (comprising the automated synthetic platform and electrochemical setup) [74].

Dworschak *et al.* also established an automated electrochemical synthesis-analytics platform through the integration of custom-built electrochemical instrumentation with robotic synthesis systems, achieving cost-effective autonomous experimentation [74]. The modular, expandable discovery and understanding synthesis apparatus "MEDUSA" executes precise stoichiometric mixing of metal-ligand solutions before transferring aliquots to parallel electrochemical cells. Electrochemical characterization employs an open-source workstation implementing cyclic voltammetry (CV) and differential pulse voltammetry (DPV) protocols. Experimental data streams are processed in real-time through ChemOS 2.0 [35], with synchronized storage in a structured database (Figure 13) [74]. The system implements quality control through reference electrode calibrations and makes autonomous experimental decisions to ensure operational continuity. Using this framework, the researchers successfully compiled a repository comprising 400 chronoamperometric datasets from 100 unique metal-ligand complexes derived from 10 metal ions and 10 ligands. With its modular, scalable architecture and cost-efficient design, the platform provides valuable flexibility for diverse electrochemical investigations. Present implementations show particular strength in aqueous systems, while ongoing refinements aim to expand compatibility with organic electrolytes and simplify the user experience for researchers across disciplines.

2.12 Dr. Kuangbiao Liao's group (Guangzhou Laboratory)

Addressing the limitations of current models in molecular structure-aware generative tasks, Liao *et al.* engineered SynAsk: a multimodal language processing platform with domain-specific capabilities for organic synthesis planning and analysis [24]. The workflow initiates with multimodal input processing, accepting vocal commands or textual descriptions. Inputs are parsed and decomposed into

executable subtasks using a transformer-based architecture. The LangChain framework [75] integrates cheminformatics tools for molecular retrieval, reaction prediction, retrosynthesis, literature extraction, and advanced modules (YieldPredict and Retrosynthesis). For example, during yield prediction, the LLM extracts substrate details from prompts to classify reaction types, and YieldPredict employs ML models/reaction templates to evaluate yield feasibility, returning optimized conditions. Retrosynthesis recursively designs synthetic routes from target molecules to purchasable precursors, outputting pathways in text/image formats (Figure 14) [24]. the architecture combines LLM fine-tuning with external tool orchestration, effectively enhancing domain-specific capabilities and practical utility. While opportunities remain for improvement—such as optimizing yields for intricate transformations, and reducing retrosynthesis computation times—this platform marks meaningful progress in automating chemical research workflows.

3. Concluding remarks and future outlook

The advent of autonomous laboratories is driving a profound transformation in chemical synthesis. We present an overview of recent advancements in autonomous laboratory systems from leading global research groups, focusing on their applications in synthetic chemistry (Table 1).

BO algorithms are particularly well-suited for complex chemical optimization tasks [9,76], such as material discovery and drug development, owing to their ability to handle uncertainty, noise, and high-dimensional search spaces. RL algorithms, in contrast, demonstrate superior performance in multi-step decision-making processes [10,77,78], enabling efficient reaction path planning and optimization in applications such as quantum dot synthesis and heterogeneous catalyst screening. Meanwhile, neural networks and DNN leverage their robust pattern recognition capabilities to analyze multivariate experimental data and predict intricate structure-property relationships. The modularity and computational efficiency of these algorithms further determine their adaptability: highly modular systems facilitate flexible integration across diverse experimental workflows, while computationally efficient implementations enable rapid exploration of complex chemical spaces, significantly accelerating the discovery of novel materials and synthetic pathways. Thus, the judicious selection of algorithms based on specific chemical requirements is critical for optimizing the performance and scalability of autonomous laboratory systems.

Early systems reduced repetitive task burdens through rudimentary mechanical systems and early automation, yet retained significant human oversight and high operational costs. Recent progress in AI algorithms and ML has enabled autonomous laboratories to achieve unprecedented predictive accuracy in controlling complex reaction processes through the integration of computational models, algorithms, and large-scale data analytics. This synergy enhances synthetic efficiency while minimizing human-induced errors, elevating chemical research to new levels of sophistication.

As autonomous laboratories evolve, modular design and flexible system architectures are becoming critical directions for advancing their capabilities. Modular experimental platforms enable scientists to configure and integrate functional units (such as synthesis modules, analytical instruments, and robotic systems) tailored to experimental requirements. For instance, mobile robotic systems integrated with existing laboratory equipment facilitate efficient workflows without incurring the high customization costs associated with traditional automated laboratories [79]. This modular approach reduces costs while enhancing operational flexibility and scalability, allowing laboratories to address diverse chemical synthesis challenges.

Furthermore, the integration of closed-loop feedback mechanisms with ML algorithms is progressively becoming a standard feature in autonomous laboratories [80]. Through closed-loop systems, experimental protocols can be dynamically optimized in real time using continuous data streams, significantly enhancing synthesis efficiency and product quality. This mechanism relies on ML algorithms with real-time analytical and decision-making capabilities, enabling dynamic adjustments to experimental parameters based on live data, thereby improving efficiency and success rates. Concurrently, advancements in explainable AI (XAI) [81,82], are enabling researchers to better interpret autonomous systems' decision-making processes, shifting their roles from routine experimentation to supervising outcomes and deriving scientific insights.

Despite their transformative potential for addressing critical challenges across energy, medicine, and materials science, autonomous laboratories still face significant hurdles that hinder their widespread adoption. Key challenges include interoperability bottlenecks among heterogeneous hardware and software systems, disrupting seamless workflow integration; the inherent "black box" nature of advanced ML models, which complicates reproducibility and erodes trust in automated decision-making; and prohibitive initial costs coupled with specialized maintenance demands, which disproportionately limit accessibility for smaller research institutions. To overcome these barriers, strategic interventions are required. First, the development and adoption of universal communication protocols (such as SiLA2 [26] or AnIML [83]) could standardize cross-platform compatibility, thereby streamlining interoperability. Second, hybrid human-AI validation systems, in which critical synthetic steps undergo dual verification, could enhance reliability while preserving the efficiency gains of automation. Third, decentralized resource-sharing models, such as cloud-based simulation platforms and shared equipment hubs, could democratize access by reducing capital expenditures and operational costs. Concurrently, fostering interdisciplinary training programs and promoting open-source platforms aligned with FAIR [84,85], (Findable, Accessible, Interoperable, Reusable) data principles are critical to ensuring transparency, scalability, and the equitable advancement of autonomous laboratory technologies. Addressing these challenges through collaborative, community-driven efforts will not only refine system architectures and cost-effectiveness but also establish ethical frameworks for data management, thereby ultimately accelerating the integration of autonomous systems into mainstream scientific research In summary, autonomous laboratories represent a transformative shift in chemical synthesis, offering unprecedented opportunities while requiring careful addressing of technical and ethical challenges. As these systems mature, they will become foundational to scientific discovery, driving innovation across disciplines.

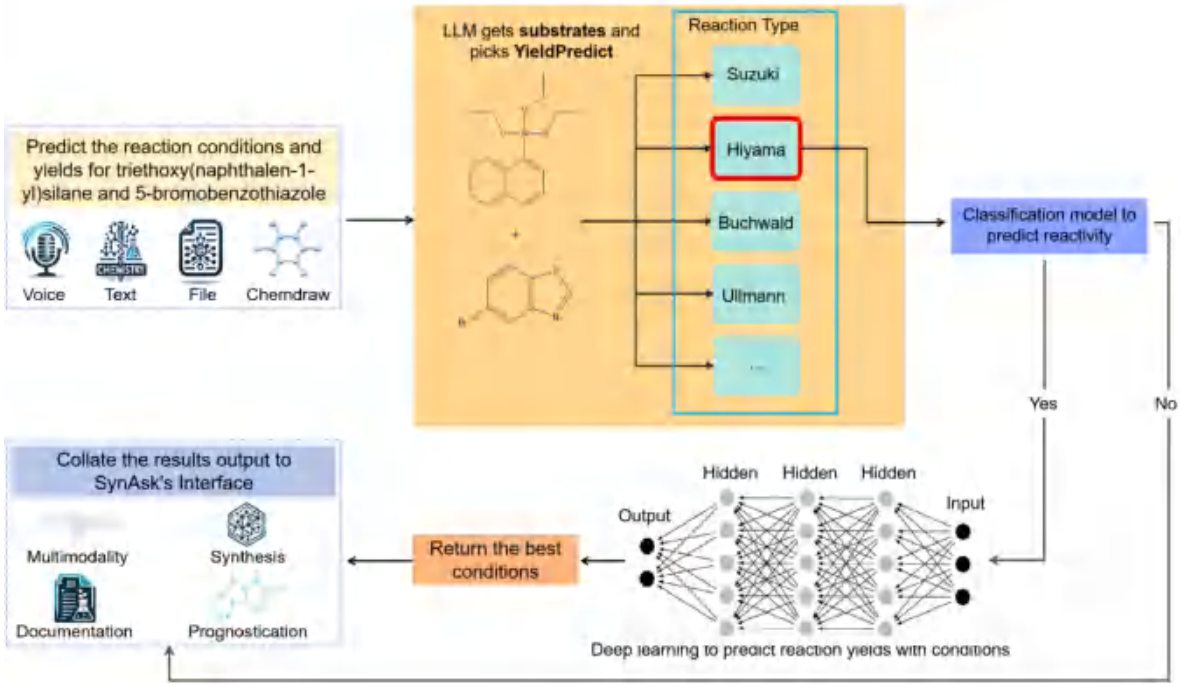

Figure 14. An example of the YieldPredict tool workflow for predicting the reaction yield of triethoxy(naphthalen-1-yl)silane and 5-bromobenzothiazole [24]. Copyright 2025 Chemical Science under Creative Commons CC-BY license, https://creativecommons.org/licenses/by/3.0/.

Table 1. Performance comparison of autonomous laboratories developed by different research teams.

Research institution	Main achievements	Model	Degree of modularity	Operating efficiency	Adaptability to chemical scenarios
University of Toronto	ChemOS [13,25]	BO	High	High	Material discovery, drug development
	Ada [34]	BO	Medium	High	
	ChemOS2.0 [35]	BO	High	High	
	CLT [38]	BO	Medium	Medium	
	Cloud-based experimental planning platform [39]	GNN, GP	High	High	
University of Amsterdam	Automated continuous-flow platform [14]	-	Medium	High	Photocatalytic reaction
	RoboChem [41]	BO	Medium	High	
Massachusetts Institute of Technology	Reconfigurable continuous flow platform [15]	-	Medium	High	Flow chemistry
	MINLP [43]	-	High	High	
	BO-driven platform [44]	BO	High	High	
North Carolina State University	QDExer [16]	-	Medium	Medium	Quantum dot synthesis, catalysis
	Artificial Chemist system [17]	NN, BO	High	High	
	AlphaFlow [49]	RL	High	High	
	Fast-Cat [50]	DNN, BO	High	High	
University of Glasgow	Chemputer [58]	-	High	Medium	Organic synthesis
University of Liverpool	Mobile robotic chemistry platform [18]	BO	High	High	Material discovery, catalysis
	ARChemist [59]	BO	High	High	
	Chemspeed ISynth platform [61]	-	High	High	
Autonomous Discovery of Alloys	CAMEO [19]	BO	Medium	Medium	Alloy development, electrochemistry
	High-throughput scanning droplet cell platform [62]	GP	Medium	Medium	
University of Science and Technology of China	AI-Chemist [20]	NN, BO, GPT-4	High	High	Multidisciplinary chemical research
Zhejiang University	AROPS framework [21]	GP	High	High	Organic synthesis
	LLM-RDF [73]	GPT-4	High	High	
Samsung Advanced Institute of Technology	Synbot [22]	-	High	High	Organic synthesis
Helmholtz Institute Erlangen-Nuremberg	Integrated data management system [23]	-	High	High	Electrochemistry
	Automated electrochemical synthesis-analytics platform [74]	BO	Medium	Medium	
Guangzhou Laboratory	SynAsk [24]	LLM	High	High	Organic synthesis

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Appendix

Full name	Abbreviation
artificial intelligence	AI
Bayesian optimization	BO
Reinforcement learning	RL
machine learning	ML
hole-transporting materials	HTMs
closed-loop transfer	CLT
organic solid-state lasers	OSL
graph neural networks	GNN
graphical user interface	GUI
process analytical technology	PAT
mixed-integer nonlinear programming	MINLP
computer-aided synthesis planning	CASP
perovskite quantum dot	PQD
lead halide perovskite	LHP
deep neural networks	DNN
indirect hard modeling	IHM
variable time normalization analysis	VTNA
gas chromatography	GC
powder X-ray diffraction	PXRD
high-throughput virtual screening	HTVS
X-ray diffraction	XRD
gaussian process	GP
oxygen evolution reaction	OER
aggregation-induced emission	AIE
high-entropy alloy	HEA
horseradish peroxidase	HRP
probability of improvement	PI
large language models	LLMs
structured query language	SQL
cyclic voltammetry	CV
differential pulse voltammetry	DPV
explainable artificial intelligence	XAI