

Engineering principles for self-driving laboratories

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The chemical engineering field stands at a pivotal moment of transformation, driven in part by the convergence of process automation, robotics and artificial intelligence into self-driving laboratories (SDLs) to accelerate scientific discoveries. This Comment explores how process intensification principles can guide the development of SDLs to accelerate innovation while ensuring efficient use of resources across the multiscale chemical domain.

Chemical engineering has been a driving force behind the industrial revolution, enabling transformative innovations ranging from the discovery and manufacture of life-saving pharmaceuticals to the large-scale production of essential goods. These advancements have profoundly enhanced global quality of life by enabling access to critical products and services. However, the rapid expansion of chemical manufacturing has also introduced substantial environmental and resource consumption challenges, including climate change, ecosystem degradation and the depletion of finite resources¹. This urgency is further underscored by time-sensitive energy, environment and healthcare targets, necessitating swift and deliberate action. Meeting these challenges requires global collaboration efforts and rethinking scientific innovation. Self-driving laboratories (SDLs) have recently emerged as a promising tool to enhance research efficiency and speed. However, their development must be informed by a forward-looking approach that aligns with broader sustainability and societal goals.

SDLs offer an integrated framework for accelerating research in domains where the scale and complexity of experimental design surpass what individual researchers can feasibly manage. By automating the design–make–test–analyze cycle, SDLs leverage both prior knowledge and simulated experiments, dynamically refining their knowledge model in real time with minimal human supervision. Central to this workflow is an artificial intelligence (AI)-assisted decision-making system that orchestrates the entire process – analyzing incoming data, pinpointing promising experimental pathways and iteratively updating predictive models. SDLs have demonstrated success in rapid discovery, optimization, process development and manufacturing of advanced materials and (bio)molecules². A key aspect of the SDL operation lies in the interplay between its digital and physical components: physical modules handle (bio)chemical formulation, transport, synthesis, purification and characterization, while digital modules automate data

collection, analysis and experimental design. This closed-loop coordination of (qu)bits and atoms substantially boosts the speed, precision and information density of scientific research³ (Fig. 1).

Combining human expertise with AI agents for decision-making can improve the efficiency of navigating vast chemical landscapes within SDLs. By refining strategies in real time, the AI agent of SDLs identifies the most promising experimental routes in high-dimensional chemical spaces that would otherwise be intractable². The AI agent's decision-making performance depends on robust, unbiased and reproducible data. Reliable datasets result from systematically designed experiments, and they guide predictive models. In this way, data and AI form a feedback loop that fuels scientific progress. As Thomas Kuhn observed in *The Essential Tension*⁴, true scientific breakthroughs often arise not from deeper pattern recognition alone, but from the creative disruption of established frameworks – suggesting that future advances may require new forms of AI or computing, capable of transcending existing paradigms.

Extending a chemical engineering analogy, each 'process unit' within an SDL should be optimized not only to produce valuable materials but also to generate high-quality, information-rich datasets that enhance the AI agent's predictive power. The chemical engineering toolbox includes several frameworks that have transformed the way we design, assess and improve chemical processes in terms of efficiency, safety and sustainability. Among these, process intensification (PI) stands out as a systematic framework influencing all scales of chemical engineering innovations. A process can be viewed as any task or series of tasks necessary to accomplish a goal, in the traditional chemical engineering standpoint; such tasks can be categorized by scale or by unit operations or 'process units' (for example, storage, transport, mixing, separation, reaction and characterization). Intensifying a process translates to achieving intended goals with drastically enhanced performance while minimizing required resources – such as materials, time and capital – or any other relevant process metric. Taken holistically, PI has driven the development of novel equipment, methods and their synergistic integrations across different scales⁵.

In this Comment, we briefly discuss how to harness PI principles for designing resource-efficient SDLs for a given research problem. The classical vision of PI has been established through four fundamental principles: (1) maximizing the effectiveness of intra- and intermolecular events; (2) giving each molecule the same processing experience (uniform reaction conditions); (3) optimizing driving forces while maximizing specific surface areas; and (4) maximizing synergistic effects from partial processes. These principles are traditionally achieved through four fundamental approaches in different domains: structure (spatial), energy (thermodynamic), synergy (functional) and time (temporal)⁵. The convergence of SDLs and PI gives rise to the concept of data intensification. Through the iterative nature of SDLs' closed-loop decision-making, data intensification strategies lead to substantial

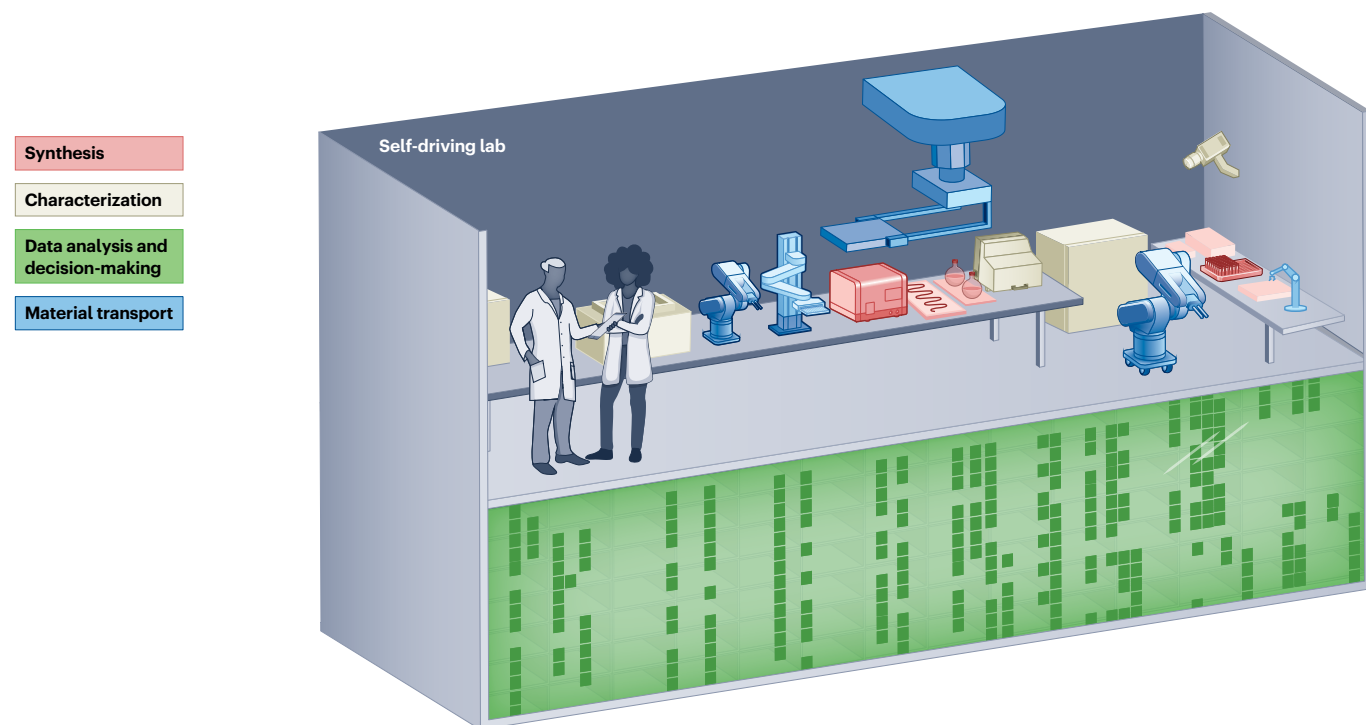


Fig. 1 | An SDL architecture. Integration of physical and digital components of SDLs. The virtual model of the SDL highlights the synergistic interaction of key laboratory process units, encompassing autonomous data analysis and decision-making (green), synthesis (pink), material transport (blue) and characterization (beige). SDLs integrate traditionally siloed physical laboratory environments,

including chemical synthesis laboratories, data analysis and decision-making hubs, and analytical characterization facilities into a compact, fully integrated workspace capable of executing autonomous design–make–test–analyze cycles with enhanced efficiency and precision.

improvements in experimental data quality across multiple metrics: amount (volume), rate (cost per data), reliability (precision) and scope (capability space coverage). Data utility and efficiency can be drastically improved from the standard gridded-domain search by employing AI-guided optimization campaigns that leverage prior knowledge that influences a decision-making policy to propose a next experiment (or trajectory of experiments) that increases the likelihood of meeting a task's goal (or objective). Furthermore, data itself could be considered both an approach to and an outcome of PI – better data enables better understanding and control of molecular events, processing conditions, driving forces and synergistic effects, which in turn generates higher-quality data for its decision-making process unit (Fig. 2).

SDLs designed by chemical engineering principles leverage the PI frameworks through integration of the four fundamental approaches – structure, energy, synergy and time – to optimize experimental workflows and accelerate research. When rate-limiting phenomena are identified in a reaction process unit – whether mass transfer, heat transfer, reaction kinetics or photon flux – these are addressed through the optimization of driving forces and enhancement of specific surface areas⁶. A prime example is the widespread adoption of microreactor technology across SDLs, from materials discovery to pharmaceutical process development. These miniaturized reactors (Fig. 2) reduce reaction volumes from milliliters to microliters while providing unprecedented control over reaction conditions through enhanced heat and mass transfer rates. The high surface-to-volume ratio of microreactors enables rapid mixing and efficient heat transfer, leading to improved

yields and selectivities. Furthermore, parallelization of miniaturized batch reactors allows for faster chemical domain exploration in micro-well plate reactors, while continuous flow synthesis can exploit transient data to approximate steady-state conditions owing to instantaneous changes in process parameters⁷. When integrating the intensified reactor unit with the characterization unit, one should choose a characterization timescale that matches the upstream process, to avoid a bottleneck in the SDL workflow. To achieve this, most SDLs choose a multi-modal and multi-fidelity strategy (Fig. 2), combining rapid in situ measurements for real-time decision-making with more detailed ex situ characterization for comprehensive material analysis⁸. This approach allows for rapid screening and process control while still gathering the detailed data needed for fundamental studies and validation. PI-empowered SDLs can reduce materials and molecular discovery and development timelines by orders of magnitude compared with the status quo while minimizing resource consumption and waste generation⁹.

When a process requires work-up steps such as washing, separation, or other pre- and/or post-treatments, SDLs can benefit from maximizing synergistic effects between partial processes through integration and simplification of process units. For example, AlphaFlow, a self-driven fluidic laboratory that combines droplet-based microfluidics, in-line phase separation and real-time analytics for autonomous multi-step synthesis, exemplifies this integration¹⁰. AlphaFlow was tasked with the discovery and optimization of colloidal atomic layer deposition – a precision synthesis technique for growing hetero-nanostructures

Principles of process intensification

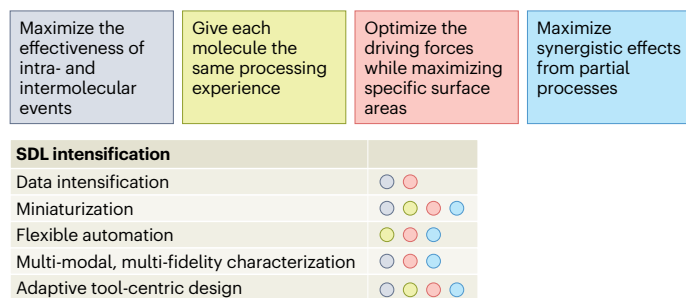


Fig. 2 | Intensification of SDL process units. Mapping the intensification of SDL process units (data analysis and decision-making, synthesis, material transport, and characterization) to fundamental PI principles. Data intensification: AI-guided sampling of the parameter space leverages prior knowledge to inform a decision-making policy, shifting from a conventional grid search approach to an optimized trajectory for subsequent experiments. This data-driven intensification strategy substantially reduces the number of experiments required to achieve a desired objective, enhancing efficiency and accelerating discovery. Miniaturization: synthesis miniaturization enhances PI by reducing material consumption, improving control over reaction conditions and enabling the simultaneous exploration of a broader chemical space – both in batch and flow – compared with larger-scale alternatives. Flexible automation: transitioning from manual to automated material transport techniques – utilizing pumps, robotic arms and other automation technologies – reduces variability in controlled parameters while substantially increasing experimental throughput. Multi-modal, multi-fidelity characterization: reliance on single high-fidelity characterization techniques can create bottlenecks in the experimental cycle time of SDLs. Adopting a multi-modal characterization approach with varying levels of fidelity enables the rapid acquisition of lower-precision data to capture general trends for automated decision-making while concurrently collecting high-fidelity data to validate or refine the decision-making policy. Such a data-intensification strategy optimally balances the selection of multi-modal, multi-fidelity characterization techniques to enhance efficiency. Adaptive tool-centric design: modular tools integrated within a shared framework allow flexible, reconfigurable experimentation, thus supporting faster workflow creation and enabling processes to evolve through layered integration and continuous refinement.

with monolayer control. AlphaFlow's transport process unit was controlled through modular fluidic micro-processors, enabling seamless integration of formulation, synthesis, characterization and phase separation operations within an end-to-end, automated workflow (Fig. 2). Using reinforcement learning, AlphaFlow autonomously explored and optimized a 40-dimensional parameter space, consuming less than 1/500th of the materials required by conventional methods while generating data at a rate equivalent to over 100 researchers working simultaneously. Without any prior knowledge of conventional colloidal atomic layer deposition sequences, AlphaFlow discovered a novel, more efficient multi-step synthetic route that achieved superior optical properties compared with literature protocols. AlphaFlow exemplifies how the convergence of PI principles with autonomous experimentation can lead to improved material properties and more sustainable, intensified research practices in SDLs.

While the introduction of intensified technologies into SDLs has accelerated scientific research, the design, building and implementation of SDLs remain slow. This bottleneck stems from the diverse requirements and unique complexities of process units needed for

specific research goals. The lack of standardized process units has undermined PI's widespread adoption and consequently hindered SDL development cycles. Modularity, a complementary concept to PI, offers a solution through reconfigurable process units that can be readily integrated and adapted¹¹. Such process units, whether off-the-shelf commercial solutions or retrofitted low-cost units, must share common interfaces and protocols to enable rapid assembly of new SDLs and modification of existing ones. Achieving this goal is facilitated by open innovation initiatives (for example, open-sourcing and expertise sharing) from researchers worldwide to democratize their SDL hardware and software modules.

Beyond hardware considerations, data handling and processing must follow modular principles. Modular intensified SDL deployment enables successful, distributed and decentralized SDL networks capable of tackling complex research objectives. Each intensified process (sub-)module must comply with all PI principles. Giving all molecules the same processing experience is particularly crucial, as it ensures reproducibility across SDLs sharing standard (sub-)modules. This standardization is exemplified in a distributed continuous flow chemistry-based SDL, where a pharmaceutically relevant aldol condensation reaction across different locations with a shared commercial reactor module was explored¹².

For bespoke SDLs, reproducibility requires comprehensive documentation of the fundamental PI approaches employed in each (sub-)module, including structural (standard molecular descriptors and reactor geometry), thermodynamic (form, amount, moment and position of applied energy field), functional (data-driven models of the synergistic effects) and temporal (dynamic states, periodicity or continuous processing characteristics) domains of intensification. Recent work has demonstrated how a standardized chemical language can facilitate the transfer of experimental instructions for batch systems¹³. Such standardized frameworks and abstractions could enable knowledge transfer while maintaining the benefits of PI across diverse SDL implementations¹⁴.

In this Comment article, we explored PI as a foundational framework for designing sustainable SDLs, but broader chemical engineering principles, including circular chemistry, must also be integrated to maximize the impact of SDLs. Moving beyond a linear trajectory, SDLs should embrace a sustainable, closed-loop model that accounts for not only efficiency gains but also auxiliary material consumption, waste reduction and resource regeneration. Achieving this vision necessitates rethinking both hardware and software paradigms – developing modular, reusable and reconfigurable process units while establishing standardized experimental workflows and data architectures. A concerted effort within the chemical engineering community is essential to implement common standards that enable seamless knowledge transfer across SDLs, ensuring that intensification strategies remain scalable and adaptable. By treating both physical resources and experimental data as co-products of scientific discovery, SDLs can leverage data intensification to maximize knowledge extraction – where even transient, previously discarded data can inform decision-making with minimal system reconfiguration. This holistic integration of PI and sustainability principles will accelerate scientific breakthroughs and also create a globally connected network of SDLs that democratize access to powerful research capabilities¹⁵. If successfully implemented, PI-empowered SDLs will serve as a scalable blueprint for sustainable research acceleration across chemical engineering and beyond, demonstrating how foundational principles can drive technological progress while safeguarding planetary integrity.

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Competing interests

The authors declare no competing interests.