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Review

The future of sustainable chemistry and process: Convergence of artificial intelligence, data and hardware

Xin Yee Tai[a], Hao Zhang[b], Zhiqiang Niu[a], Steven D.R. Christie[c], Jin Xuan[a,*]

[a] Department of Chemical Engineering, Loughborough University, Loughborough LE11 3TU, United Kingdom
[b] School of Engineering, The University of Edinburgh, Edinburgh EH9 3FB, United Kingdom
[c] Department of Chemistry, Loughborough University, Loughborough LE11 3TU, United Kingdom

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ABSTRACT

Sustainable chemistry for renewable energy generation and green synthesis is a timely research topic with the vision to provide present needs without compromising future generations. In the era of Industry 4.0, sustainable chemistry and process are undergoing a drastic transformation from continuous flow system toward the next level of operations, such as cooperating and coordinating machine, self-decision-making system, autonomous and automatic problem solver by integrating artificial intelligence, data and hardware in the cyber-physical systems. Due to the lack of convergence between the physical and cyber spaces, the open-loop systems are facing challenges such as data isolation, slow cycle time, and insufficient resources management. Emerging researches have been devoted to accelerating these cycles, reducing the time between multistep processes and real-time characterization via additive manufacturing, in-/on-line monitoring, and artificial intelligence. The final goal is to concurrently propose process recipes, flow synthesis, and molecules characterization in sustainable chemical processes, with each step transmitting and receiving data simultaneously. This process is known as 'closing the loop', which will potentially create a future lab with highly integrated systems, and generate a service-orientated platform for end-to-end synchronization and self-evolving, inverse molecular design, and automatic science discovery. This perspective provides a methodical approach for understanding cyber and physical systems individually, enabled by artificial intelligence and additive manufacturing, respectively, in combination with in-/on-line monitoring. Moreover, the future perspective and key challenges for the development of the closed-loop system in sustainable chemistry and process are discussed.

1. Introduction

The sustainable chemical process is a scientific concept that seeks to satisfy the present needs without sacrificing the resources and the environment for future generations. In recent years, continuous flow chemistry is gaining momentum and has progressed considerably from basic laboratory techniques to complex, multistep processes in practice. Compared with the traditional batch system, it offers the advantages of fast mixing, heat transfer, effective reaction time control, and experiment safety with toxic and highly reactive chemicals. Besides, continuous flow chemistry enables the faster discovery of green chemistry products and synthetic routes, which significantly reduce the emission of pollutants in the lab- [1] and industrial scales [2]. Continuous flow chemistry is the mini-continuous plant in the lab. It is considered as the stepping stone for the sustainable chemical process to be scaled-up from scientific research to engineering production. One of the remarkable examples of sustainable chemical processes is the laminar flow-based fuel cells, which utilise liquid fuels as the sustainable resources to continuously generate energy and produce water as the by-product in the microchannel without negatively affecting the environment [3]. Besides, solar energy, an enormous, reliable, and practically inexhaustible energy sources with uniform irradiation can be easily integrated with continuous flow reactors to generate chemical and electrical energy in flow solar cells [4], such as producing singlet oxygen [5] and removal of toxic components from the water [6]. The concept of sustainable chemical process was also seen in the carbon capture and utilisation, in which the greenhouse gases are captured continuously in the form of microcapsules [7] or in the microfluidic device [8] and then converted into greenly synthesised products [9].

The Fourth Industrial Revolution, also referred to Industry 4.0, is creating an evolution, and the impact has been witnessed across sectors, especially manufacturing. In the Industry 4.0 context, the sustainable

* Corresponding author.
E-mail address: j.xuan@lboro.ac.uk (J. Xuan).

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chemical process potentially becomes a smart lab, connecting cyber-physical systems with advanced AI and robust detection techniques. It will also create a closed-loop system consisting of cooperating and coordinating machines, self-decision-making systems, autonomous problem solver and learning systems. The goal of the smart lab for the sustainable chemical process is to produce fully flexible production as fast as possible by adapting the principle of 'Plug and Process'. The robust sensing techniques are allowed to embed agilely in the multistep reaction and separation process for real-time monitoring [10]. Therefore, 3D printing offers the best solution because of its unique properties of being flexible and customisable, enabling a quick realisation of the principle of 'Plug and Process'. Furthermore, adopting a data-driven strategy in the smart lab allows improving the flexibility and smart manufacturing level. This strategy is massively depending on data quality and quantity, which can be assured by utilising advanced sensing techniques through the process of in-/on-line monitoring. Moreover, the smart lab is also known as 'dark lab', 'lights out lab', or 'unmanned lab', where no human power is required. It employs artificial intelligence to practice the methodologies of prediction, automation and autonomy, self-behaving and self-decision-making and performing the intelligence control, scheduling, design, process control quality as well as maintenance in the sustainable chemical process. For example, BASF is implementing Industry 4.0 in its deployment of 3D printing for site facilities [11], connected systems and advanced predictive and analytics models for process management and control and virtual plant commissioning [12]. Schneider Electric employed the 3D printing, advanced AI and advanced sensors, which led to an improvement of productivity by 2–7% [13], energy utilisation increase by 30% [14] and operating cost reduction by 50% [15]. Applying additive manufacturing, advanced AI and robust sensors in the industrial-scale process show a significant momentum to improve the process efficiency, energy utilization and cost-effectiveness.

As discussed above, AI, data and hardware are the foundation modules of the smart lab. AI is a simulation of human intelligence, which is programmed in the machines to enable them think and act like 'scientist', such as learning and problem-solving. In the sustainable chemical process, AI algorithms such as neural network [16,17], machine learning [18,19] and genetic algorithms [20,21] are the common data-driven approaches in the monitoring, optimisation and control. Therefore, employing in-/on-line monitoring by embedding advanced sensing techniques into the multistep processes can assure the quality and quantity of data, which are the primary concern in the data-driven approaches. Through in-/on-line methods real-time data from the chemical processes can be obtained, such as reactants usage, product yield, as well as operation conditions like pH, temperature, and pressure, which are inaccessible by off-line analysis techniques. In-line methods directly measure the process stream without the removal or diversion of the sample, whereas on-line methods automatically analyse the sample materials without distributing the process [22]. Integrating advanced sensing techniques into reaction chambers requires a flexible design of hardware, which can be facilitated by the additive manufacturing (AM). AM, also known as 3D printing, is a green manufacturing technology, building 3D physical outputs from digital inputs without conventional tooling. This bespoken tool offers excellent advantages for this application which demands customisation, flexibility and design complexity. The advances of using AM were also widely discussed in the fuel cells [23], flow chemistry [24] and other energy generation devices [25].

In addition to that, there is also a high desire to bring AI, data and hardware together into the lab-scale research to ease the up-scaling process later. To date, many works have discussed the cyber and physical systems of the smart factory separately. The cyber system refers to the integration of AI and data, where the data is generated through advanced sensing techniques and being utilised by the AI algorithms to perform tasks such as self-optimisation and prediction in the cloud space. In contrast, the physical system describes smart labs' hardware such as multistep reactors, separator and detection technology, where they can be integrated physically for in-/on-line monitoring, enabled by AM technology. In such cyber and physical systems, if, without AM, the robustness of the cyber system will be hindered by the low customisability to connect with powerful detection techniques, resulting in the loss of high-quality data for building a reliable model. On the other hand, if, without AI, the physical system will only be performing real-time monitoring with no intelligence feedback and control, limiting the extendibility and functionality of the physical system. Therefore, the integration of AI, data, and hardware can realise both the physical and virtual meanings of the smart sustainable chemistry.

2. Smart physical system enabled by additive manufacturing and in-/on-line monitoring

Here, the physical system refers to the hardware of the smart lab for sustainable chemical processes such as reactor, separator, and advanced detection. Due to the demand for real-time information, there is a need to integrate them in housing and casing by additive manufacturing to allow the in-/on-line monitoring. AM could reduce the cycle time to produce the customized reaction chamber integrated with advanced detections. This unparalleled approach could encourage researchers to perform a more iterative approach to embed specific geometries in the existing hardware. Therefore, the design can be modified immediately based on the requirement of the processes. Moreover, it can also avoid the loss of detection of the valuable but short-lived intermediates [26].

Currently, various detection techniques such as temperature monitoring, spectroscopy, and imaging have been reported in sustainable chemistry applications via 3D printing for in-/on-line monitoring. For example, Monaghan had developed multi-material structure spectroscopy by ultrasonic additive manufacturing (UAM), embedding fibre-optics into the metallic microreactor for *in-situ* monitoring of B-vitamin nicotinamide and fluorescein [27], as shown in Fig. 1A. Via AM-enabled *in-situ* monitoring, researchers can obtain real-time data from reactants usage, product formation and intermediates generation and will therefore not be visible using off-line analysis techniques [27]. Maier et al. had developed the stainless-steel reactors with in-line oxygen sensor through selective laser melting (SLM) [28]. It was proven as a promising method for investigating the oxidation of Grignard reagents in the flow. Both works show the robustness of AM technology to fabricate highly complex metallic devices suitable for high temperature and pressure application in sustainable chemical processes whilst maintaining high accuracy of measurement in a more freeform design [27]. In another application for air pollution monitoring, fused filament fabrication (FFF) was used to fabricate the photocatalytic gas phase reactor with an embedded semiconductor air quality sensor, which measures electrical resistance changes [29]. This 3D printed gas sensor is fabricated by inexpensive method and assembled with the off-the-shelf components such as photocatalytic filter and analogue-to-digital converter [29].

Adopting AM technology also allows the installation of more powerful detections units and improves the evaluation of system performance. For instance, in fuel cell systems, current density and power density are the standard real-time information to evaluate the performance. Fused deposition modelling (FDM) was employed to embed electron paramagnetic resonance (ERP) spectroscopy on the high temperature polymer electrolyte fuel cells for cathode conductivity measurement [30]. Polyjet technology provided a rapid and cost effective way to design a fixture small enough to achieve good signal-to-noise ratio when using low intensity X-ray provided by commercial X-ray computed tomography scanners for water distribution visualization (Fig. 1B) that would be otherwise be difficult to manufacture through conventional machining [31]. The works highlighted the opportunity for real-time monitoring of laminar flow-based fuel cell using the robust sensors. Menzel et al. presented a 3D-printed chemical synthesis system including reactor, separator, pressure regulator and pump as shown in Fig. 1C through FDM, which creates a complete continuous flow system for multistep chemical synthesis [32]. 3D printing of high temperature and chemically resistant polymer, such as polyether ether ketone (PEEK) on a low-cost 3D print-

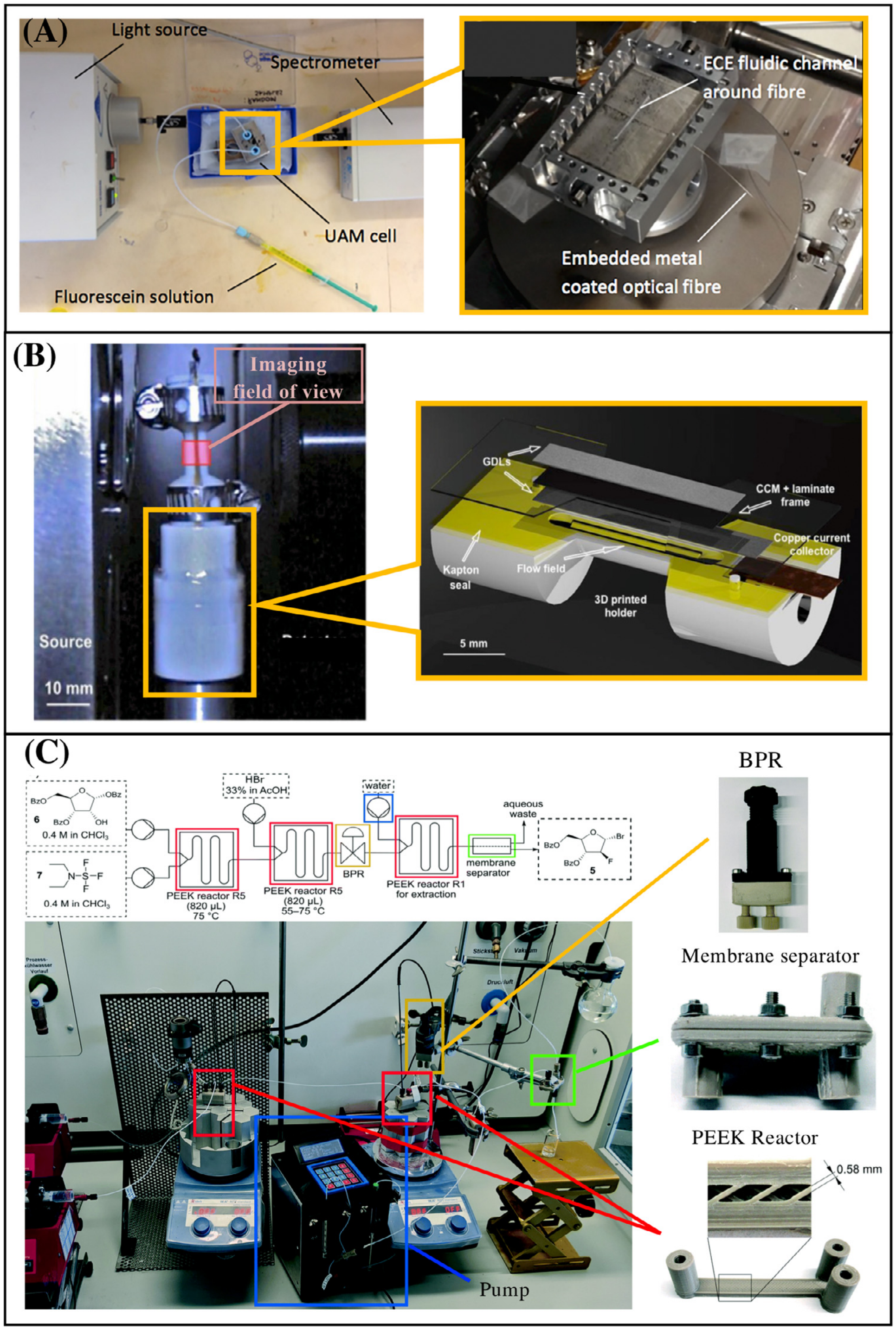

Fig. 1. (A) The schematic diagram of spectrographic measurement by UAM cell featuring embedded the coated optical fibre perpendicularly to the microfluidic channel for the analysis of fluorescein solutions [27] (B) Visualization set-up inside the X-ray computed tomography system with the 3D-printed cell holder with flow field fixture [31] (C) Photography of the multistep synthesis with 3D printed reactors, pump, BPR and membrane separator [32].

ing technology creates opportunities for high temperature and corrosive applications in the sustainable chemical process [32].

3. Smart cyber systems empowered by artificial intelligence and in-/on-line monitoring

In sustainable chemical processes, the cyber system adopts the smartness offered by AI to execute tasks such as self-optimisation and prediction using the data generated by in- and on-line detections. Previously, AI had been utilised in the off-line data analysis where the data was used to build (typically) surrogate models and performing tasks such as prognostic health state [16], prediction [17] and optimisation [20]. The results have shown the ability of off-line data analysis in trends observation and big image visualisation. However, human power is still required to keep an eye out on the process and taking control. Recently, sustainable chemistry is gradually being developed into 'dark labs' with self-optimisation approach, where AI algorithms replace human work, integrated with in-/ on-line detection and control techniques to perform a closed-loop of interactive, self-behaviour and autonomy operation.

To date, direct search methods such as stable noisy optimisation by branch and fit (SNOBFIT) [33] is one of very few single-objective optimisers which have been successfully applied for self-optimisation in the multistep process [34], downstream process [35], and product synthesis [36]. Clayton et al. employed SNOBFIT algorithm to maximise

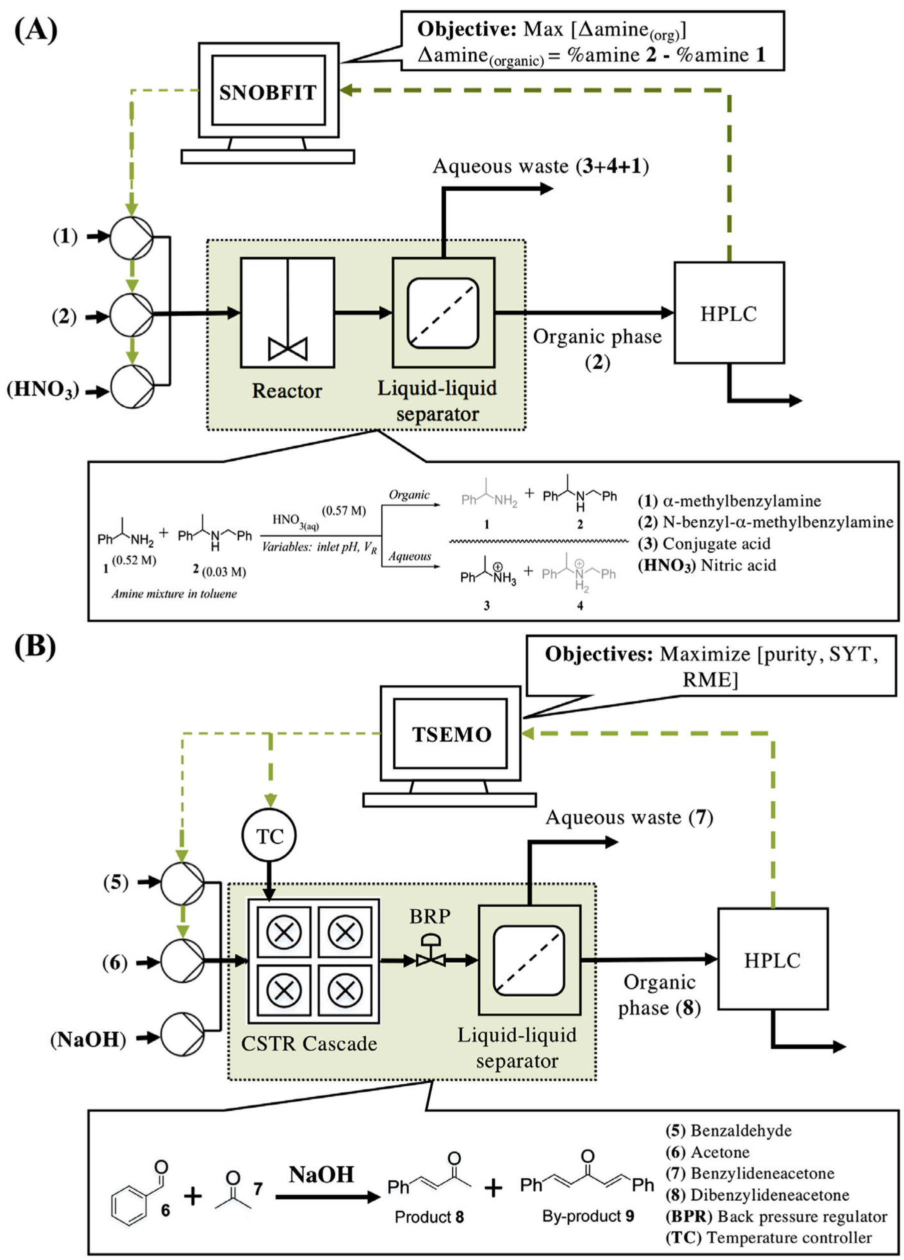

Fig. 2. (A) SNOBFIT algorithm was employed in the single objective self-optimization of multistep reaction-extraction system by manipulating the flow rate of α-methylbenzylamine and N-benzyl-α-methylbenzylamine for solvent volume ratio and nitric acid for pH value, adopted from [34] (B) TSEMO algorithm was utilized in the multiple objectives self-optimization of multistep Claisen-Schmidt condensation process by adjusting the flow rate of benzaldehyde and acetone for solvent ratio and temperature controller from CSTR, adopted from [21].

the concentration of α-methylbenzylamine in the aqueous phase from the multi-step reaction-extraction process [34], as shown in Fig. 2. By manipulating the inlet pH and feed volume ratio, this single-objective optimiser converged and finally provided 90% of separation efficiency. The same algorithm was applied in the reactive-extraction process to optimise the yield by reducing the generation of side product that would cause clogging in the reactor [35]. The reaction achieved 66% of yield by strictly controlling over the reaction parameters such as feed flow rate, feed volume ratio and temperature [35]. A single optimisation of inhibitor synthesis achieved 89% of yield by regulating four parameters such as feed flow rate, feed volume ratio, temperature and residence time [36].

However, in practice, economic and environmental factors should also be considered during the optimisation. A solution has been proposed via introducing a set of optimal solutions called Pareto front, where a non-dominated solution is one which cannot be improved without having a detrimental effect on the other [37]. It enabled multitarget optimisation, automated learning of feasible process conditions, and improved material utilisation due to the low number of experiments required [38]. Later, Clayton et al. developed Thomson sampling efficient multi-objective optimisation (TSEMO) algorithms to maximise the product purity, space-time yield (STY) and reaction mass efficiency (RME) simultaneously in multistep Claisen-Schmidt condensation reaction [21], as shown in Fig. 2B. Multi-objective TSEMO algorithm converged to Pareto front which was successfully highlighted the complete trade-off between product purity, STY and RME. It enabled the optimisation of multi-step processes concerning multiple objectives simultaneously from Pareto front, and potentially to improve the resource utilisation and decision-making during process design [21]. Besides continuous flow chemical processes, TSEMO can be used for batch-sequential design.

The flexibility of applying optimisation algorithms, multi-objective genetic algorithm (MOGA) cooperating with mechanistic and data-driven approaches to evaluate the performance of chemical processes was recently reported. Yan et al. and Xu et al. respectively compiled MOGA with artificial neural network (ANN) [39] and deep neural net-

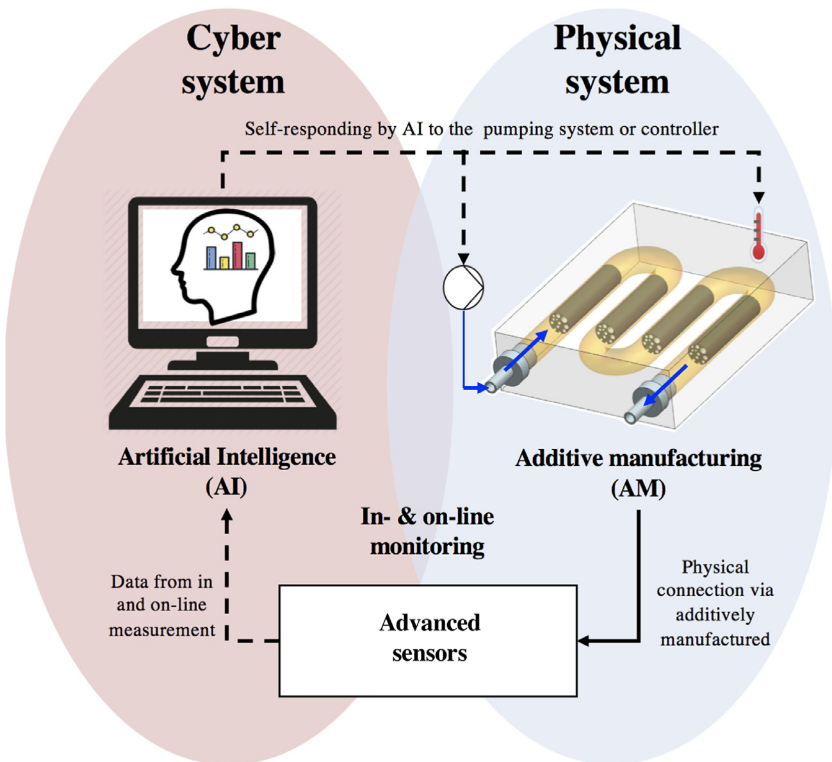

Fig. 3. Visualization of the combination of AI, AM and in-/on-line monitoring in the sustainable energy chemistry and process to create a closed-loop system.

work (DNN) [40] to assess the performance of solid oxide fuel cell. The data-driven algorithms effectively resolve the correlations between the inputs and outputs, while non-dominated sorting genetic algorithm (NSGA-II) was competent to optimise the multi-objective functions. However, DNN and ANN are the data-driven 'black-box' method in which the description of the process with input and output of data is not clear, which has limited extrapolation with poor interpretability. To address this issue, Yang et al. presented a hybridisation of data-driven and mechanism-driven to improve not only the interpretability of data-driven model, but also the traceability of the first-principle models in the fluid catalytic cracking simulation [41]. The result shows the effectiveness of the hybrid model, presenting better data correlation [41]. Collaborating hybrid model with optimization algorithms would be a new direction in the sustainable chemistry and process.

4. Future perspectives and opportunities

The previous works have shown the in-/on-line monitoring could be physically and virtually enhanced by AM and AI, respectively to achieve system smartness. Yet, a clear gap still exists, where the physical system requires powerful AI algorithms for smart feedback control, while the cyber system needs data from integrated sensing techniques customisable by AM. Therefore, we envision that a closed-loop paradigm need to be created for sustainable chemical processes by closely integrating the physical and cyber systems, as shown in Fig. 3. This closed-loop system can potentially create a future lab framework with an extension of AI beyond cyber space and the automation of physical hardware such as highly integrated system, self-evolving process, inverse design approach, automated science discovery and service-orientated platform.

4.1. Highly integrated system

Due to the demand for automatic and autonomous operation in the chemical process, many robust sensors are required in the multistep processes to continuously generate accurate real-time process data. However, connecting advanced sensing techniques to the complex processes usually is inconvenient due to the requirement of nonstandard components. The connected systems are usually space-intensive and bulky with much cabling, which increases the electromagnetic interference (EMI) [42]. AM technology is competent to fabricate bespoke and sophisticated 3D objects in various dimensions and enhances the manufacturing agility with 'Plug and Process' principle. The fast fabrication speed also helps propagate the design innovation with an agile-iterative approach by adopting a 'fail fast, fail often' strategy, as shown in Fig. 4A. Therefore, an AM-enabled highly integrated system is expected to eliminate the boundary and creates a compact assembly, allowing advanced detection techniques to dial in the multistep process flexibly and thus improving the manufacturing agility. The highly integrated unit offers the benefits of downsizing, light weight, and less cabling, which is beneficial to reduce the EMI [42]. Besides, the data quality could be assured in a highly integrated system to improve the transparency of the system and the accuracy of the AI algorithms. The highly integrated system has recently been developed in the lab-on-chip and organ-on-chip through AM technology [43]. For example, researchers at Berkeley Lab has produced an all-liquid 3D-printed lab-on-chip device, potentially to be programmed to carry out multistep, complex chemical reactions on demand [44]. Besides, 3D printing offers the possibility to introduce multi materials into the same integrated system to create an on-demand assembly that can easily connect to other parts [45]. Such smart hardware, when integrating into the cyber space, will offer a convenient route to scale up, and bring new possibilities to move from proof-of-concept lab-based high integrated systems to more practical systems, such as factory-on-chip [46].

4.2. Service-orientated platform for end-to-end synchronization and self-evolving system

Currently, due to the lack of convergence between physical process and virtual space, the information from distributed nodes in the chemical process such as feed data, equipment data, process parameter data and sensory data are largely isolated, fragmented, and stagnant. Therefore, centralized information management, for example, a service-

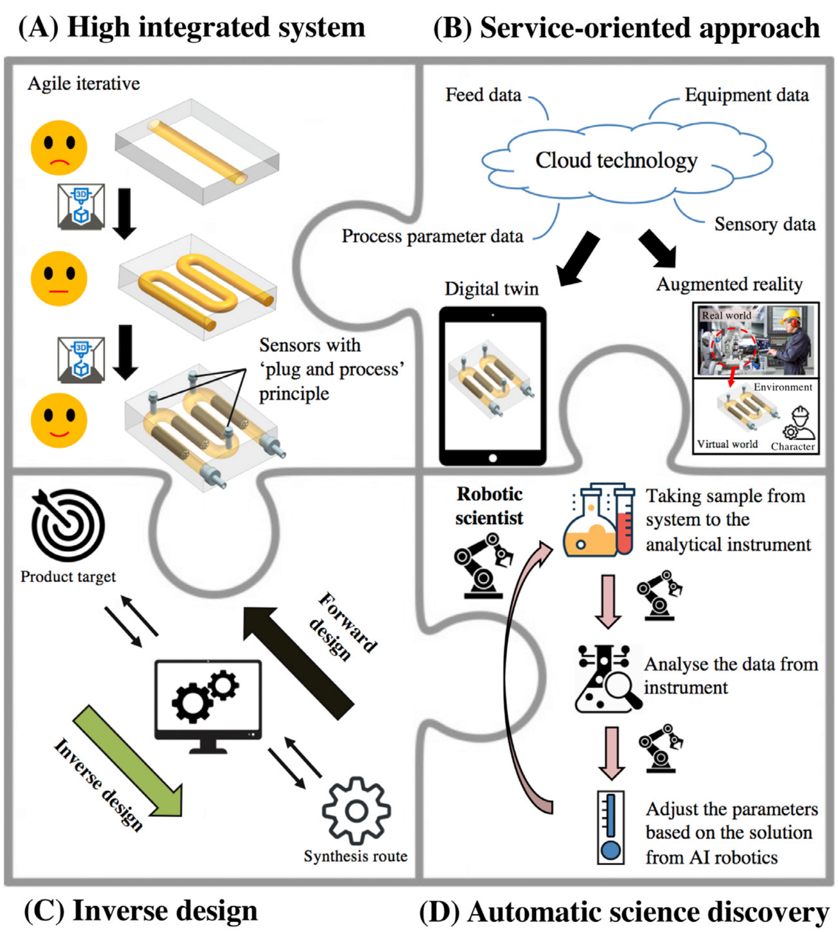

Fig. 4. A closed-loop system able to create (A) High integrated system. The ability of AM technology to create a high integrate system with 'plug and process' principle in agile iterative approach (B) Service-orientated platform. A service-orientated platform is developed through cloud technology to aggregate the data from distributed nodes, allowing to implement through digital twin and augmented reality platforms (C) Inverse design. Inverse mapping focuses on the design aspect of chemistry informatics towards flow chemistry recipe while forward mapping mainly deals with molecules prediction given process recipe (D) Automatic science discovery. Robotic scientist works like the human and successfully speed up the science discovery in the light-out environment.

orientated platform as shown in Fig. 4B, is required to aggregate the information through cloud technologies. Digital twin offers end-to-end synchronization on a service-orientated platform, virtually representing the physical multi-step process and allows monitoring, control, and fault detection to overcome the challenge of geographical distance. Maiwald group has developed a digital twin approach to demonstrate reactors with NMR on the screen through a cloud server [46,47]. Besides, the service-orientated platform is also able to create a self-evolving system empowered by AI technology. The self-evolving system adopts AI algorithms as the active learning machine to continuously improve and adapting themselves from the new-incoming information to create a super-predictive model. Zhang et al. proposed a concept of inverse augmented reality [47]. In the inverse augmented reality, the characters and environment agents in the virtual world can self-develop and evolved by learning from the physical world. Therefore, the service-orientated architecture mirrors the physical process in the digital twin platform and develops into the self-evolving system.

4.3. Inverse design

In multistep flow synthesis, developing high purity of green molecules requires more in-depth insights and search into the process recipes. Until recently, exploring targeted properties of molecules through using experiences built upon existing synthesis recipes has become the general strategy. However, this forward design strategy is usually time-consuming and costly. Promptly solving the recipes is one of the challenges for future sustainability. To accelerate the design process, the inverse design has emerged as a significant sustainable chemistry informatics platform enabled by powerful AI algorithms. Based on the chemistry data, the flow chemistry recipes (e.g. flow rate, temperature, pressure) would be deduced with pre-defined target properties of products or processes (e.g. purity and conversion). The AI-based mapping directions, such as forward and inverse, in chemistry informatics, are shown in Fig. 4C. Recently, the inverse design approach has been widely discussed in materials exploration. Sanchez-Lengeling proposed a data-driven generative model that can generate unseen materials with desired properties by learning property distributions of the existing materials [48]. Besides, European Large-Scale Research Initiative 'Battery 2030+' has implemented Battery Interface Genome – Materials Acceleration Platform (BIG-MAP) [49] to accelerate the discovery of ultra-high performance batteries with the inverse computational design of battery materials and interfaces empowered by AI, high-performance computing and autonomous synthesis robotics [50]. Analogising to these initiatives, adopting inverse design in the cyber-physical system will bring new possibilities to speed up the discovery of sustainable flow synthesis recipes as well.

4.4. Automatic science discovery

The relatively slow cycle time within sustainable chemistry from synthesis to characterization remains a challenge obstructing the scientific discovery. Likewise, the complexity of experiments and simulation scales exponentially with the number of variables, confining most research in narrow areas of material space. Therefore, an autonomous robotic driven by a robust AI algorithm is required to take the scientist out of the loop system. Recently, Cooper et al. designed a robot assistant to search for photocatalysts [51], as shown in Fig. 4D. The robot had continuously worked for 22 h a day over eight days and performed 688 experiments within a ten-variable experimental space. With the advanced laser scanning and tactile feedback of the robot, this mobile robotic chemist was able to operate in lights-out operation, which is also an advantage when carrying out the light-sensitive photochemical reactions [51]. Besides, Macleod et al. developed a self-driving laboratory for autonomously synthesizing and characterizing solar cell materials [52]. The breakthroughs clearly show a vision that the extension of AI beyond cyber space and the automation of physical hardware brings an accelerated and automated scientific study.

Conclusion

It is now apparent that the sustainable chemical research is undergoing a philosophical transformation by coupling AI, data, and hardware to create a closed-loop cyber-physical system. This transformation will be developing the 'lab of the future' to a self-decision-making manner, interactive machines, autonomous problem solvers, and learning machines through AM, AI, and in-/ on-line monitoring. A closed-loop system constitutes a highly integrated system enabled by AM technology, enhancing the integration of advanced sensors into multistep processes. Adopting cloud technology in the cyber-physical system eliminates the barrier between physical equipment and virtual space. It will develop end-to-end synchronization and self-evolving system through centralized information management such as service-orientated platforms. The closed-loop system will also offer an advanced searching platform to explore the greener synthesis route from the targeted properties of products or processes such as purity and conversion through inverse design. Finally, the cyber-physical system will also provide remarkable breakthroughs for science discovery in an accelerated and automated fashion via robotics driven by powerful and robust AI technology.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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