Review

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Review

Recent Developments in Automated Reactors for Plasmonic Nanoparticles

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Abstract: Automated reactors are revolutionizing nanomaterial synthesis, streamlining processes through advanced machine-driven execution and data collection. By delegating repetitive tasks—such as experimental execution and data acquisition—to automation, researchers can focus more on critical analysis and creative problem-solving. Unlike traditional approaches that primarily manipulate starting materials, autonomous systems now enable precise control over morphology at various growth stages. This capability is crucial for applications such as efficient chemical space exploration and adaptive manufacturing. Despite these advancements, transitioning from single-step automation to complex, multistep syntheses remains a major challenge due to the intricate structural diversity of nanomaterials and the interdependent chemical and physical processes involved. Robotic batch and continuous-flow platforms are progressively evolving into more versatile systems, expanding access to a broader range of chemistries required for autonomous multistep fabrication. Advancements in process analytical technologies have significantly improved real-time monitoring of interconnected reactions, accelerating data collection while ensuring stringent safety standards and high product quality. The integration of these monitoring tools with advanced control software establishes adaptive feedback loops, enabling flexible multistep screening and self-optimizing synthesis strategies. This mini review explores recent developments in automated reactor technologies for plasmonic nanomaterial synthesis, focusing on both batch and continuous-flow platforms and giving an outlook on what's next for the field.

Keywords: automated reactors; plasmonic nanoparticles; continuous flow platform

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Introduction

Automated reactors have revolutionized chemical and nanomaterial synthesis by increasing efficiency, precision, and reproducibility.[1–5] These platforms allow researchers to focus on process optimization and creative problem-solving rather than repetitive manual labour.[6] Plasmonic nanoparticles (PNPs), such as gold and silver, play a crucial role in biomedical engineering, optics, and catalysis, necessitating precise control over their size, shape, and surface properties.[7–9] While batch synthesis remains widely used, continuous flow platforms offer several advantages, including enhanced reproducibility, scalability, and process optimization.[10] The global nanomaterials market is expected to grow significantly, driven by increasing demand for precision-engineered nanoparticles in various fields such as healthcare, electronics, and sustainable energy solutions.[11–13] Autonomous self-optimization of nanoparticle synthesis has emerged as a crucial area of development, allowing researchers to achieve user-defined nanoscale geometries that are otherwise challenging to fabricate.[14] By integrating continuous flow synthesis with advanced automation techniques, researchers can unlock novel synthetic methodologies, ensuring safety, reproducibility and scalability in nanoparticle manufacturing.[10,15]

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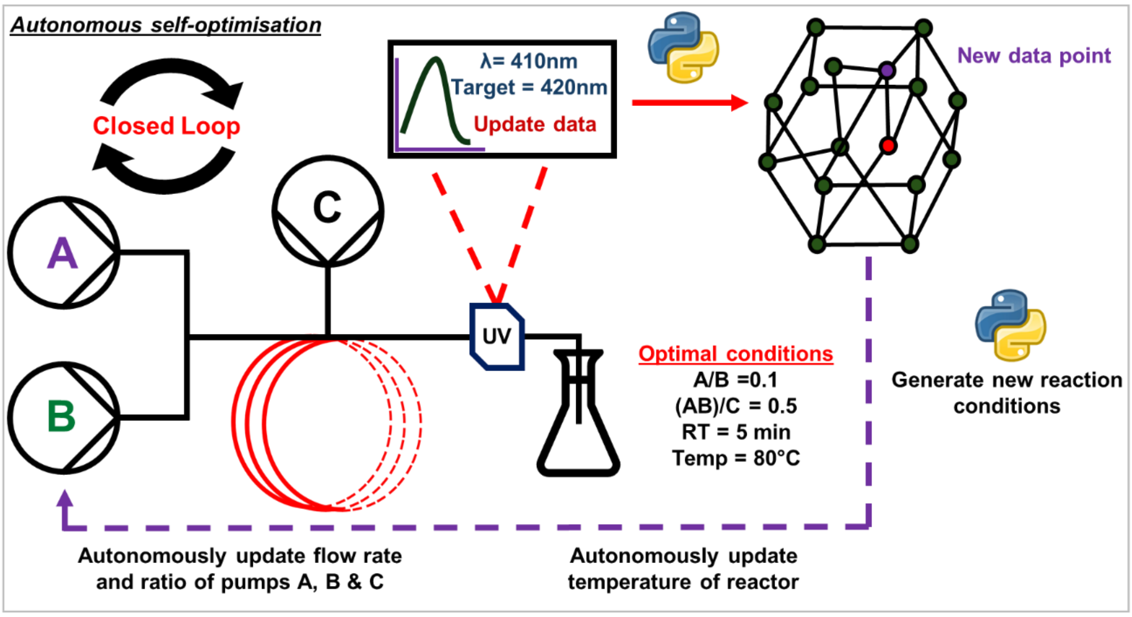

Figure 1. Pictographic representation of a simple autonomous self-optimising platform using UV-Vis as the inline analysis.

Recent advancements in continuous flow reactors have demonstrated their potential in optimizing the synthesis of plasmonic nanoparticles.[16] These platforms enable real-time monitoring, adaptive feedback control, and rapid fine-tuning of reaction parameters to achieve high-quality nanoparticles with tailored optical, electrical, and catalytic properties. Additionally, integrating microfluidic reactors into continuous flow synthesis has significantly improved reaction kinetics, mixing efficiency, and heat transfer, allowing for superior control over nanoparticle morphology and composition.[17–20] Furthermore, autonomous self-optimization enables safer and more efficient nanoparticle synthesis by incorporating real-time toxicity assessment and Bayesian optimization algorithms.[21] These algorithms iteratively refine reaction conditions based on real-time feedback, enhancing reproducibility while reducing experimentation time.[22,23] This capability is particularly beneficial in biomedical applications, where precise control over nanoparticle properties is essential for drug delivery, biosensing, and imaging applications.[24] As the field continues to evolve, the integration of AI-driven predictive models and machine learning algorithms will further enhance the efficiency and adaptability of automated reactors.[25] By addressing key challenges such as reactor fouling, process scalability, and inline characterization limitations, future advancements will pave the way for next-generation nanofabrication technologies.

This mini-review explores recent developments in automated reactor technologies, highlighting their impact on plasmonic nanomaterial synthesis and potential applications in diverse industries.

Batch Platforms

The advent of batch-based automated reactors has significantly improved the synthesis of PNPs. Batch synthesis remains the most widely used method for nanoparticle production due to its straightforward implementation and scalability. However, the emergence of automation in batch platforms has led to notable advancements in nanoparticle synthesis, enhancing reproducibility and efficiency. The automation of batch reactors primarily focuses on integrating artificial intelligence, real-time feedback mechanisms, and advanced spectroscopic techniques to achieve higher precision.

Wolf *et al.* (2022) integrated the Chemputer platform into inorganic synthesis, demonstrating its potential in achieving colloidal stability for silver nanoparticles.[26] Their study utilized small-angle X-ray scattering and dynamic light scattering for characterization, highlighting automation's role in precise nanoparticle fabrication. However, a limitation of this approach is its reliance on predefined reaction conditions, which may not be adaptable to varying synthesis environments.

Yoo *et al.* (2024) introduced an AI-guided batch synthesis system that linked a UV-Vis spectroscopy module with a Bayesian optimization model. This approach optimized silver

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nanoparticle formation at room temperature within 200 iterations.[27] A notable strength of this work is its self-adjusting mechanism, which rapidly adapts to changing synthesis parameters. However, its reliance on a single analytical technique may limit comprehensive real-time monitoring.

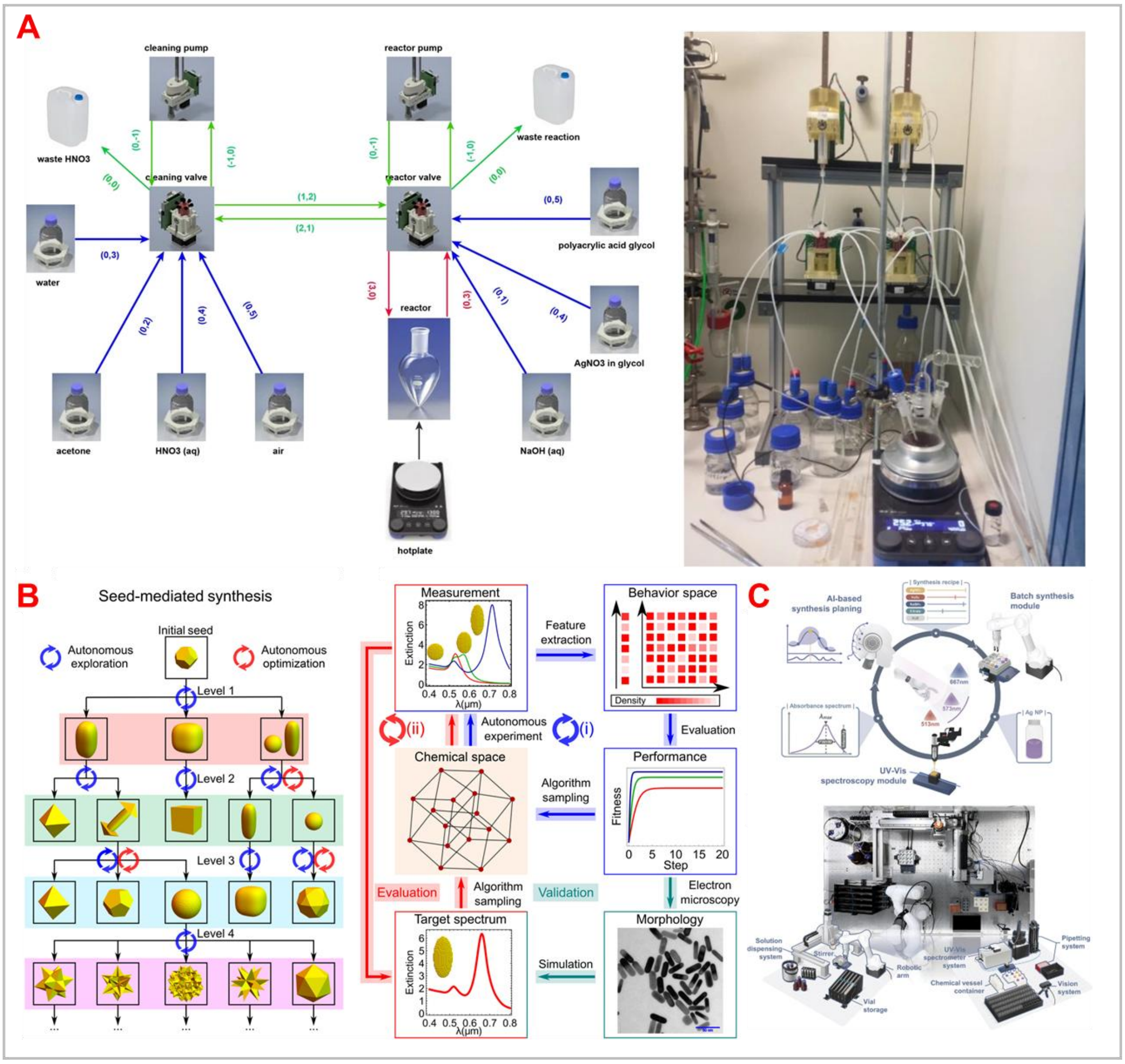

Figure 2. A) Chemputer schematic (left) and physical setup (right) showing components, metadata, and tubing connections for automated nanoparticle synthesis. Reproduced from [26] under a Creative Commons 4.0 CC BY license B) The closed-loop approach toward exploration and optimization in the seed-mediated synthesis of nanoparticles. Reproduced from [14] under a Creative Commons 4.0 CC BY license C) The autonomous laboratory platform for bespoke NP design with target optical properties. Reproduced from [27] under a Creative Commons 4.0 CC BY license [14,26,27].

Salley *et al.* (2020) developed a genetic algorithm-driven robotic platform for gold nanoparticle synthesis, further advancing self-optimizing reactors.[28] The system autonomously adjusted reaction conditions based on experimental fitness scores obtained through UV-Vis spectroscopy, enabling the production of various nanoparticle morphologies, including rods and octahedral structures. This work demonstrated that AI-driven batch synthesis could lead to novel material discovery and enhanced control over nanoparticle characteristics. Jiang *et al.* (2022) expanded on this work, incorporating theoretical modelling and machine learning to improve nanostructure design with a 95% yield. Their platform integrated real-time spectroscopic feedback, allowing for continuous adjustments to reaction conditions, thereby reducing material waste and improving consistency.[14]

Despite these advancements, automated batch synthesis platforms face several challenges. One significant drawback is the need for intermittent human intervention to handle unexpected variables

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such as impurity accumulation, inconsistent precursor quality, or undesired side reactions. Additionally, while parallel combinatorial experimental techniques have been applied to nanomaterials, they have not yet been effectively integrated into autonomous experimentation systems. Another limitation is the lag time in sample characterization, which, despite real-time analytical tools, still requires validation through offline techniques such as electron microscopy. The accumulation of byproducts and the need for extensive purification steps also contribute to increased waste and environmental impact, making continuous flow platforms an attractive alternative.

Continuous Flow Platforms

Continuous flow synthesis has revolutionized nanofabrication by providing enhanced control over reaction conditions, enabling inline analysis, and ensuring precise reagent handling.[29,30] Unlike batch processing, which often faces challenges with inconsistencies in particle size, morphology, and reproducibility, continuous flow methods utilize controlled flow rates, residence times, and reaction environments to achieve superior uniformity and scalability.[31–33] Despite these advantages, challenges such as energy consumption, reactor clogging, and the integration of real-time analytical techniques persist. This section critically evaluates key studies that have advanced the field of continuous flow nanomaterial synthesis.

Pinho and Torrente-Murciano (2021) introduced the "Dial-a-Particle" system, a microfluidic reactor platform designed for the precise manufacturing of plasmonic nanoparticles.[34] This innovative system combines fast, integrated multipoint particle sizing with a modular "plug-n-play" platform, featuring reactors in series and distributed feed capabilities. The real-time early growth information obtained allows for accurate prediction and control of particle properties, enabling automated synthesis of nanoparticles with tunable sizes ranging from approximately 4 to 100 nm. This approach represents a significant advancement toward reproducible nanomaterial production. However, the study primarily utilized UV-Vis spectroscopy for characterization, which offers limited insight into detailed morphological features. Future work could benefit from integrating advanced analytical techniques, such as electron microscopy or dynamic light scattering, to enhance characterization accuracy.

Mekki-Berrada *et al*. (2021) proposed a two-step machine learning framework for the high-throughput microfluidic synthesis of silver nanoparticles with desired optical properties.[35] The approach combines Gaussian process-based Bayesian optimization with a deep neural network, enabling the rapid production of silver nanoparticles tailored to specific absorbance spectra. While this method effectively optimized particle shape and size, it required extensive data acquisition prior to model training, presenting a considerable drawback. This study highlights the classic trade-off in machine learning-based synthesis: large datasets improve predictive accuracy but can slow down the optimization process. Future advancements could focus on transfer learning or active learning strategies to reduce the data acquisition burden while maintaining model performance.

Hall *et al.* (2021) demonstrated the integration of autonomous optimization within a continuous flow system for nanoparticle-catalyzed reactions.[36] They developed an automated continuous flow reactor equipped with inline analysis, applying it to the self-optimization of a gold nanoparticle-catalyzed 4-nitrophenol reduction reaction. The system optimized experimental conditions to achieve maximum conversion in under 2.5 hours. Data obtained from this optimization facilitated the generation of a kinetic model, allowing for the prediction of reaction outcomes under varying conditions. This study exemplifies the potential of AI-driven synthesis for catalytic applications, particularly in dynamically optimizing reaction conditions. However, it also underscores a critical bottleneck: the necessity for advanced inline analytical techniques to complement AI-driven decision-making. Without robust real-time monitoring, the system's ability to make precise adjustments is constrained, limiting its broader applicability.

Wu et al. (2025) introduced a self-driving laboratory designed for the photochemical synthesis of plasmonic nanoparticles with specific structural and optical characteristics.[37] This autonomous system integrates real-time monitoring and adaptive feedback mechanisms to fine-tune reaction parameters, ensuring the production of nanoparticles that meet predefined criteria. The study highlights the potential of combining artificial intelligence with photochemical processes to achieve

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precise control over nanoparticle synthesis, paving the way for advancements in materials science and nanotechnology. However, the implementation of such autonomous systems necessitates sophisticated inline analytical tools capable of providing accurate, real-time data to inform the AI-driven adjustments. The development and integration of these advanced analytical techniques remain a significant challenge, critical for the broader application of self-optimizing synthetic platforms.

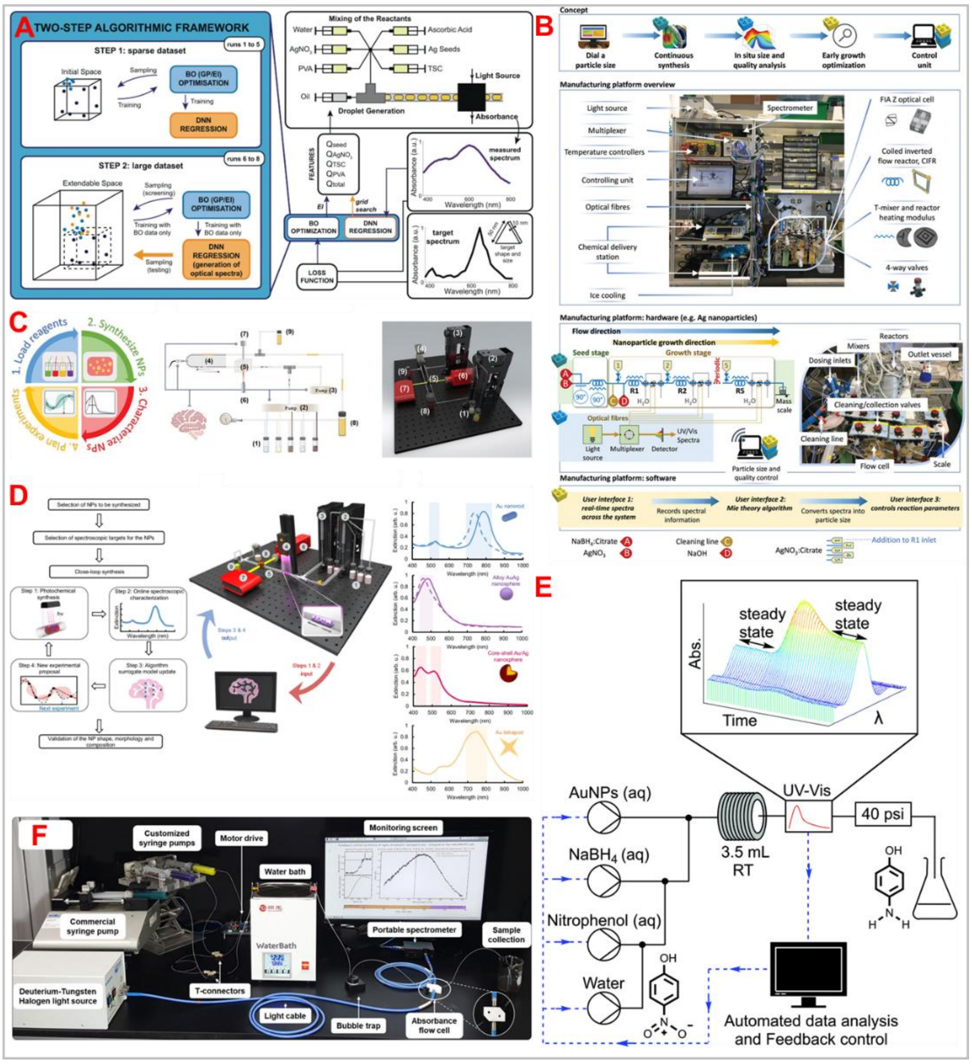

Figure 3. A) Autonomous self-optimisation of AgNPs through a two-step optimization algorithmic framework. Reproduced from [35] under a Creative Commons 4.0 CC BY license. B) Autonomous self-optimisation of specific size Au and AgNPs. Reproduced from [34] under a Creative Commons 4.0 CC BY license. C) Self-driving platform for different size AuNPs. Reproduced and adapted from [38] under the terms of CC BY-NC 4.0 with permission from the Authors. D) Autonomous Fluidic Identification and Optimization Nanochemistry (AFION) self-driving lab showing the workflow and synthesised NPs. Reproduced from [37] under a Creative Commons 4.0 CC BY license. E) Closed loop self-optimising platform for AuNP catalysis. Reproduced from [36] under a Creative Commons 4.0 CC BY license. F) A digital image showing the automated flow system for the synthesis of AgAu alloy nanoboxes with tailored optical properties. Reproduced from [39] under a Creative Commons 4.0 CC BY license.[34–39].

Tao *et al.* (2021) developed a self-driving platform that integrates oscillatory microfluidics, online spectroscopy, and machine learning for the autonomous synthesis of metal nanoparticles.[38] This innovative system employs machine learning algorithms to analyse real-time spectroscopic data, enabling the dynamic adjustment of synthesis parameters to achieve desired nanoparticle properties without human intervention. The study demonstrates the platform's capability to efficiently navigate complex reaction spaces, optimizing conditions to produce nanoparticles with specific characteristics.

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This approach not only accelerates the discovery and development of new nanomaterials but also enhances reproducibility in nanoparticle synthesis. However, the successful implementation of such autonomous systems relies heavily on the integration of advanced inline analytical techniques that provide accurate, real-time data. Ensuring the precision and reliability of these analytical components is crucial for the system's ability to make informed decisions during the synthesis process.

Bui *et al.* (2024) introduced an automated flow chemistry system employing proportional–integral (PI) feedback control to synthesize silver–gold (AgAu) alloy nanoboxes with precise optical properties.[39] This system utilizes a PI control algorithm based on a first-order plus dead-time model, correlating precursor flow rates with the maximum absorbance peaks of the resulting nanoboxes. By iteratively adjusting the flow rate in response to real-time UV–vis absorbance measurements, the system achieves the target optical characteristics of the AgAu nanoboxes. This approach enhances the consistency and reliability of nanoparticle synthesis, minimizing human intervention. However, the effectiveness of this automated system depends on the accuracy of real-time analytical measurements and the robustness of the feedback control algorithm, which are critical for maintaining the desired product specification.

Collectively, these studies underscore the transformative potential of continuous flow synthesis in nanomaterial fabrication. The integration of real-time monitoring, machine learning, and autonomous optimization not only enhances precision and reproducibility but also addresses scalability and efficiency challenges. Ongoing research focusing on overcoming existing limitations, such as reactor design optimization and advanced inline analytical integration, will be pivotal in fully realizing the capabilities of continuous flow nanomanufacturing.

Challenges and Future Outlook

The future of automated plasmonic nanoparticle synthesis lies in the integration of advanced machine learning algorithms and real-time adaptive control mechanisms. AI-driven predictive models will enable researchers to fine-tune reaction conditions dynamically, leading to improved process efficiency and reduced material wastage. Additionally, hybrid systems that combine the strengths of batch and continuous flow platforms could provide greater flexibility for complex nanoparticle synthesis. Another promising area is the expansion of inline characterization techniques. While UV-Vis spectroscopy is widely used, the incorporation of complementary methods such as Raman spectroscopy, mass spectrometry, and electron microscopy (*in situ* liquid TEM) will allow for a more comprehensive understanding of nanoparticle properties.[40] This will enhance the ability to produce nanoparticles with tailored optical, electronic, and catalytic properties. Scalability remains a significant challenge for both batch and continuous flow synthesis. While continuous flow systems offer inherent scalability advantages, further advancements in modular reactor design and process standardization will be required for industrial-scale implementation. Collaborative efforts between academia and industry will be crucial in bridging this gap, ensuring that automated nanoparticle synthesis technologies are both practical and commercially viable.

Conclusion

In conclusion automated reactors are transforming the field of plasmonic nanoparticle synthesis, with batch and continuous flow systems offering unique advantages and challenges. While batch platforms have demonstrated high-throughput capabilities, continuous flow methods provide superior reproducibility and real-time optimization. Integrating AI, machine learning, and advanced analytical tools will further enhance the potential of these systems, paving the way for next-generation nanofabrication technologies.

Declaration of Competing Interest: The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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