



From Chemistry 4.0 to Chemistry 5.0: Digital Transformation, Sustainability, and Human-Centred Innovation

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DOI: <https://doi.org/10.68050/JAMS.2026.738>

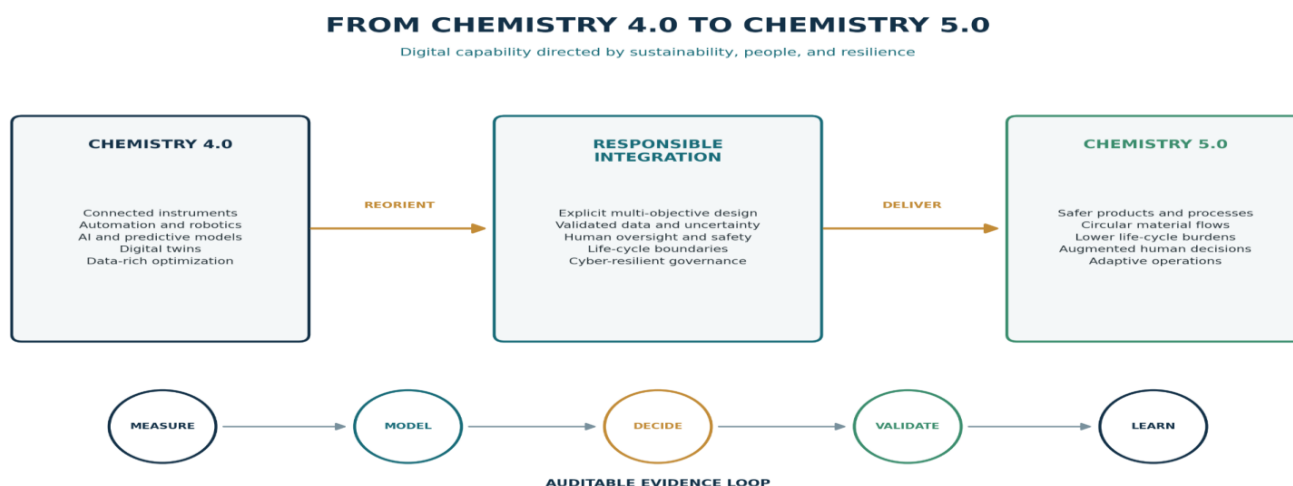
Received: 02 October 2026; Accepted: 10 October 2026; Published: 15 October 2026

ABSTRACT

Chemistry 5.0 connects digital chemical technologies with measurable sustainability, human-centred design, and operational resilience. This critical narrative review examines artificial intelligence, autonomous experimentation, digital twins, green chemistry, and circular resource use across chemical research and process engineering. Foundational and recent literature is synthesized through four analytical domains: digital capability, environmental performance, human oversight, and resilience. The review proposes an implementation framework that links data and models to explicit design constraints, validation, decision authority, and life-cycle boundaries. Two technology and implementation tables map capabilities to benefits, risks, and staged actions. The resulting framework identifies practical indicators for yield, material intensity, safety, data quality, workforce participation, and system robustness. These indicators require documented baselines and system boundaries; the framework itself has not yet been empirically validated. Chemistry 5.0 is therefore presented as a testable approach for directing digital tools toward safer and more sustainable chemical processes, with future research needed to compare measured outcomes across scales.

Keywords: artificial intelligence; circular economy; digital twins; green chemistry; human-centred innovation; sustainable chemical engineering

Graphical abstract



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1.0 INTRODUCTION

The fourth industrial transformation brought connected instruments, advanced analytics, cloud computing, automation, and cyber-physical systems into laboratories and chemical plants. In chemistry, these capabilities support faster screening, real-time process monitoring, predictive maintenance, and data-rich design. Yet digital sophistication alone does not guarantee safer products, lower life-cycle burdens, circular material flows, or better work. A highly optimized process can still depend on hazardous substances, fossil feedstocks, opaque algorithms, fragile supply chains, or poorly defined end-of-life routes.

Industry 5.0 reframes technological progress around three mutually reinforcing dimensions: human-centricity, sustainability, and resilience [1, 8, 9]. Chemistry 5.0 translates this logic into molecular discovery, formulation, reaction engineering, separations, manufacturing, and education. It preserves the useful infrastructure of Chemistry 4.0 while changing the objective function: efficiency remains important, but it is evaluated together with safety, environmental performance, circularity, transparency, and human agency.

This review has three objectives: to define the conceptual boundary between Chemistry 4.0 and Chemistry 5.0; to examine how digital technologies can support sustainable and circular chemical practice; and to propose an implementation architecture with measurable technical, environmental, and human outcomes. The central argument is that Chemistry 5.0 is not a new collection of devices. It is a governance and design paradigm for directing digital capability toward demonstrable public and environmental value.

2.0 REVIEW METHODOLOGY AND SCOPE

A critical narrative-review approach was adopted because Chemistry 5.0 remains an emerging and inconsistently labelled field. The synthesis was anchored in established sources on Industry 4.0 and 5.0, green chemistry, circular economy, digital twins, autonomous experimentation, and sustainable process design. The cited literature was used as seed literature and expanded conceptually across the period in which digitally enabled chemistry and Industry 5.0 became prominent.

Sources were retained when they contributed directly to at least one of four analytical domains: digital capability, sustainable chemistry, human-centred design, or operational resilience. Policy documents were used to define Industry 5.0; peer-reviewed articles and scholarly books were used for scientific and engineering concepts. Claims requiring raw Scopus or Web of Science exports—such as publication rankings, co-occurrence networks, correlations, and precise screening totals—were excluded. Consequently, this article offers a transparent conceptual synthesis rather than a bibliometric or PRISMA systematic review.

The evidence was organized by comparing the dominant purpose, unit of optimization, decision authority, performance indicators, and failure modes of Chemistry 4.0 and Chemistry 5.0. The resulting framework was then translated into an implementation pathway and indicator set suitable for laboratories and chemical-process organizations.

3.0 RESULTS AND DISCUSSION

Industry 4.0 integrated physical production with digital communication and computation, enabling decentralized control and data-driven manufacturing [2]. Chemistry 4.0 applies this logic to laboratory and process environments through connected analytical instruments, laboratory information systems, robotic experimentation, process analytical technology, and computational models. Its main contribution is the conversion of fragmented operations into observable and optimizable systems.

Chemistry 5.0 does not reject this foundation. It adds constraints and purposes that are frequently external to conventional productivity optimization. A candidate molecule is not preferred solely because a model predicts high activity; its synthesis, toxicity, feedstock origin, persistence, and end-of-life implications must also be considered. Likewise, a process is not superior solely because it increases yield or throughput if the improvement shifts burdens to energy demand, solvent use, worker exposure, or downstream waste.



The transition is therefore from tool adoption to responsible system design. Chemistry 4.0 asks how digital technologies can improve chemical work. Chemistry 5.0 asks what chemical work should be improved, for whom, under which environmental limits, and with what evidence and accountability.

3.1 Digital intelligence in chemical discovery and development

Machine learning can extract relationships from molecular, spectroscopic, reaction, and process data that are difficult to identify using one-factor-at-a-time experimentation. In molecular design, models can prioritize candidates, estimate properties, and guide synthesis planning. In formulation and process development, surrogate models can connect composition and operating conditions with multiple responses, reducing experimental burden when the domain of applicability is respected.

Autonomous laboratories combine algorithmic experiment selection, robotic execution, automated analysis, and iterative learning [3]. Their principal sustainability opportunity lies in choosing more informative experiments, not merely performing more experiments. Closed-loop optimization can reduce reagent consumption and development time, but only when objective functions include safety and environmental criteria alongside yield, selectivity, or functional performance.

The principal limitations are data quality, hidden bias, weak extrapolation, and loss of mechanistic scrutiny. Chemical datasets often combine measurements made under different protocols or omit unsuccessful experiments. Accordingly, model documentation should record provenance, uncertainty, applicability domain, excluded data, and the human decisions that shaped the pipeline. Human review remains essential where a prediction affects hazardous operations, product safety, or environmental release.

3.2 Digital twins and cyber-physical chemical systems

A digital twin is a dynamically updated virtual representation of a physical asset, process, or system. Unlike a static simulation, it receives operational data and can support diagnosis, prediction, and scenario testing [4]. In chemical engineering, twins can connect mechanistic models, soft sensors, process historians, and control systems to evaluate energy use, product quality, equipment condition, and abnormal situations.

For Chemistry 5.0, the twin should extend beyond production efficiency. Environmental inventories, material provenance, solvent recovery, emissions, and waste routes can be associated with operating states. This makes it possible to test whether a local improvement creates a life-cycle burden elsewhere. A formulation twin may similarly connect composition and processing with quality, stability, release behaviour, safety, and end-of-life assumptions.

A twin is only as credible as its validation and data governance. Model drift, sensor failure, undocumented changes, and cyberattack can convert apparent precision into operational risk. Version control, calibration history, access management, uncertainty reporting, and human override must therefore be treated as functional requirements rather than administrative additions.

3.3 Green chemistry and circular economy as design constraints

Green chemistry established a preventive approach in which hazard and waste are addressed through molecular and process design [5, 10]. The circular economy adds a systems perspective concerned with maintaining value, slowing and closing resource loops, and avoiding the regeneration of waste under a new label [6]. Together, these concepts give Chemistry 5.0 its environmental direction.

Digital tools can accelerate solvent selection, reaction-condition optimization, safer-substitute screening, waste-stream characterization, and material-flow analysis. However, optimization requires explicit constraints. A model trained only to maximize yield may prefer conditions with high energy demand or problematic solvents. Multi-objective functions should therefore include atom economy, mass intensity, solvent hazard, energy demand, renewable content, durability, recovery, and expected exposure as appropriate to the application.

Circular claims require particular discipline. Bio-based origin does not automatically imply low toxicity, biodegradability, or reduced life-cycle impact. Recyclability demonstrated under ideal laboratory conditions is not equivalent to recovery in an available system. Chemistry 5.0 should distinguish intrinsic material

properties from system-level outcomes and should report boundaries, allocation rules, uncertainty, and infrastructure assumptions.

3.4 Human-centred and resilient chemical practice

Human-centricity places technology in service of people rather than positioning people as residual components of automation [1]. In chemical work, this includes safer interfaces, reduced exposure, meaningful human control, accessible training, and recognition of tacit knowledge. Operators and laboratory professionals should participate in system design because they understand deviations, maintenance realities, and informal adaptations that are rarely visible in clean datasets.

Augmentation is preferable to indiscriminate substitution. Decision-support systems can integrate large data streams and expose trade-offs, while accountable professionals interpret context and authorize consequential actions. This division requires calibrated trust: users must understand what the system knows, where uncertainty is high, and how to challenge its recommendation.

Resilience concerns the capacity to anticipate, absorb, and adapt to disruption. Digital twins and scenario models can evaluate feedstock shortages, utility failures, climate-related events, and equipment constraints. Yet interconnected systems also create dependencies. Modular design, local fallback procedures, secure architectures, interoperable data, and diversified supply options are therefore core Chemistry 5.0 attributes.

3.5 Integrated Chemistry 5.0 architecture

Figure 1 organizes Chemistry 5.0 as an integration layer among digital intelligence, sustainable chemistry, human-centred practice, and resilient operations. None of these domains is sufficient alone. Digital intelligence without sustainability can optimize the wrong target; sustainability without reliable measurement can become assertion; automation without human-centred design can erode responsibility; and connected operations without resilience can amplify disruption.

The unifying mechanism is an evidence loop: measure, model, decide, validate, and learn. Each cycle should preserve the relationship between data and physical reality, record the criteria used for a decision, and test whether expected benefits occur. This architecture is deliberately iterative because chemical development and production are affected by scale, variability, ageing, supply changes, and evolving knowledge.

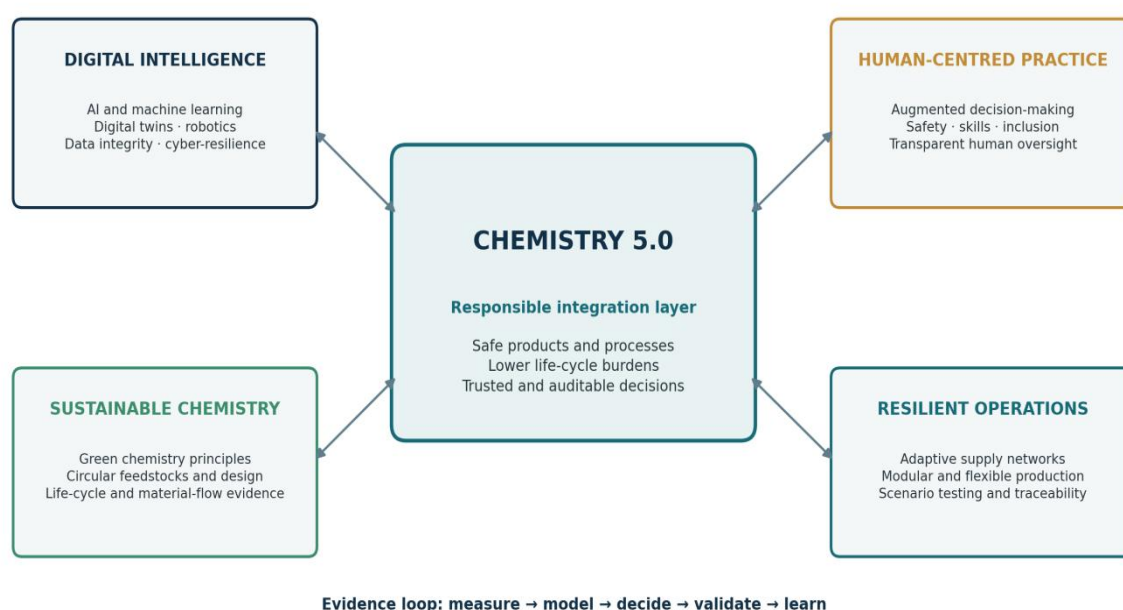


Fig. 1 Integrated scientific architecture for Chemistry 5.0. Digital intelligence, sustainable chemistry, human-centred practice, and resilient operations are connected through an auditable evidence loop.



3.6 Technology and value mapping

Table 1 maps major digital capabilities to their Chemistry 5.0 value, evidence needs, and characteristic risks. The table emphasizes that a technology becomes compatible with Chemistry 5.0 only when its deployment includes relevant safeguards and outcome measures.

Table 1 Digital capabilities mapped to Chemistry 5.0 value, evidence, and safeguards.

Capability	Primary value	Minimum evidence	Principal safeguard
Machine learning	Property prediction; candidate and condition prioritization	External validation, uncertainty, applicability domain, data provenance	Human review; bias and drift monitoring
Autonomous experimentation	Efficient closed-loop selection and execution of experiments	Baseline comparison; reagent, energy, and time accounting	Multi-objective constraints; physical interlocks
Digital twins	Dynamic scenario testing, control, and predictive maintenance	Calibration, update frequency, residual analysis, version history	Cybersecurity; fail-safe operation; human override
Connected analytical systems	Traceable real-time quality and process information	Validated methods, metadata completeness, instrument status	Access control; audit trails; interoperability
Life-cycle and material-flow models	Detection of burden shifting and circularity constraints	Declared boundaries, inventories, allocation, uncertainty	Independent review; sensitivity analysis
Immersive and decision-support interfaces	Training, visualization, and safer task execution	Usability, comprehension, error and workload evaluation	Participatory design; accessibility; clear accountability

3.7 Staged implementation pathway

Implementation should begin with a bounded use case and a documented baseline. Organizations often purchase advanced platforms before defining the decision they are intended to improve. A better sequence starts with the chemical, environmental, safety, or resilience problem; identifies minimum data and validation needs; then selects the least complex digital intervention capable of addressing it.

Pilot studies should be evaluated against the baseline using technical and non-technical indicators. Scale-up should follow only after the data pipeline, model limits, user roles, cybersecurity controls, and life-cycle implications have been reviewed. Table 2 summarizes a six-stage pathway that can be adapted to research laboratories, pilot plants, and manufacturing facilities.



Table 2 Staged pathway for implementing Chemistry 5.0.

Stage	Core action	Decision gate	Representative outputs
1. Define	Specify problem, stakeholders, system boundary, hazards, and baseline	Is the use case material and sufficiently bounded?	Problem statement; baseline; responsibility map
2. Govern data	Establish provenance, quality rules, access, metadata, and retention	Are data fit, lawful, secure, and representative?	Data plan; validation protocol; audit trail
3. Model and design	Select mechanistic, statistical, or hybrid approach; define objectives and constraints	Does the design encode safety, environmental, and human requirements?	Model card; objective function; risk register
4. Pilot	Test with physical validation and user participation	Does performance exceed baseline without burden shifting?	Pilot report; uncertainty; user evaluation
5. Scale	Assess transferability, infrastructure, cybersecurity, and life-cycle effects	Are scale-dependent risks controlled and benefits reproducible?	Scale-up plan; LCA or screening; contingency plan
6. Learn	Monitor drift, incidents, outcomes, and changing assumptions	Should the system continue, be revised, or be withdrawn?	Dashboard; review record; controlled updates

3.8 Indicators for Chemistry 5.0

A balanced indicator set should prevent gains in one domain from concealing losses in another. Technical indicators may include predictive error, yield, selectivity, throughput, robustness, and deviation rate. Environmental indicators may include process mass intensity, solvent intensity, energy demand, greenhouse-gas emissions, hazardous input fraction, renewable content, recovery yield, and waste destination. Human-centred indicators may include exposure reduction, usability, training completion, override frequency, reported workload, and participation in design. Resilience indicators may include recovery time, supply-source diversity, fallback capability, and performance under simulated disruption.

Not every project requires every indicator. Selection should follow materiality: the metrics must represent the most consequential effects of the specific system. Baselines, system boundaries, units, uncertainty, and data sources should be stated. Composite scores can assist communication but should not conceal trade-offs or permit poor safety performance to be compensated numerically by efficiency gains.

3.9 Challenges and research agenda

The first challenge is semantic and methodological. Chemistry 5.0 risks becoming a promotional label unless authors specify what changed relative to ordinary digitalization and how sustainability, human-centredness,



and resilience were measured. Comparative studies should test integrated objective functions against conventional performance-only optimization.

The second challenge is infrastructure inequality. High-quality automation and data systems remain concentrated in well-resourced organizations. Research is needed on modular, interoperable, and lower-cost architectures that allow smaller laboratories and institutions to participate without surrendering data control. Shared standards should support reuse while protecting confidential and sensitive information.

The third challenge is validation across scales. Models trained on microscale experiments may not capture mixing, heat transfer, impurity accumulation, or equipment constraints at larger scales. Hybrid models that combine mechanistic understanding with data-driven learning are promising because they can improve interpretability and reduce unreasonable extrapolation [7].

Finally, education must integrate chemical fundamentals, statistics, programming, safety, ethics, and life-cycle reasoning. The future chemist or chemical engineer should be able to interrogate an algorithmic recommendation as critically as a spectrum or mass balance. Chemistry 5.0 will be credible only if professional judgment grows with computational capability.

4.0 CONCLUSION

Chemistry 5.0 is best understood as a responsible operating paradigm for chemical science and engineering. It retains the connected instruments, models, automation, and data infrastructures of Chemistry 4.0 but redirects them toward safer chemistry, circular resource use, human agency, and resilient operation. Its defining feature is not a particular technology; it is the integration of technical and public-value objectives within auditable decision cycles.

Artificial intelligence, autonomous laboratories, and digital twins can reduce experimental burden, reveal complex relationships, and improve process control. Their benefits are conditional on validated data, explicit system boundaries, uncertainty reporting, cybersecurity, and human oversight. Green and circular outcomes must be demonstrated rather than inferred from digitalization or bio-based content.

The proposed architecture, technology mapping, implementation pathway, and indicators provide a practical basis for research and institutional adoption. Future work should test the framework through transparent case studies that report both successes and failed assumptions. In short, Chemistry 5.0 begins where optimization stops being the final question and responsibility becomes part of the objective function.

Acknowledgements

The authors acknowledge the Federal University of São João del-Rei (UFSJ), the National Council for Scientific and Technological Development (CNPq), and the Coordination for the Improvement of Higher Education Personnel (CAPES) for institutional and infrastructure support.

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Paula Cristina Santana Cardilli: Investigation, Literature review, Data curation, Formal analysis, Writing – original draft.

Boutros Sarrouh: Methodology, investigation, literature synthesis, visualization, writing—original draft, writing—review and editing, and final approval of the manuscript.

Renata Carolina Zanetti Lofrano: Conceptualization, methodology, investigation, literature synthesis, visualization, writing—original draft, writing—review and editing, and final approval of the manuscript.

Funding

This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors declare no competing financial or non-financial interests.

Data availability

No new datasets were generated or analyzed for this critical narrative review. The sources supporting the synthesis are cited in the manuscript.

Ethics approval and consent to participate

Not applicable. This article does not report research involving human participants or animals.

Consent for publication

All authors must approve the final submitted version.

Declaration of generative AI and AI-assisted technologies

During manuscript preparation, AI-assisted tools were used to support language refinement, structural editing, and development of the conceptual figure. The authors are responsible for reviewing and verifying the content, references, and final submitted version.

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