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REVIEW ARTICLE

Advancing sustainability in bioprinting through artificial intelligence

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Abstract

Sustainable bioprinting is a transformative approach in tissue engineering and regenerative medicine, offering solutions to environmental challenges while advancing functional outcomes. However, achieving true sustainability remains complex, requiring reductions in material waste and energy use, and scalable, resource-efficient fabrication without compromising biological performance. Artificial intelligence (AI) provides a powerful means to meet these demands through data-driven material design, predictive process optimization, and intelligent control systems that improve both efficiency and environmental impact across the bioprinting workflow. This review examines the integration of AI into sustainable bioprinting across four key areas: hydrogel material discovery and development, bioink screening, process parameter optimization, and AI-assisted intelligent printing. AI facilitates the design of eco-friendly hydrogels by predicting molecular interactions and tailoring structural properties. It also improves bioink formulation by optimizing printability, biocompatibility, and mechanical strength, thereby reducing reliance on resource-intensive trial-and-error experimentation. Furthermore, AI algorithms streamline workflows by dynamically adjusting printing parameters to improve fidelity and reduce waste, while advanced AI-assisted systems demonstrate the feasibility of multi-material, contactless bioprinting, aligning with sustainability goals.

Keywords: Artificial intelligence; Biomaterials; Bioprinting; Sustainability

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1. Introduction

Bioprinting is an advanced additive manufacturing technique that precisely deposits bioinks, which are composed of cells, biomaterials, and sometimes growth factors, in a layer-by-layer manner to fabricate complex, functional biological structures.[1–3] It is a transformative technology at the intersection of materials science, biology, and engineering.[4] It allows customization of bioink placement and control over architectural features and cell density, significantly enhancing the level of biomimicry of the native cell niche.[5–7] It also enables the fabrication of complex, patient-specific structures tailored for personalized medicine and provides highly relevant, less invasive biological models for comprehensive systemic investigations and evaluations.[8–11] Hydrogels play a pivotal role as bioink materials due to their high water content, biocompatibility, and ability to mimic the extracellular matrix.

The increasing adoption of bioprinting places sustainability challenges at the forefront of the field. Conventional hydrogel materials, while effective, often rely on finite resources or involve manufacturing processes that generate chemical waste, consume high energy, or raise environmental and ethical concerns. As the demand for bioprinting scales up, particularly in fields such as regenerative medicine, drug screening, and tissue modeling, the need for sustainable, eco-friendly alternatives becomes increasingly urgent.[12,13] In this context, sustainable bioprinting refers to the development and implementation of bioprinting systems, materials, and workflows that minimize environmental impact, optimize resource use, and enhance scalability without compromising biological or functional performance. This includes using hydrogels derived from renewable or recycled sources, such as plant-based polysaccharides, waste-derived biopolymers, or repurposed synthetic polymers, which reduce reliance on petroleum-based feedstocks and promote material circularity. It also involves lowering the carbon footprint of fabrication by optimizing energy consumption during hydrogel synthesis, crosslinking, and printing processes, for instance, through low-temperature curing methods or solvent-free fabrication. Additionally, minimizing material waste during formulation and printing can be achieved through precise control of deposition parameters, reusability of support materials, and predictive modeling that reduces failed prints and redundant experiments. Together, these strategies contribute to a more resource-efficient, environmentally responsible bioprinting workflow aligned with broader sustainability goals in biofabrication and healthcare innovation.

However, implementing these sustainability strategies introduces new challenges. Renewable or recycled hydrogels often exhibit variability in composition and mechanical properties, making it difficult to ensure consistent printability and biological performance. Similarly, optimizing fabrication parameters to reduce energy use or material waste requires fine control over complex, interdependent variables such as viscosity, crosslinking dynamics, nozzle speed, and cell viability. Traditional trial-and-error methods are not only time-consuming and inefficient but also generate additional waste, counteracting sustainability goals. Moreover, the growing diversity of biomaterials, printing techniques, and application-specific design constraints further complicates sustainable bioprinting workflows.

Artificial intelligence (AI) offers a transformative solution to these challenges, providing data-driven insights and predictive capabilities to sustainable bioprinting.[14–16] AI can accelerate the discovery and optimization of hydrogels by predicting their performance based on molecular structure and interactions.[12,13,17] This contributes to the development of hydrogels tailored for specific applications in tissue engineering and drug delivery, and reduces the need for extensive physical testing. Furthermore, AI enables intelligent screening of bioink formulations for printability and functionality, optimizing rheological properties and crosslinking conditions.[14] Beyond material development, AI-assisted algorithms enhance bioprinting processes by optimizing printing parameters, minimizing waste, and improving printing fidelity and performance.[18] Integrating AI into bioprinting enables researchers to address sustainability challenges by accelerating the development process of sustainable biomaterials for bioprinting, minimizing material waste by eliminating unnecessary experimental iterations, and advancing the functionality of this technology.

While previous studies have explored the roles of AI in bioprinting[16,18,19] or discussed general principles of sustainability in biofabrication and AI's potential,[20] a comprehensive synthesis linking these domains remains limited. This review uniquely addresses this gap by proposing a structured, four-pillar framework illustrating how AI directly enhances sustainability in bioprinting: (i) accelerated material discovery (e.g., AlphaFold 3 for biomolecular prediction), (ii) data-driven bioink formulation screening, (iii) dynamic parameter optimization, and (iv) intelligent printing systems. This structure is shown in Figure 1. Furthermore, the review critically discusses implementation challenges and provides a comprehensive roadmap, advancing the current discourse by explicitly integrating AI methodologies with sustainability targets across the entire bioprinting workflow.

2. Bioprinting

2.1. Bioprinting techniques

This review categorizes bioprinting techniques based on their principles for stimuli-responsive deposition of bioinks into four main methods: inkjet bioprinting (using thermal and piezoelectric effects), extrusion-based bioprinting (utilizing air pressure or mechanical forces), laser-assisted bioprinting (using laser for droplet deposition), and stereolithography (using light for solidification), as shown in Figure 2.

Inkjet bioprinters dispense bioink droplets in the picoliter range using either thermal or piezoelectric mechanisms.[22,23] Thermal inkjet printers heat bioink to create pressure pulses that propel droplets, while piezoelectric printers generate acoustic waves to break

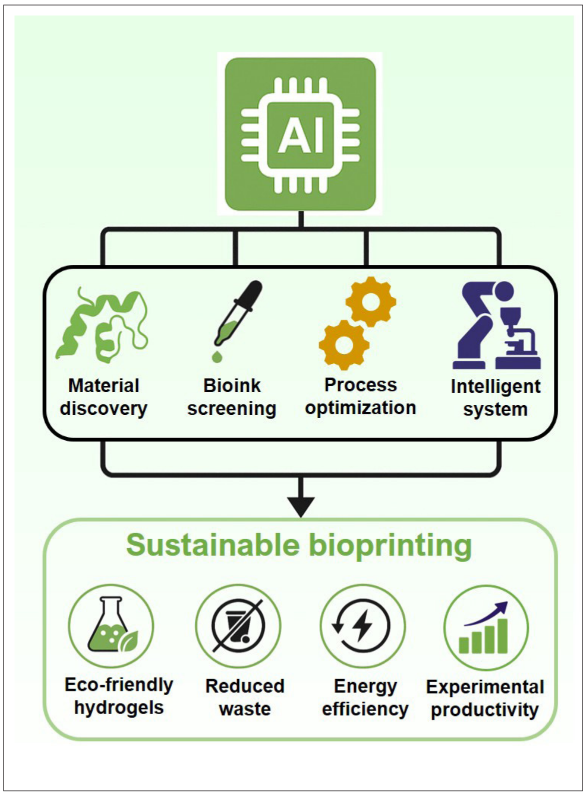

Figure 1. Overview of the structure of this review, which explores how artificial intelligence (AI) supports sustainable bioprinting across four key domains: material discovery, bioink screening, process optimization, and intelligent system integration. These AI-driven strategies contribute to the development of eco-friendly hydrogels, the reduction of material waste, improved energy efficiency, and experimental productivity.

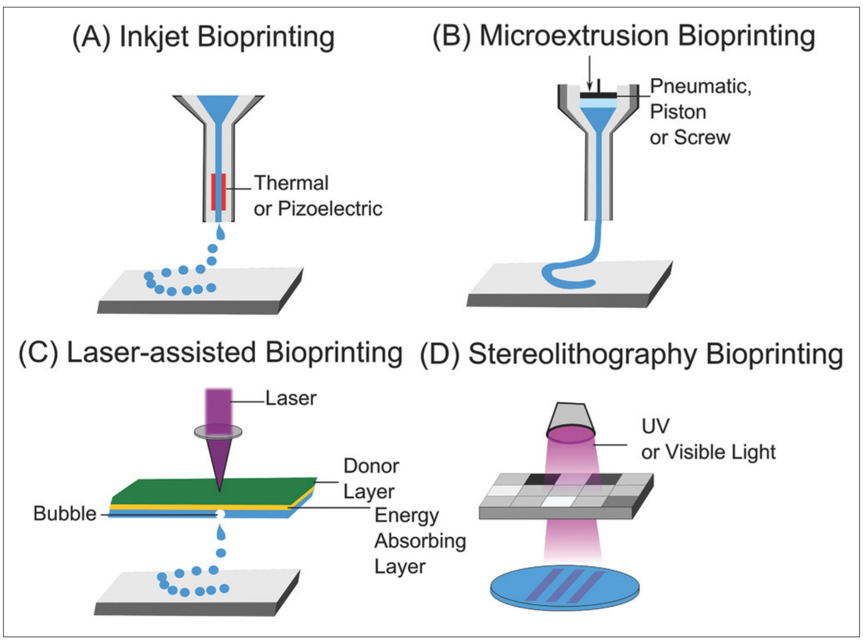

Figure 2. Schematic representation of the four main bioprinting methods. (A) Inkjet bioprinting utilizes piezoelectric or thermal actuators to eject precise, small droplets of bioinks containing hydrogels and cells. (B) Microextrusion bioprinting deposits filaments of viscous bioinks continuously through a nozzle, driven by pneumatic or mechanical (piston or screw-based) force. This technique excels in fabricating constructs with high cell densities and structural integrity. (C) Laser-assisted bioprinting uses a focused laser pulse to vaporize a thin donor layer (typically metallic or energy-absorbing material), generating high-pressure bubbles that propel droplets of bioink onto the substrate. (D) Stereolithography bioprinting employs ultraviolet (UV) or visible light to selectively polymerize photoreactive bioink layer-by-layer, creating a three-dimensional construct. Reprinted from Foyt et al.[21]

bioink into droplets.[23] Inkjet printing is cost-effective and widely available but faces challenges such as cell damage from heat or sound, inconsistent droplet size, and nozzle clogging.[24]

Extrusion-based bioprinters use mechanical or pneumatic systems to deposit continuous bioink filaments with high precision across *x*-, *y*-, and *z*-axes.[25] This method accommodates a wide range of bioink viscosities, supporting structural integrity with higher viscosities or promoting cell viability with lower ones.[26,27] It excels in printing bioinks with varying cell densities and mechanical properties.[28,29]

Laser-assisted bioprinting employs laser-induced forward transfer to deposit bioinks with cell-level precision.[30,31] A laser pulse vaporizes the metal film or bioink layers, creating bubbles that propel droplets onto the substrate. This technique offers exceptional patterning accuracy but is limited by low flow rates, high costs, metallic residues, and small print sizes, restricting its use for larger tissue or organ fabrication.[31]

Stereolithography bioprinting uses photopolymerization to solidify bioink layer-by-layer with ultraviolet (UV) or visible light.[32,33] A light source selectively cures bioink in precise patterns to form complex three-dimensional (3D) structures. As an entire layer is solidified simultaneously with the light projection, this layer-by-layer process can often increase printing speeds.[34] However, its reliance on light-sensitive materials and the potential cytotoxicity of unpolymerized residues may pose challenges.

2.2. Sustainable hydrogels for bioprinting

Hydrogels stand out as bioink materials and are becoming indispensable in bioprinting due to their high-water content, biocompatibility, and ability to mimic the extracellular matrix, supporting cell adhesion, proliferation, and differentiation.[2,35,36] Traditional hydrogels often pose environmental challenges, including resource-intensive production and limited recyclability. Sustainable hydrogels are therefore becoming a focal point in bioprinting due to their potential to address both functional and environmental challenges associated with conventional materials.[37–39] These hydrogels are specifically designed to meet the rigorous demands of bioprinting, such as biocompatibility and biodegradability, while maintaining environmental responsibility. Unlike traditional materials that may rely on finite resources or involve energy-intensive production processes, sustainable hydrogels emphasize minimal environmental impact by utilizing renewable or recycled materials.[40,41] This dual focus on functionality and sustainability makes them an essential component for advancing bioprinting technologies while adhering to eco-friendly principles.

These sustainable hydrogels can be broadly categorized based on their origin and composition, including natural hydrogels, derived from renewable biopolymers, and recycled hydrogels, made from repurposed polymers engineered for reusability.[42,43]

2.2.1. Biopolymers

Biopolymers, which are derived from natural plants, microbes, and other organisms, are more sustainable than synthetic polymers.[44] Hydrogels made from biopolymers are also inherently biocompatible and biodegradable, mimicking the extracellular matrix to promote cell attachment and proliferation. However, their mechanical properties often require enhancement through chemical modifications or blending with other materials to meet the structural demands of bioprinting.

Common biopolymers used for bioprinting include alginate, collagen, and gelatin. Alginate is a natural, water-soluble material primarily derived from brown seaweed and bacteria.[45] It has been used successfully for maintaining a chondrogenic phenotype of chondrocytes and enhancing neocartilage formation.[46,47] Its ionic crosslinking property facilitates printing of stable structures, contributing to its widespread use in bioprinting. Collagen is the main structural protein in the articular cartilage and meniscus extracellular matrix, and can be isolated from numerous biological tissues, retaining key signalling, adhesive, and other biochemical cues.[48] Gelatin is a water-soluble and biodegradable polypeptide produced through collagen hydrolysis. It has been extensively integrated with natural or synthetic hydrogels to enhance the biological properties of hydrogel composites.[47,49,50]

2.2.2. Recycled/upcycled polymers

Recycled or upcycled hydrogels offer another avenue for sustainability.[51] These materials not only reduce environmental waste but also align with circular economy principles by repurposing byproducts into functional biomaterials.[52] These hydrogels prioritize resource efficiency by enabling reuse through chemical or physical modifications, such as phase separation or crosslinking, retaining functionality across bioprinting cycles.[42,51]

Recent advances in hydrogel design have introduced recyclable and upcycled polymers that support sustainable bioprinting by reducing material waste and enabling multiple reuse cycles. Charlet et al.[42] developed recyclable double-network granular hydrogels with a disulfide-based network that allows selective degradation and microgel recovery while preserving printability. Xu et al.[53] created phase-separated supramolecular hydrogels with enhanced toughness and recyclability under extreme conditions. Ji et al.[54] introduced a salting-out-based method using poly(N-isopropylacrylamide) hydrogels, enabling reversible solidification and dissolution without chemical crosslinkers or post-processing. Collectively, these approaches maintain mechanical performance while promoting circular material use, offering promising pathways for integrating sustainability into future bioprinting workflows.

3. Artificial intelligence for sustainable bioprinting

Despite advances in sustainable hydrogels for bioprinting, challenges remain in balancing printability, biocompatibility, biodegradability, and mechanical strength.[18,55,56] Hydrogels must exhibit optimal rheological properties for smooth deposition while maintaining structural integrity.[57] However, materials often excel in one attribute at the expense of another—for example, natural hydrogels offer high biocompatibility but lack the mechanical robustness needed for complex structures. Beyond material selection, ensuring efficient, reproducible bioprinting is equally complex. Traditional trial-and-error methods lead to resource inefficiencies, waste, and prolonged development cycles. Variability in bioink properties, processing parameters, and post-printing conditions further impacts cell viability, tissue functionality, and print success, undermining sustainability.

AI offers a transformative solution by enhancing material discovery, process optimization, and print quality. Coined by John McCarthy, the term AI refers to the intelligence demonstrated by machines.[58] Early rule-based AI relied on predefined "if-then" rules, facilitating data analysis and automation.[59,60] Classical AI introduced knowledge-based systems that integrated expert reasoning for problem-solving.[61,62] The emergence of machine learning (ML) revolutionized AI, enabling systems to learn from large datasets, recognize complex patterns, and predict material and print outcomes beyond the limitations of predefined rules.[63–66]

By combining the structured, efficient automation of classical AI with the adaptability and predictive capabilities of ML, AI is currently transforming sustainable bioprinting across multiple dimensions.[67–71] In hydrogel design, AI accelerated the discovery of materials that balance functionality, printability, and sustainability by predicting their behavior under diverse conditions and minimizing the resource-intensive nature of traditional development.[17] AI-driven approaches also enhanced material screening processes, ensuring bioinks meet the specific mechanical, biological, and environmental requirements for bioprinting.[14,72,73] Furthermore, AI optimized printing parameters in real-time, improving construct fidelity, reducing waste, and advancing efficiency.[19,74–76] Lastly, AI-assisted intelligent bioprinting technologies enabled powerful bioprinting capabilities with improved sustainability. Together, these innovations demonstrate AI's pivotal role in driving sustainable bioprinting forward, aligning with both ecological and functional demands. AI applications are categorized not only by technical functions but also by their potential impact on sustainability.

3.1. Material discovery and development

AI has revolutionized the incorporation of bioactive molecules into hydrogels, significantly enhancing their functionality for bioprinting applications.[77] Tools like AlphaFold, a deep learning model for protein structure prediction, enable precise identification of molecular interactions, facilitating the integration of bioactive components such as growth factors, peptides, and enzymes into hydrogel matrices for functionalization. AI-driven methods allow the design of hydrogels with tailored properties.

One notable example of AI's potential in modeling molecular interactions is AlphaFold, which has redefined protein structure prediction. AlphaFold, developed in three successive versions (AlphaFold 1, 2, and 3), has revolutionized protein structure prediction. AlphaFold 1 introduced neural networks to predict inter-residue distances, demonstrating significant advancements in protein modeling by leveraging evolutionary data and achieving superior accuracy during the Critical Assessment of Structure Prediction 13.[12] It is used on multiple sequence alignments (MSAs) and gradient descent algorithms to model protein structures, achieving notable success in free modeling domains, particularly for proteins lacking homologous templates. AlphaFold 2 advanced this by incorporating Evoformer blocks to integrate spatial and evolutionary relationships, enabling atomic-level accuracy in 3D structural predictions, as shown in the Critical Assessment of Structure Prediction 14.[13] It achieved near-experimental accuracy for most targets, effectively modeling long-range residue interactions and folding pathways, but remained computationally intensive due to its reliance on MSAs. AlphaFold 3 further enhanced capabilities with a diffusion-based architecture, replacing Evoformer with Pairformer[17] (Figure 3). This eliminates MSA dependency while enabling accurate modeling of protein complexes, including protein–ligand and protein–nucleic acid interactions. Its experimental results demonstrated superior performance in predicting multi-component systems, with applications extending to chemically modified residues and novel biomolecular assemblies.

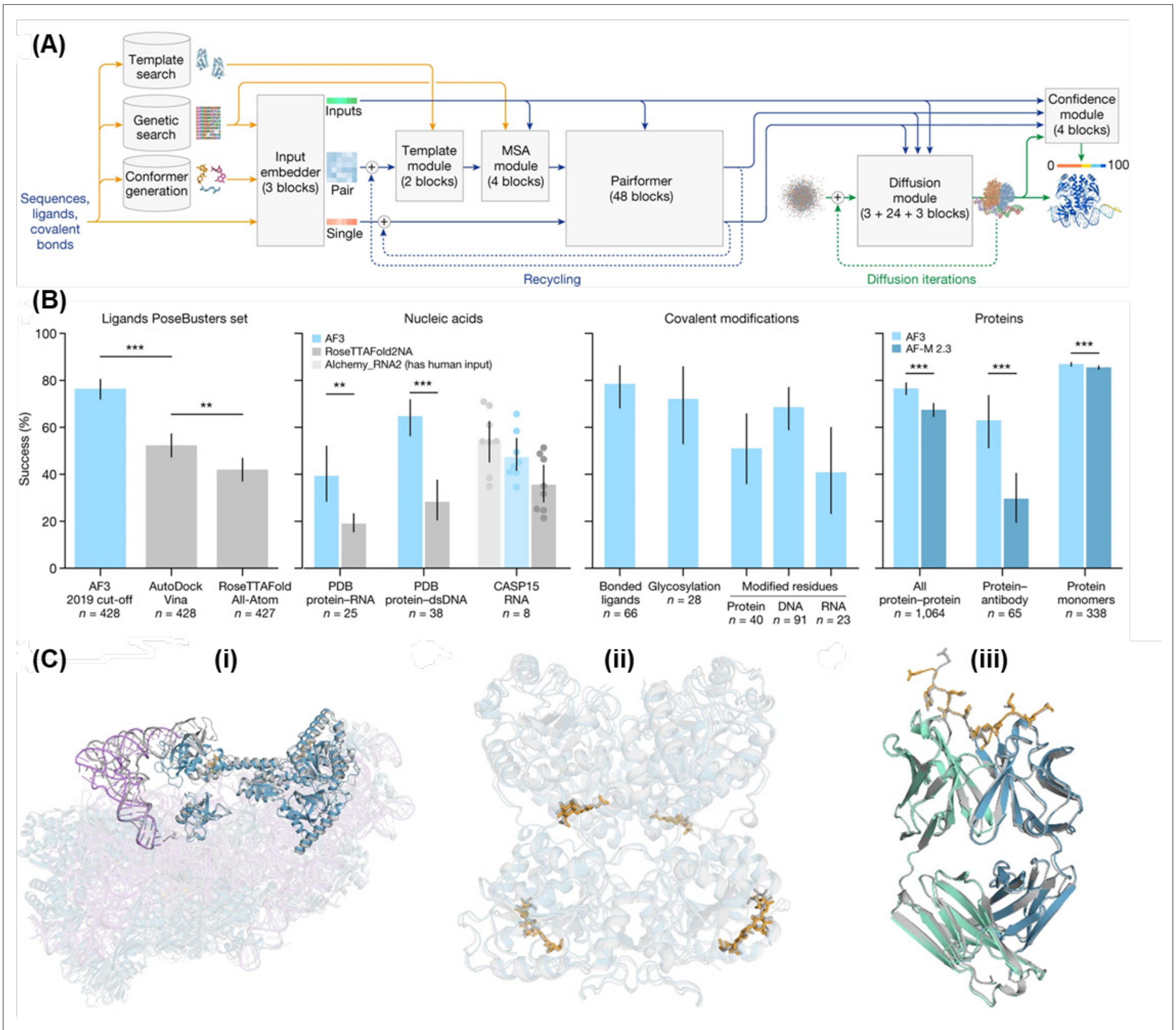

Figure 3. AlphaFold 3 is capable of accurately predicting protein structures, protein–ligand interactions, and multi-component biomolecular complexes using its advanced diffusion-based architecture and Pairformer module. (A) The Pairformer module and diffusion-based architecture of AlphaFold 3 enable precise predictions of biomolecular interactions without reliance on multiple sequence alignments, showcasing its innovative approach to modeling complex biological systems. (B) Success rates in predicting diverse biomolecular complexes, including protein–protein, protein–ligand, and protein–nucleic acid interactions, highlight its capability to identify key functional interactions relevant for material design. (C) Real-world applications of AlphaFold 3 in discovering and modeling biomolecular materials: (i) protein–nucleic acid complexes, (ii) protein–ligand systems, and (iii) ribosomal subunits, demonstrating its potential to guide the development of bioactive hydrogels and other sustainable bioprinting materials. Reprinted from Abramson et al.[17]

Despite AlphaFold's transformative impact on protein modeling, developing comparable AI tools for biomaterial design in bioprinting remains limited by fundamental challenges. One fundamental challenge among these is the absence of large, standardized, and well-annotated open-source datasets that link bioink composition to rheological properties, printability, and biological performance. Unlike protein sequences with defined formats and abundant data, bioinks lack universal representations, and the available datasets are often small, heterogeneous, and inaccessible. This hinders model training, validation, and benchmarking, making it difficult to achieve generalizable or reproducible outcomes. Additionally, the performance of hydrogels often depends not only on molecular configuration but also on mesoscale properties (e.g., porosity, swelling, rheology), which are difficult to encode or predict purely from primary composition. Addressing these limitations requires community-wide efforts in data sharing, standardization, and the development of open benchmarks to accelerate progress in predictive modeling for bioprinting.

To circumvent these limitations, researchers are turning to other AI strategies, such as multi-objective optimization, that focus on synthesis pathways rather than structural modeling alone. Hardian et al.[78] applied support vector machines and a multi-objective genetic algorithm to optimize the green electrochemical synthesis of zeolitic imidazolate framework-8. Their approach enabled simultaneous prediction and optimization of synthesis parameters to maximize product quality while minimizing environmental impact. The AI-optimized conditions achieved a high yield of 88%, crystallinity of 86%, and 100% purity, while keeping energy consumption at 7 kWh/kg of product, an E-factor of 11 kg waste/kg product, and a carbon footprint of 27 kg carbon dioxide-equivalent/kg product. These results demonstrate the potential of AI to identify synthesis conditions that balance performance with sustainability. Although focused on metal–organic frameworks, the methodology is highly transferable to bioprinting contexts such as bioink and scaffold development, where similar multi-objective trade-offs between material function and environmental impact must be addressed.

These advancements represent a transformative opportunity for sustainable hydrogel and biomaterial discovery in bioprinting. Emerging ML approaches enable predictive modeling at multiple scales, from atomic-level biomolecular interactions to macroscopic material performance, facilitating the rational design of bioinks with optimized mechanical strength, biocompatibility, and biodegradability. Tools like AlphaFold exemplify how deep learning can predict protein–material interactions to guide the development of functional bioactive hydrogels. Complementing this, other AI-driven frameworks have demonstrated the ability to optimize synthesis pathways by balancing material yield with environmental metrics such as energy consumption and carbon footprint. Together, these approaches highlight the broader potential of AI in accelerating sustainable material development for bioprinting. By integrating high-throughput computational modeling with multi-objective optimization, AI reduces reliance on trial-and-error experimentation, conserves resources, and enables the targeted design of novel, eco-friendly bioinks, thus contributing to more efficient and sustainable biofabrication.

3.2. Bioink formulation screening

Once promising hydrogel materials are discovered and selected based on their functional properties tailored to specific applications, the next step is bioink formulation screening to assess their practicality and reliability for bioprinting applications. This requires a detailed analysis of performance indicators, including printability, rheological behavior, crosslinking efficiency, and cellular response under various printing conditions. This stage ensures that hydrogel formulations not only meet theoretical design criteria but also perform effectively during bioprinting. The integration of AI-driven methodologies, such as ML models, enables rapid evaluation and prediction of hydrogel performance, minimizes trial-and-error experimentation, and ensures sustainable, high-quality outcomes in bioprinting applications.[79]

Ink printability is a crucial aspect of 3D printing as it greatly influences the integration and function of printed implants.[2] ML has been used to predict printability from biomaterial formulations to guide the development of inks. Chen et al.[14] used ML learning algorithms to predict printable biomaterial formulations for direct ink writing. The data used in their study consisted of 210 ink formulations with two ink systems: the hydrogel-based system (including both natural and synthetic hydrogels) and the polymer organic solution-based system. The biomaterials include polymers of a range of molecular weights, properties, and functional fillers with different sizes and functions. The inks were 3D-printed using the direct ink writing technique, and their printability was assessed. The ML algorithms (decision tree, random forest, and deep learning) successfully predicted the printability of biomaterial formulations with high accuracy (>88%), as shown in Figure 4A. In addition, a printability map of biomaterial composites was generated using the trained ML algorithms to guide the ink design (Figure 4B). This study has paved the way for using ML in guiding the selection of materials with a range of properties for different types of 3D printing.

AI-driven models can screen potential hydrogel candidates based on their physicochemical and mechanical properties, such as viscosity, shear-thinning behavior, and crosslinking efficiency. Nadernezhad and Groll[80] employed a random forest algorithm to predict the printability of hyaluronic acid-based hydrogel inks based on their rheological properties. They quantitatively assessed the significance of various rheological parameters and identified 13 critical measures that defined the printability of hydrogel formulations. Their trained model statistically predicted that a printable formulation should demonstrate high yield viscosity and minimal plasticity before initiating flow.

Lee et al.[81] presented a ML-based strategy for bioink design, focusing on elastic modulus for shape fidelity and yield stress for extrusion feasibility (Figure 4B). Data

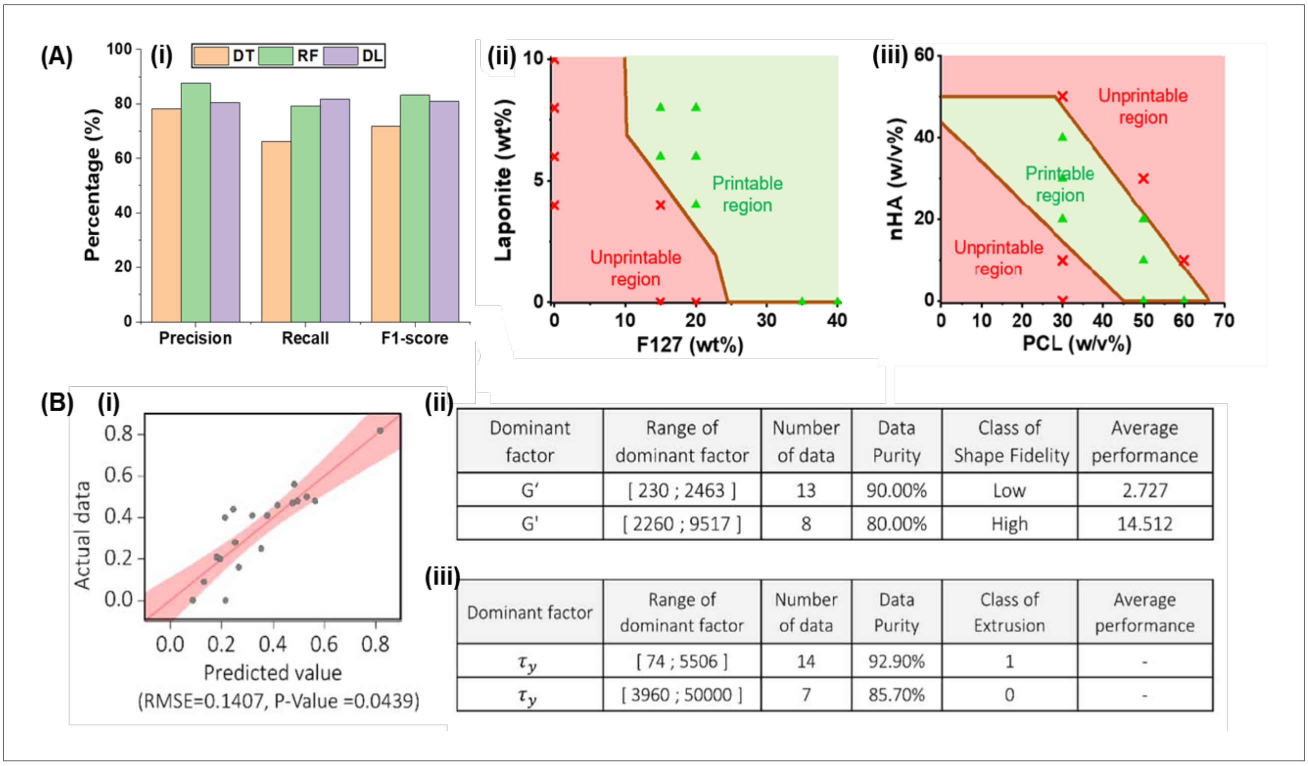

Figure 4. Machine learning in material screening for bioprinting. (A) Machine learning in predicting the printability of biomaterials for direct ink writing. (i) Prediction performance among decision tree (DT), random forest (RF), and deep learning (DL) models.[14] Reprinted from Chen et al.[14] (B) Machine learning analysis of bioink printability. (i) Correlation between predicted and actual data (root mean squared error [RMSE]: 0.1407, p-value 0.0439) showing model accuracy. (ii) Shape fidelity classification based on elastic modulus. (iii) Extrusion classification based on yield stress. Reprinted with permission from Lee et al.[80] Copyright © 2020, IOP Publishing Ltd.

includes 25 bioink formulations composed of collagen, hyaluronic acid, and fibrin, with input features including component concentrations and output targets such as elastic modulus, yield stress, extrusion feasibility, and shape fidelity. ML analysis correctly classified 84.6% of cases for shape fidelity and 89.5% for extrusion feasibility, demonstrating strong predictive performance. Bioinks with an elastic modulus above 2260 Pa exhibited high shape fidelity, while those with a yield stress above 3960 Pa led to nozzle clogging. Multiple regression analysis (p-value: 0.0439) further validated a predictive model for optimizing bioink composition based on collagen, hyaluronic acid, and fibrin concentrations. Future work can focus on expanding the dataset beyond the initial 25 formulations and making it openly available to support more robust model training and improve generalizability across a wider range of bioink materials.

AI-driven bioink formulation screening has the potential to significantly improve the efficiency and accuracy of selecting high-performing bioinks by predicting printability, rheological properties, crosslinking behavior, and cell compatibility. ML models trained on large datasets of hydrogel compositions can rapidly identify optimal formulations, reducing the need for trial-and-error experimentation and minimizing material waste. These advancements ensure that selected bioinks meet the necessary structural and biological requirements, accelerating the development of sustainable and functional materials for bioprinting applications. Current studies often rely on small or focused datasets, such as the 25 formulations in Lee et al.,[81] which may lack model generalizability and reproducibility. While Nadernezhad and Groll[80] and Chen et al.[14] incorporated more datasets (180 and 210 samples, respectively), their scope remains confined to specific material systems. Future efforts should focus on expanding the diversity and scale of training data, incorporating broader input parameters such as crosslinking kinetics and cell viability. Most existing models focus primarily on predicting printability based on rheological or mechanical properties. Thus, future work should broaden predictive targets to include crosslinking behavior, degradation profiles, and biological performance metrics such as cell viability and tissue integration, enabling more holistic and application-specific bioink screening.

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3.3. Processing parameters optimization

Besides optimizing bioink formulations, achieving consistent and high-fidelity bioprinted constructs also depends on precise control of printing parameters such as extrusion speed, nozzle pressure, and layer stacking accuracy. Variations in processing conditions can significantly impact construct stability, resolution, and cellular viability.[67,82,83] Traditional approaches to address these challenges involve extensive trial-and-error experiments to fine-tune such parameters and can be time- and resource-consuming. Addressing these complexities through AI-driven optimization offers a transformative approach to enhancing bioprinting efficiency and accuracy.[71,84]

Bone et al.[85] introduced a hierarchical ML (HML) framework for optimizing 3D bioprinting alginate biopolymer (Figure 5A). The dataset included 48 alginate hydrogel prints, with input parameters of ink concentration, flow rate, nozzle speed, and nozzle diameter, and output targets defined as print fidelity metrics (line width and corner radius errors). The HML approach leverages domain knowledge, incorporating integrated system variables (e.g., nozzle speed, flow rate, ink concentration) with middle-layer physical relationships (e.g., effective shear rate, viscosity, proportionality laws) to predict and optimize print fidelity. Experimental validation demonstrated that the HML framework accurately predicts optimal printing parameters, achieving high-fidelity prints with less than 10% dimensional error. The study also highlights the trade-offs in optimizing specific features, such as linewidths and corner radii, emphasizing the need for multi-objective optimization.

Chen et al.[86] demonstrated an AI-driven approach to optimizing 3D bioprinting parameters, enhancing both efficiency and sustainability (Figure 5B). The AI-assisted high-throughput printing–condition–screening system integrates a programmable pneumatic extrusion bioprinter with an AI-powered image-analysis algorithm, systematically optimizing key parameters such as printing pressure, nozzle speed, and printing distance. The model was trained on 280 labeled images of alginate–gelatin hydrogel prints, using deep learning to classify extrusion states and predict optimal print conditions. By automating the screening process, the AI-assisted high-throughput printing–condition–screening system eliminates reliance on extensive trial-and-error experimentation, reducing material waste while ensuring high-quality scaffold fabrication. Experimental results demonstrated that the AI-assisted approach led to a 45% reduction in optimization time, significantly lowering the consumption of bioinks and resources. The optimized hydrogel scaffolds exhibited improved mechanical stability, uniform fiber alignment, and enhanced porosity, factors critical for promoting cell proliferation and tissue regeneration. *In vivo* diabetic wound healing models showed that AI-optimized scaffolds accelerated re-epithelialization, improved collagen deposition, and enhanced vascularization, demonstrating superior therapeutic potential over conventionally printed scaffolds. This AI-assisted workflow minimizes resource consumption, ensures reproducibility, and enhances the scalability of bioprinting.

Fu et al.[87] investigated the effects of printing parameters on the printability of Pluronic F127 hydrogels in extrusion-based 3D bioprinting and introduced an ML-guided optimization framework (Figure 5C). The researchers examined the influence of nozzle temperature, nozzle gauge, path height, and material composition on printability, using the width index as the primary output metric. They trained a support vector machine model on 12 data points selected via uniform design across three key parameters—concentration, nozzle temperature, and path height—and generated a 3D process map that predicted optimal printing regions with over 75% probability of high-fidelity output. While the study demonstrates the potential of ML to reduce trial-and-error and improve parameter selection, the small dataset limits generalizability. Future work should focus on expanding the parameter space and dataset size, incorporating additional variables such as crosslinking conditions and cell viability, and establishing standardized printability metrics to enable broader applicability and model reproducibility across materials and platforms.

Xu et al.[88] developed a predictive framework for assessing cell viability in stereolithography-based 3D-bioprinted gelatin structures, addressing the limitations of physics-based models through an ensemble ML approach combining ridge regression, k-nearest neighbors, random forest, and neural networks. The model was trained and validated on 405 cell viability data points collected from 81 bioprinting conditions, using gelatin methacrylate concentration, UV intensity, UV exposure time, and layer thickness as input features. Results showed that UV exposure time had the greatest impact on cell viability, followed by layer thickness, gelatin methacrylate concentration, and UV intensity.

Zhang et al.[89] developed an integrated framework combining advanced rheological modeling, computational fluid dynamics simulations, and ML to predict as-extruded cell viability in extrusion-based 3D bioprinting. The study used support vector regression to predict Cross power law parameters for alginate inks based on 76 rheological measurements across different concentrations and temperatures, and trained multilayer perceptron regressors

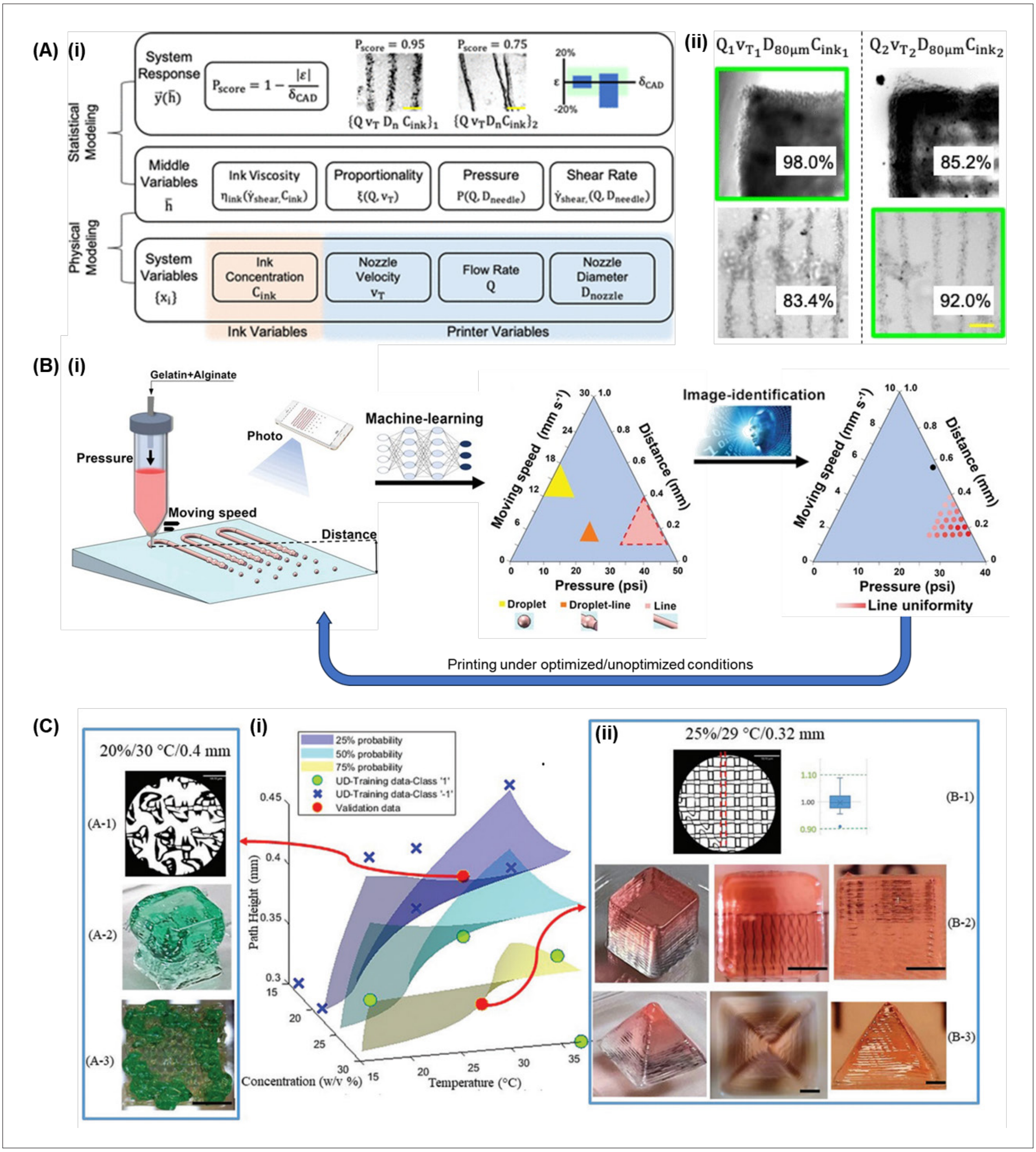

Figure 5. Machine learning in optimizing processing parameters for bioprinting. (A) A hierarchical machine learning model used for optimizing three-dimensional printing parameters. (i) The schematics of the model integrating laboratory-controlled system variables, middle-layer physical relationships, and statistical inference to predict and enhance print fidelity based on dimensional error metrics. (ii) Visualization of trade-offs in optimizing printing parameters for high-fidelity features.[85] Reprinted with permission from Bone et al.[85] Copyright © 2020, American Chemical Society. (B) Artificial intelligence (AI)-assisted high-throughput printing-condition-screening system. Real-time image recognition analyzes printed patterns, classifying them into droplets, droplet lines, or continuous lines. AI-generated phase diagrams guide parameter selection for achieving optimal print fidelity and uniformity, reducing material waste and improving sustainable bioprinting efficiency.[88] Reprinted with permission from Xu et al.[88] Copyright © 2020, Springer Nature. (C) Machine learning-guided parameter optimization in bioprinting. (i) Low-printability validation: Parameters resulted in (A-1) irregular filaments, (A-2) deformed cube, and (A-3) non-uniform grid. (ii) High-printability validation: Optimized parameters produced (B-1) uniform filaments, (B-2) well-formed cube, and (B-3) geometrically accurate pyramid.[87] Scale bar: 1.87 mm for (A-1) and (B-1); 2 mm for (A-3), (B-2), and (B-3). Reprinted from Fu et al.[87]

on 1050 labeled data points collected from simulations and experiments using four cell lines (fibroblast, stem, cancer, and endothelial cells). Input features included wall shear stress (1.0–5.0 kPa) and exposure time (100–700 ms), while the output target was cell viability. Model performance was evaluated using 20-fold cross-validation, yielding high predictive accuracy with R^2 values ranging from 0.866 to 0.964 across cell types.

Rojek et al.[90] presented an AI-driven approach to optimize 3D printing efficiency and reduce material waste by training artificial neural networks on a dataset of 238 input parameters and eight output metrics, including filament usage, cost, and print time, using experimental data from 3D-printed elbow exoskeleton components. The artificial neural network model (multilayer perceptron regressor-142-102-8) achieved strong predictive performance (mean squared error = 0.007; testing quality = 0.9132), allowing a 30-fold reduction in waste and enabling one free print for every 6.67 prints.

Wu and Xu[91] developed a data-driven ensemble learning approach to predict droplet velocity and volume in inkjet-based bioprinting. They conducted a full factorial design with 243 experiments varying polymer concentration, voltage, dwell time, and rise time, training predictive models (random forest, least absolute shrinkage and selection operator, support vector regressor, extreme boosting gradient) on these features using 10-fold cross-validation (R^2 = 0.977–0.978). The ensemble model achieved high predictive accuracy, demonstrating its potential to enhance the precision of droplet-based bioprinting, optimizing process parameters to improve reproducibility and scalability.

AI-driven approaches trained on experimental datasets and computational simulations predict optimal printing conditions, ensuring high-resolution constructs with minimal defects and material waste. They reduce the need for manual adjustments and trial-and-error experimentation, making bioprinting more efficient, scalable, and sustainable. While these developments are promising, current models, such as those by Bone et al.,[85] Fu et al.,[87] and Chen et al.,[86] are often trained on material-specific or relatively small datasets, which may limit their immediate applicability across different bioprinting platforms or bioink types. Some frameworks, like those developed by Zhang et al.[89] and Xu et al.[88] have begun to incorporate cell viability and rheological behavior, reflecting a growing interest in integrating both physical and biological outcomes into predictive models. Others, like Rojek et al.,[90] demonstrate the potential of AI in reducing material waste and energy use, aligning with broader sustainability goals. Looking ahead, expanding the diversity and scale of training datasets, including parameters such as crosslinking kinetics and biological performance, and developing real-time, adaptive control systems could further enhance the robustness and utility of AI in bioprinting.

3.4. Artificial intelligence-assisted intelligent printing

Beyond material development, bioink formulation, and parameter optimization, AI-assisted intelligent printing represents a major step toward adaptive and autonomous bioprinting systems. These systems leverage advanced algorithms, real-time monitoring, and process automation to enhance control, precision, and functionality. Advanced algorithms enable *in situ* bioprinting with acoustic levitation, allowing voxel-by-voxel and contact-free material placement on diverse substrates and expanding the possibilities of bioprinting.[92,93] AI-powered computer vision systems, feedback loops, and predictive modeling have been employed to detect and correct print defects in real time, improving print success rates.[94]

Chen et al.[92] developed an intelligent printing system, AcoustoFab, which combines a phased array of transducers and advanced control algorithms, allowing omnidirectional and multi-material *in situ* bioprinting using acoustic levitation (Figure 6A). AcoustoFab utilizes OpenMPD (multimodal particle-based displays)[95] and the boundary element method[96] algorithms to enable the formation of multiple acoustic traps in proximity to complex sound-scattering surfaces for depositing materials on these complex substrates. The OpenMPD **algorithm** dynamically calculates and updates the positions of multiple acoustic tweezers, allowing control over the levitation and omnidirectional movement of multiple droplets of bioinks in mid-air. The boundary element method algorithm simulates acoustic wave interactions with large, scattering surfaces in real-time, predicting and mitigating potential distortions in the acoustic field. This allows levitating, transporting, and *in situ* depositing of bioinks onto irregular surfaces of diverse orientations, including a human hand. AcoustoFab is capable of printing any soft materials within a wide range of viscosities (1–5,000,000 mPa·s), including biopolymers, composite hydrogels, and bioinks. The embedded cells in the hydrogels also demonstrated high viability post-printing. The contactless nature of AcoustoFab minimizes cross-contamination, mechanical wear, and substrate damage, contributing to reduced material waste and lower failure rates, which is critical in clinical applications. By integrating advanced algorithms with acoustic levitation, AcoustoFab presents a promising approach for intelligent and sustainable biofabrication.[97]

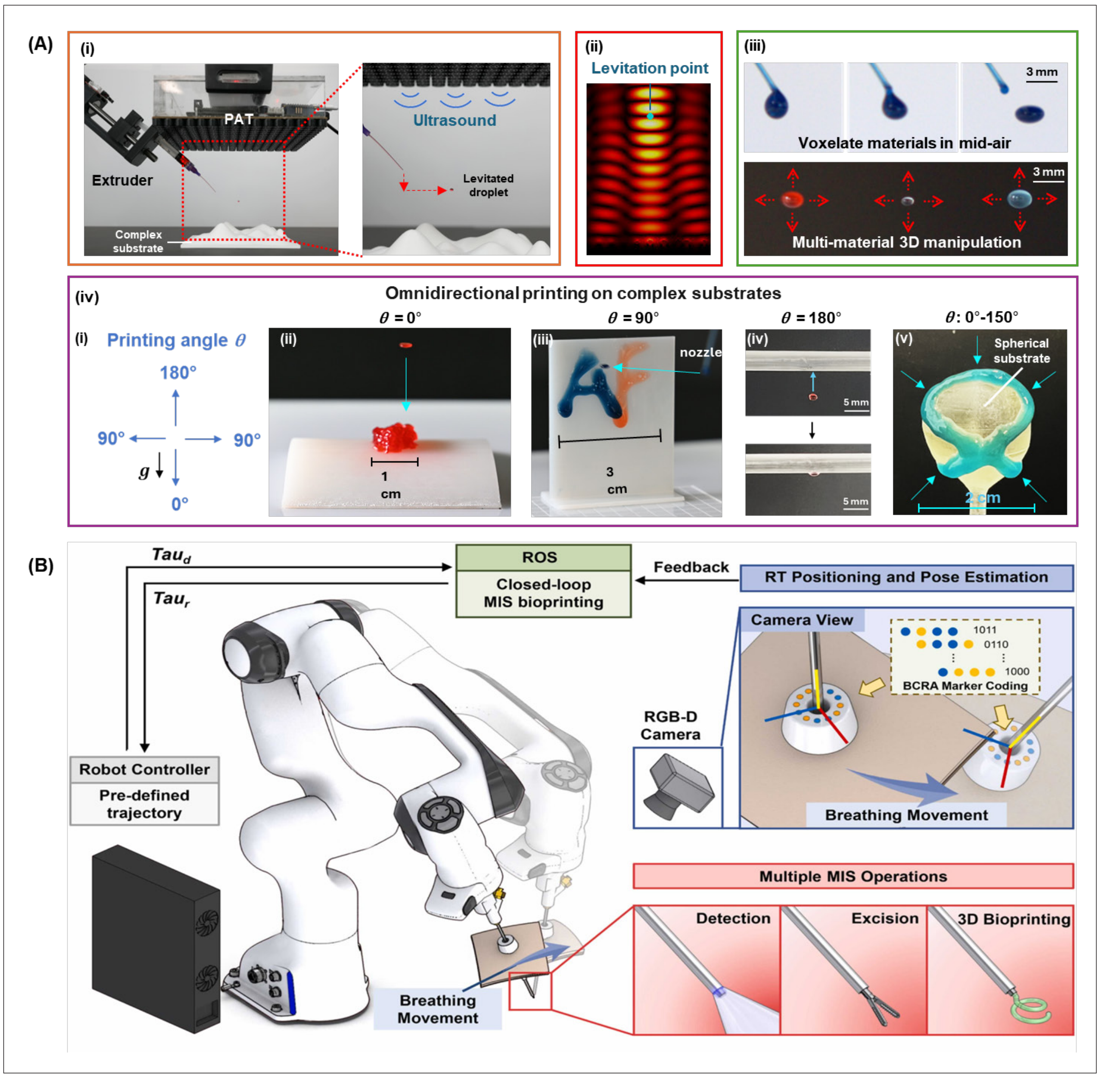

Figure 6. AI-assisted intelligent printing strategies enhance precision, adaptability, and sustainability. (A) Acoustophoretic 3D printing enables omnidirectional, multi-material fabrication. (i) A phased array transducer levitates droplets for precise deposition on complex substrates. (ii) Acoustic field visualization showing the levitation point. (iii) Mid-air voxelation and multi-material manipulation. (iv) Omnidirectional printing at varied angles (0°–180°) on flat (scale bar: 1 cm), vertical (scale bar: 3 cm), inverted (scale bar: 5 mm), and spherical (scale bar: 2 cm) surfaces, demonstrating adaptive and contactless printing.[92] Reprinted from Chen et al.[92] (B) A closed-loop minimally invasive 3D bioprinting system. A seven-axis robotic arm guided by real-time feedback from a RGB-D camera adaptively compensates for dynamic breathing-induced motion. AI-driven path planning minimizes error and material overuse, enhancing printing accuracy, efficiency, and safety in dynamic environments. This supports sustainability by reducing procedural waste and optimizing resource use.[94] Reprinted with permission from Zhao et al.[94] Copyright © 2023, Elsevier. Abbreviations: 3D, three-dimensional; AI: artificial intelligence; BCRA, binary chromatic ring array; MIS, minimally invasive surgery; RGB-D: red green blue-depth; ROS, robot operating system; RT, real-time.

Zhao et al.[94] introduced a closed-loop, AI-assisted bioprinting system that enhances precision, adaptability, and sustainability in minimally invasive surgery (Figure 6B). By integrating robotic-assisted printing, real-time computer vision, and adaptive feedback control, the system dynamically aligned the bioprinting end-effector with moving biological structures, reducing errors and minimizing material waste. A binary chromatic ring array marker enabled automatic trocar tracking, ensuring high accuracy while reducing the need for manual intervention. Additionally, the use of an optimized methacrylate gelatin/poly(ethylene glycol) diacrylates/polyacrylic acid-N-hydroxysuccinimide hydrogel facilitated efficient crosslinking and strong tissue adhesion, promoting targeted biofabrication with minimal excess material usage. The system's millimeter-scale precision, adaptive alignment at 30 Hz, and low-force application not only improved bioprinting efficiency but also enhanced resource conservation and sustainability by reducing biomaterial waste and optimizing printing parameters in real time. This AI-driven, closed-loop approach exemplifies the potential of intelligent bioprinting systems to advance eco-friendly, high-precision fabrication strategies, contributing to the sustainable evolution of regenerative medicine and biomedical engineering.

Zboinska et al.[98] investigated the robotic 3D printing of cellulose nanofibril-alginate hydrogel membranes for sustainable architectural applications, analyzing the impact of toolpath design and ambient drying on structural integrity, shrinkage, and aesthetics. Results showed that solid deposition with multiple layers led to high shrinkage (~31%) and deformation, while lattice deposition with high porosity reduced shrinkage (~8%) and improved dimensional stability. Asymmetric toolpaths caused non-uniform distortions, and ambient drying significantly affected membrane curvature and flexibility. To enhance scalability and efficiency, classical AI-driven automation can optimize toolpath generation, extrusion control, and drying conditions, ensuring consistent deposition, reducing material waste, and improving sustainability.

AI-assisted intelligent printing marks a significant shift toward adaptive, real-time, and sustainable bioprinting systems. By integrating ML, computer vision, and robotic control, these systems enable precise material deposition on complex or dynamic substrates while minimizing human intervention, error, and material waste. Collectively, these innovations contribute to greater print success rates, reproducibility, and resource efficiency. However, current implementations often remain platform-specific and are tailored to narrow material or geometric constraints, limiting broader applicability. Moving forward, research should focus on developing generalizable AI control frameworks, standardizing performance evaluation metrics, and improving cross-platform interoperability. Additionally, expanding the use of real-time feedback loops, multimodal sensing, and automated decision-making will be key to achieving fully autonomous and clinically scalable intelligent bioprinting systems.

Table 1 presents a comparative overview of recent studies integrating AI or ML with 3D bioprinting, evaluated through the lens of sustainability. Each study is classified by the method used, materials and printing technique employed, and the relevant sustainability contributions. The following sustainability indicators are used:

(i) Sustainable bioink use: Utilization of bioinks derived from renewable, recyclable, or biodegradable sources to reduce environmental impact at the material level.

(ii) Material efficiency: Minimization of material consumption and waste through efficient deposition or improving formulation success rates.

(iii) Process efficiency: Optimization of printing parameters (e.g., speed, temperature, pressure) to reduce errors, enhance energy/resource use during fabrication, or improve throughput.

(iv) Experimental productivity: Application of ML to reduce empirical trial-and-error, accelerate parameter tuning, and improve data yield per experimental cycle.

4. Discussion

4.1. Challenges and potential solutions

The integration of AI into sustainable bioprinting has significantly advanced material development, bioink screening, processing parameter optimization, and intelligent printing. Despite these advancements, challenges remain in realizing the full potential of AI in sustainable bioprinting. Robust AI models require large, diverse, and well-annotated data[99,100]; however, existing datasets frequently suffer from inconsistency in parameter reporting and limited data annotation. This complexity arises from the extensive variability in bioink compositions, bioprinting techniques, and biological systems involved.[74,101] Additionally, standardized metrics to comprehensively measure sustainability in bioprinting are currently lacking. While several general frameworks exist for sustainable manufacturing like the sustainable process index (ecological impact of industrial processes),[102] life cycle assessment (environmental impacts of a product's life cycle),[103,104] and helix of sustainability (industrial raw material use and reuse onto natural processes),[105,106] their direct application to bioprinting remains limited due to the field's unique processes and materials. This absence of universally accepted standards hinders systematic assessment and comparison of sustainable practices, complicating the optimization of sustainability efforts within bioprinting processes.

Another significant challenge is the generalizability of AI models across various materials, bioprinting methods, and evolving conditions.[107,108] AI systems typically perform well within the confines of their training datasets but sometimes struggle when confronted with new, unfamiliar, or dynamically changing scenarios.[109] Factors contributing to this limitation include data scarcity for novel materials, the complexity of accurately modeling intricate multi-material interactions, and the variability in environmental and operational conditions during bioprinting. Addressing these issues will require enhanced AI methodologies, robust validation strategies, and diverse training datasets

Table 1. Summary of artificial intelligence-driven studies in sustainable bioprinting

Study	Artificial intelligence algorithms	Bioink material	Bioprinting process	Sustainability indicators
Chen et al.[14]	Decision tree, random forest, deep learning	Composite hydrogel, polymer	Direct ink writing	Sustainable bioink use; material efficiency; experimental productivity
Lee et al.[81]	Multiple regression	Collagen, hyaluronic acid, fibrin	Extrusion	Process efficiency; experimental productivity
Nadernezhad and Groll[80]	Random forest	Hyaluronic acid-based hydrogel	Extrusion	Sustainable bioink use; process efficiency; experimental productivity
Bone et al.[85]	Hierarchical machine learning	Alginate-based	Extrusion	Sustainable bioink use; process efficiency; experimental productivity
Chen et al.[86]	Image recognition, random forest	Hydrogel scaffold	Extrusion	Material efficiency; process efficiency; experimental productivity
Fu et al.[87]	Support vector machine	Pluronic F127	Extrusion	Process efficiency; experimental productivity
Xu et al.[88]	Ensemble (ridge regression, k-nearest neighbor, random forest, neural network)	Gelatin methacrylate	Stereolithography	Process efficiency; experimental productivity
Zhang et al.[89]	Support vector regressor, multilayer perceptron regressors	Alginate-based	Extrusion	Sustainable bioink use; process efficiency; experimental productivity
Wu and Xu[91]	Random forest, least absolute shrinkage and selection operator, support vector regressor, extreme boosting gradient	Inkjet-compatible polymers	Inkjet	Sustainable bioink use; process efficiency; experimental productivity
Chen et al.[92]	Open multimodal particle-based displays, boundary element method	Soft materials	Direct ink writing	Sustainable bioink use; material efficiency
Zhao et al.[94]	Vision + adaptive feedback	Gelatin-based	Extrusion	Material efficiency; process efficiency
Zboinska et al.[98]	Artificial intelligence-assisted toolpath	Cellulose nanofibril-alginate	Extrusion	Sustainable bioink use; material efficiency

that encompass a broad spectrum of materials, processes, and conditions.[16,18,110,111]

To overcome these challenges, the creation of open-source platforms and collaborative databases is helpful. Such platforms would centralize diverse datasets, reflecting the variety of bioinks, printing parameters, and application-specific conditions, thus enabling more representative and comprehensive AI model training.[112,113] Establishing standardized sustainability metrics such as material efficiency, energy consumption, and waste minimization should also be an integral part of these centralized datasets. Quantifying these aspects would provide clear, measurable insights for sustainable bioprinting, enabling data-driven decisions to optimize AI algorithms, improve resource efficiency, and minimize environmental impact.[114] Collaborative efforts could streamline data collection, eliminate redundancy, and foster a cohesive research community. Furthermore, integrating advanced AI techniques like transfer learning and domain adaptation can enhance AI model generalizability, facilitating adaptability to new materials and dynamic printing environments.[74,115] These initiatives, combined with interdisciplinary collaboration and technological innovation, will help overcome current limitations, paving the way for AI-driven sustainable bioprinting to achieve its full potential.

4.2. Roadmap for artificial intelligence in sustainable bioprinting

In addition to addressing current challenges, a strategic roadmap for future development suggests several directions that could advance sustainability alongside technological progress. In material discovery and development, AI-assisted platforms can leverage hybrid modeling approaches that merge AI-driven predictive models with physics-based simulations to enhance accuracy, reduce experimentation, and minimize resource usage.[77,116,117] Integrating life cycle assessment indicators such as embodied energy, carbon footprint, and toxicity profiles alongside mechanical and biological performance metrics would allow the design of truly sustainability-aware hydrogel. Open-source datasets that capture both material origin and functional outcomes—such as printability, biocompatibility, and mechanical properties—will be critical in supporting these efforts.

For bioink formulation screening, while predictive models have shown success in assessing printability and rheology, there is a pressing need for AI systems that can generalize across a wider spectrum of bioink chemistries, including those derived from recycled polymers, chemically modified natural materials, and hybrid composites. Future platforms can also integrate a broader array of input features, such as crosslinking kinetics under different conditions, degradation rates over time, and dynamic cell compatibility data, including proliferation, differentiation, and immune responses. These features can be embedded into multi-objective optimization frameworks capable of balancing trade-offs between print fidelity, mechanical integrity, biological performance, and environmental impact.[118]

In processing parameters optimization, future bioprinting equipment should integrate real-time monitoring, feedback control, and adaptive optimization algorithms. This will enable continuous improvement in print quality, significantly reducing material waste and energy consumption during fabrication.[101,119–121] Advanced AI models that incorporate environmental sensors and historical print data could be used to build predictive maintenance systems, flagging deviations before print failure occurs. Furthermore, multimodal sensor fusion (e.g., combining acoustic, visual, and rheological inputs) could enable richer representations of print conditions, allowing for more granular and adaptive parameter control. Reinforcement learning algorithms, in particular, offer great potential for autonomous tuning of parameters in real time by learning optimal action policies based on performance feedback.[122]

Regarding AI-assisted intelligent printing, the development of autonomous bioprinting systems empowered by AI decision-making capabilities should be prioritized. These systems can dynamically adapt to complex and evolving substrates and environmental conditions, improving precision, throughput, and sustainable resource management.[119,120] Advanced systems could combine robotic control, computer vision, and probabilistic planning to enable in situ material placement with high spatial precision, even under uncertain or moving conditions. Real-time reconstruction of the target geometry using multimodal imaging—paired with predictive modeling—could allow these printers to adjust tool paths in real time, minimizing material waste and improving procedural outcomes. A promising approach to achieving this capability is the use of digital twin frameworks, which simulate and update a virtual replica of the bioprinting environment and printed construct in real time based on sensor feedback.[123] Finally, enhancing educational initiatives and workforce training programs that focus on AI, bioprinting technologies, and sustainability principles will be essential to build interdisciplinary expertise and foster widespread adoption of environmentally responsible bioprinting practices.[124,125]

Looking forward, as bioprinting technologies progress toward clinical translation and industrial adoption, integrating sustainability considerations early in the development process is essential. AI's significance in sustainable bioprinting is poised to expand as bioprinting processes become more complex with more intensive data. Continued advancements in computational speed, robustness, and interdisciplinary collaboration will be vital in addressing current limitations and ensuring AI-driven sustainable bioprinting meets both environmental and technological advancement goals in healthcare and biofabrication.

5. Conclusion

The integration of AI in sustainable bioprinting represents a transformative advancement in addressing environmental and functional challenges inherent in conventional bioprinting processes. AI's capabilities in predicting material performance, optimizing bioink formulations, dynamically adjusting printing parameters, and supporting intelligent bioprinting systems substantially reduce reliance on resource-intensive trial-and-error approaches, leading to significant enhancements in sustainability and efficiency. Despite notable progress, significant challenges remain, including dataset standardization, model generalizability, and comprehensive sustainability measurement. Future efforts must prioritize collaborative data-sharing platforms, advanced AI methods, and standardization initiatives. By systematically addressing these challenges, the full potential of AI in sustainable bioprinting can be realized, substantially contributing to ecological responsibility and advancing technological innovations in biofabrication and healthcare applications.

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