Genome Publications
https://doi.org/10.61096/ 978-81-981372-6-5_12

Chapter 12

Emerging Trends in 3D Bioprinting

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Abstract: Recent advancements in 3D bioprinting have propelled the field beyond traditional scaffold-based fabrication into a realm where dynamic, intelligent, and interactive systems are redefining biomedical engineering. This chapter explores the cutting-edge trends reshaping 3D bioprinting, beginning with smart bioinks that respond to environmental stimuli such as pH, temperature, or light, enabling the development of more biomimetic and functional tissue constructs. The integration of microfluidic technologies with bioprinting particularly within organ-on-chip platforms offers new pathways for precision modeling of physiological and pathological states. Concurrently, organoid and spheroid printing is emerging as a powerful strategy for recapitulating complex tissue architectures and enhancing cellular functionality. An especially transformative trend is 4D bioprinting, which introduces a temporal dimension, allowing constructs to evolve post-fabrication. This innovation opens the door to dynamic tissue constructs capable of shape-shifting or adapting their function over time. Furthermore, artificial intelligence (AI) and machine learning are becoming integral to optimizing print parameters, enhancing reproducibility, and predicting biological outcomes. Novel applications such as wearable and point-of-care bioprinters promise decentralized manufacturing, offering vital clinical solutions in emergency and battlefield scenarios. Finally, cloud-based platforms are enabling remote design, data sharing, and collaborative biofabrication, further democratizing access to this disruptive technology. Collectively, these trends underscore a paradigm shift, positioning 3D bioprinting as a cornerstone of future personalized and regenerative medicine.

Keywords: Smart Bioinks, 4D Bioprinting, Organoid Printing, AI in Bioprinting, Microfluidic Systems

Citation: Vishnu Pulavarthy, SK Abdul Rahaman, Vaishnavi Vasantrao Khandre, Nayan Govind Keshavshetty. Emerging Trends in 3D Bioprinting. *3D Bioprinting: Advances, Challenges and Fabricating the Future.* Genome Publications. 2025; Pp195-206. https://doi.org/10.61096/978-81-981372-6-5_12

12. 0 INTRODUCTION

As 3D bioprinting steadily matures from a niche research interest to a clinical and industrial tool, it is simultaneously undergoing a transformative evolution marked by an influx of interdisciplinary innovations. The foundational capabilities of layer-by-layer deposition of bioinks have enabled notable breakthroughs in tissue modeling and regenerative medicine, yet persistent limitations remain particularly concerning structural complexity, functional integration, and long-term viability of printed constructs. To overcome these challenges, the field is embracing emerging trends that integrate intelligent materials, real-time feedback systems, and decentralized fabrication networks. This chapter delineates several forward-looking trajectories poised to define the next phase of 3D bioprinting. Among these are smart bioinks that respond to external stimuli, the convergence of microfluidics and printing technologies, and the use of organoid and spheroid assemblies to better mimic native tissue architecture. One of the most groundbreaking shifts is the emergence of 4D bioprinting, which adds a temporal dynamic to previously static constructs. Simultaneously, the deployment of artificial intelligence and machine learning algorithms is optimizing every step from design to functional validation. Portable and wearable bioprinters further hint at a future where personalized medical devices and tissues can be fabricated at the point of care. Moreover, cloud-based systems are reshaping how data, protocols, and even entire tissue blueprints are created, shared, and implemented globally. Each section of this chapter presents a detailed examination of these technologies, substantiated by recent scientific literature, comparative evaluations, and future projections that highlight both opportunities and unresolved challenges.

A schematic overview of the major innovations shaping the future of 3D bioprinting, including smart bioinks, microfluidic bioprinting, organoid and spheroid printing, 4D bioprinting, AI and machine learning integration, wearable bioprinters, and cloud-based platforms.

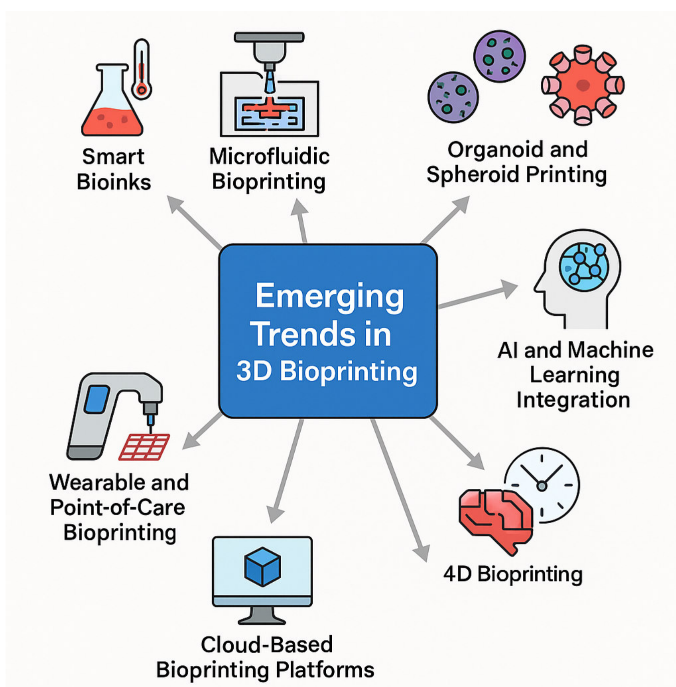

Fig 1: Emerging Trends in 3D Bioprinting

12. 1 Smart Bioinks

12. 1. 1 Stimuli-Responsive Materials

The advent of smart bioinks engineered to dynamically respond to environmental stimuli represents a significant leap in 3D bioprinting functionality. Unlike conventional bioinks that retain static physicochemical properties post-printing, smart bioinks offer an adaptive interface with their biological environment, thereby enhancing functional integration and biomimicry. These materials can be designed to undergo reversible or irreversible changes in response to specific triggers such as temperature, pH, ionic concentration, or light exposure. Thermo-responsive polymers, such as poly(N-isopropylacrylamide) (PNIPAAm), exhibit sol-gel transitions around physiological temperatures, enabling precise control over gelation and cell encapsulation during the printing process [1]. Similarly, pH-responsive hydrogels composed of chitosan or polyacrylic acid can modulate their swelling behavior in acidic or basic environments, providing cues for cell migration or controlled drug release [2]. Light-sensitive systems, especially those based on photoinitiated crosslinking, offer high spatial and temporal control, allowing selective tuning of mechanical properties within a single construct [3]. These functionalities are not only beneficial for creating more physiologically relevant tissues but also open avenues for advanced biomedical applications. For instance, smart hydrogels have been integrated into constructs for on-demand drug delivery or responsive wound healing scaffolds [4]. Moreover, researchers have developed dual-responsive hydrogels sensitive to both pH and temperature to better mimic the complex, dynamic nature of human tissues [5].

Despite their advantages, smart bioinks face challenges such as limited printability due to viscosity shifts, potential cytotoxicity of stimuli (e. g. , UV light), and difficulties in ensuring uniform response across a construct. Future research must address the synthesis of biocompatible, multi-responsive polymers that maintain high cell viability and reproducibility during and after bioprinting.

12. 2 Microfluidic Bioprinting

12. 2. 1 Integration with Organ-on-Chip Systems

Microfluidics the science of manipulating fluids at the micrometer scale has begun to synergize with 3D bioprinting, yielding unprecedented control over spatial and temporal distribution of cells and biomaterials. This integration is especially potent when applied to organ-on-chip (OoC) systems, which emulate the microscale architecture and functions of living organs. By combining microfluidics and bioprinting, researchers are now able to fabricate perfusable tissue constructs with real-time monitoring capabilities and reproducible flow dynamics. One of the primary advantages of microfluidic-assisted bioprinting lies in its ability to maintain physiological gradients such as oxygen tension and nutrient diffusion within printed tissues. Using microchannels embedded directly during the printing process, vascular-like structures can be formed to simulate perfusion and waste clearance [6]. Additionally, multi-material microfluidic printheads allow for the continuous deposition of different cell types or ECM analogs with minimal mixing, thereby enhancing tissue heterogeneity and fidelity [7]. Integration with organ-on-chip platforms has enabled the development of bioprinted mini-organs that are functionally responsive. For example, researchers have fabricated liver-on-chip and heart-on-chip models using bioprinted hepatocytes and cardiomyocytes within microfluidic scaffolds, facilitating drug screening and toxicity testing in ways that surpass conventional 2D models [8]. However, challenges persist, including device complexity, high fabrication costs, and ensuring long-term viability and function of cells in microfluidic environments. Moreover, aligning flow rates with physiological conditions while maintaining mechanical stability of printed constructs remains non-trivial. Future innovations must aim for modular, scalable systems that combine microfluidic precision with the structural capabilities of 3D bioprinting to bridge the gap between benchtop models and clinical applications.

12. 3 Organoid and Spheroid Printing

12. 3. 1 3D Cell Aggregate Printing

Organoids and spheroids self-assembled multicellular aggregates that recapitulate organ-like structures are revolutionizing tissue engineering, and their integration into 3D bioprinting workflows is emerging as a transformative strategy. Unlike dispersed single-cell suspensions used in traditional bioprinting, organoid-based bioinks capitalize on the inherent self-organizing and differentiation capacities of stem or progenitor cells. These multicellular aggregates maintain intercellular junctions, exhibit natural ECM deposition, and often contain multiple cell types, making them more representative of in vivo tissues [9]. Incorporating them into bioinks allows the bioprinter to build complex tissue layers that retain both structure and function. For instance, bioprinted liver organoids have demonstrated enhanced metabolic activity compared to their 2D counterparts, while cardiac spheroids have been used to fabricate beating myocardial patches with synchronized contractions [10]. A key challenge in organoid and spheroid printing is the precise control of spatial orientation and viability during deposition. Organoids are sensitive to shear forces and mechanical stress, necessitating the development of gentler extrusion systems or drop-on-demand techniques. Recent innovations in support bath bioprinting where spheroids are printed into a soft gel matrix—have helped mitigate these issues [11]. Future developments will likely focus on co-printing multiple organoid types to recreate multi-tissue interfaces, such as the neurovascular unit or the gut-liver axis. Moreover, coupling organoid bioprinting with microfluidics could yield dynamic models for disease research, drug discovery, and personalized medicine.

12. 4 4D Bioprinting

12. 4. 1 Time-Dependent Constructs

While 3D bioprinting has focused largely on producing anatomically accurate constructs, 4D bioprinting introduces a revolutionary paradigm where printed structures evolve over time in response to internal or external stimuli. This temporal aspect allows for adaptive behavior such as shape morphing, functional modulation, or self-healing beyond what is achievable through conventional methods. The fourth dimension time is achieved by using stimuli-responsive materials that change their physical or chemical properties post-fabrication. Examples include shape-memory polymers, hydrogels that swell or contract in response to moisture, or magnetic nanoparticles embedded in matrices that respond to external magnetic fields [12]. These materials have enabled constructs that fold, bend, or even assemble autonomously after printing, enhancing the functional complexity of bioprinted tissues. In biomedical applications, 4D bioprinting is being explored for developing stents that expand in situ, scaffolds that gradually degrade and are replaced by natural tissue, or wound dressings that conform to dynamic tissue surfaces [13]. Researchers have demonstrated a self-folding tissue patch that mimics the mechanics of embryonic folding, representing a step closer to replicating developmental biology processes [14]. Despite its promise, 4D bioprinting faces significant technical and biological challenges. Material fatigue, reproducibility of dynamic responses, and biocompatibility of smart materials remain critical concerns. Furthermore, regulatory pathways for dynamic implants are still underdeveloped. Nonetheless, with continued refinement, 4D bioprinting holds the potential to revolutionize tissue engineering by offering constructs that not only resemble but also behave like native tissues. A comparative overview of these trends is presented in Table 1, detailing their unique functions, benefits, and associated challenges in translational application.

Table 12.1: Trending Scenario for the 3D Bioprinting

Trend Category	Trend	Description	Examples	Potential Impact	References
Technological Advancements	**AI and Machine Learning in Bioprinting**	Integration of AI and machine learning to optimize bioprinting processes, predict outcomes, and improve designs.	AI-powered software for designing complex tissue structures, predictive algorithms for bioink behavior.	Increased precision and efficiency in bioprinting, reduction of human error, and accelerated research and development.	21
	Multi-Material Bioprinting	Printing with multiple materials in one go, enabling the creation of complex, multi-functional tissues.	Printing of tissues with different layers, each mimicking a distinct part of an organ (e.g., skin layers, vascular structures).	Creation of highly functional, multi-layered tissues that better mimic the complexity of human organs, advancing organ printing.	22
	4D Bioprinting	Introduction of 4D printing, where printed structures change shape or behavior in response to environmental factors.	Bioprinted materials that respond to temperature, pH, or light, enabling dynamic tissue or organ systems.	Potential for bioprinted tissues and devices that self-assemble, adapt, or repair over time, offering functional improvements.	23

Material Innovation	**Smart Bioinks**	Development of bioinks with enhanced properties such as stimuli-responsiveness, greater biocompatibility, and mechanical strength.	Bioinks with temperature sensitivity or those that can respond to chemical or electrical stimuli for specific tissue types.	Improved cell viability, structural integrity, and functional adaptability, opening doors for creating more complex tissues.	24
	Biodegradable and Sustainable Bioinks	Use of plant-based or other environmentally friendly bioinks to reduce waste and environmental impact.	Bioinks made from natural polymers like collagen, chitosan, or gelatin for sustainable bioprinting.	Development of more sustainable bioprinting methods, contributing to environmental conservation efforts in healthcare and manufacturing.	25
Clinical and Healthcare Applications	**Organ Printing and Transplantation**	Advancements in bioprinting fully functional organs, including vascularization, for transplantation.	Bioprinted kidney, heart, and liver models, with ongoing research into complex organ systems.	Potential to solve organ shortage issues by printing fully functional organs for transplantation, reducing waiting lists.	26
	Personalized Medicine	Tailoring bioprinted tissues and implants to individual patients based on their genetic and biological profiles.	Bioprinted tissue models for drug testing and custom implants for patients based on their unique anatomy.	More effective treatments and surgeries with personalized, patient-specific solutions that improve outcomes and reduce risks.	27

	Bioprinted Implants and Prosthetics	Creation of customized implants and prosthetics tailored to an individual's anatomical structure.	Bioprinted orthopedic implants, dental implants, and prosthetic limbs.	Enhanced patient comfort, quicker recovery times, and greater effectiveness in medical devices.	28
Environmental and Sustainability	**Bioprinted Environmental Sensors**	Use of bioprinting for developing low-cost, biodegradable environmental sensors to monitor pollution or natural conditions.	Bioprinted sensors for detecting water quality, soil health, or air pollution.	Cost-effective and sustainable environmental monitoring systems with minimal environmental impact.	29
	Sustainable Packaging and Materials	Bioprinting for the creation of sustainable packaging solutions that are biodegradable and non-toxic.	Mycelium-based bioprinted packaging materials and plant-based bioplastics.	Significant reduction in plastic waste, contributing to eco-friendly solutions in consumer goods and packaging industries.	30
Cross-Disciplinary Collaborations	**Integration with Stem Cell Research**	Collaborations between stem cell biologists and bioprinting researchers to develop regenerative therapies.	Bioprinted tissues using stem cells for regenerative medicine applications like skin grafts or cartilage repair.	Faster development of regenerative therapies for various diseases and injuries, including neurodegenerative diseases, burns, and arthritis.	31
	Bioelectronics and Bioprinting	Bioprinting for bioelectronics applications, including	Bioprinted flexible electronic circuits and	Enable new forms of wearable devices, real-time health tracking,	32

		integration of cells with electronic devices.	sensors embedded in tissues for healthcare monitoring.	and new treatments for chronic conditions like diabetes or cardiac diseases.	
Educational and Market Trends	**Wider Adoption in Academia and Industry**	Increased adoption of bioprinting technology in research and industrial settings, bridging gaps between academia and industry.	Universities developing bioprinting programs, collaborative research centers with industrial applications.	Acceleration of bioprinting technology into market-ready products, with a larger pool of skilled professionals driving innovation.	33
	Public and Government Engagement	Growing support from governments and the public for bioprinting-related research and initiatives.	Government-funded research projects on bioprinting, public awareness campaigns for bioprinting's potential.	Increased funding and resources for bioprinting research, leading to breakthroughs in medical applications, environmental solutions, and sustainability.	34

Table 12.1 explores the trends that will define the future of bioprinting, including cutting-edge advancements in technology, material science, clinical applications, environmental sustainability, and educational initiatives. Recent trends in bioprinting highlight significant technological advancements and their potential impacts. AI and machine learning are being integrated to optimize bioprinting processes, enhance precision, and reduce errors, while multi-material and 4D bioprinting are enabling the creation of complex, dynamic tissues. Innovations in material science, such as smart bioinks and biodegradable, sustainable bioinks, are improving biocompatibility, mechanical strength, and environmental sustainability. Clinically, bioprinting is advancing organ printing for transplantation, personalized medicine, and customized implants, offering personalized, more effective treatments. Additionally, bioprinted environmental sensors and sustainable packaging materials are supporting eco-friendly solutions. Cross-disciplinary collaborations, particularly with stem cell research and bioelectronics, are driving innovations in regenerative therapies and wearable health monitoring devices. The wider adoption of bioprinting in academia and industry, alongside growing public and

government engagement, is accelerating the technology's transition into market-ready applications, advancing medical, environmental, and industrial uses.

12. 5 AI and Machine Learning Integration

12. 5. 1 Predictive Analytics in Bioprinting

Artificial intelligence (AI) and machine learning (ML) have begun to play pivotal roles in optimizing 3D bioprinting processes by enhancing design accuracy, automating quality control, and predicting biological outcomes. These computational approaches are particularly valuable in managing the vast datasets generated during the printing process, which include parameters such as extrusion pressure, printhead velocity, bioink viscosity, and environmental conditions.

Machine learning algorithms particularly neural networks and decision trees are now being deployed to predict the viability of cells post-printing based on real-time inputs, such as shear stress, temperature fluctuations, and bioink composition [15]. Supervised learning models trained on experimental data can forecast cell survival and tissue maturation outcomes, guiding researchers toward optimal printing parameters without the need for extensive trial-and-error experiments. AI-powered design platforms have also facilitated automated construct generation. Generative design algorithms can propose novel scaffold architectures based on mechanical and biological constraints, allowing for more efficient use of biomaterials and tailored tissue-specific properties [16]. Additionally, computer vision systems integrated with AI can detect printing defects or layer misalignments in real time, enabling adaptive corrections that enhance construct fidelity and reproducibility [17]. However, challenges remain in integrating these systems into existing workflows. Data standardization, model interpretability, and limited labeled training datasets for biological systems are major barriers. Furthermore, ensuring that AI predictions are biologically meaningful and generalizable across cell types and tissue models is an ongoing research focus. Nevertheless, AI holds significant promise for transforming 3D bioprinting into a more predictive, consistent, and scalable process.

12. 6 Wearable and Point-of-Care Bioprinting

12. 6. 1 Portable Bioprinter Development

One of the most exciting and disruptive frontiers in bioprinting is the development of wearable or point-of-care (POC) bioprinting systems. These innovations aim to bring the printing process directly to the patient, whether in emergency settings, operating rooms, or even on the battlefield. The core philosophy is decentralization enabling on-demand, location-agnostic tissue repair or delivery of bioengineered constructs without the need for centralized labs or facilities. Several prototypes of handheld or mobile bioprinters have been developed. For instance, a handheld skin printer was successfully used to deliver sheets of bioink laden with skin cells directly onto burn wounds, promoting rapid re-epithelialization [18]. Another approach utilizes wearable bioprinting units integrated with robotic systems to print constructs directly onto irregular wound surfaces, such as joints or facial contours [19]. These systems typically utilize low-shear extrusion or inkjet-based mechanisms, designed to be minimally invasive and biocompatible. They are powered by compact, battery-operated systems and often feature onboard cartridge exchange for different bioink formulations. Some designs are augmented with real-time imaging tools (e. g., ultrasound or optical coherence tomography) to guide precise deposition. The implications for trauma medicine and regenerative care are profound. Soldiers injured in combat zones could receive immediate cellularized patches for wound stabilization.

In disaster scenarios, first responders might carry compact bioprinters to provide emergency care where hospital infrastructure is inaccessible. Nevertheless, these devices face notable limitations: bioink stability over time, device sterilization, consistent dosing control, and regulatory hurdles surrounding in situ biomanufacturing. Future directions involve improving the ergonomics, scalability, and clinical validation of portable bioprinters for widespread adoption.

12. 7 Cloud-Based Bioprinting Platforms

12. 7. 1 Remote Collaboration and Data Sharing

The digital transformation of biomedical research has extended into 3D bioprinting, with the emergence of cloud-based platforms that enable remote design, simulation, and collaborative fabrication of bioprinted constructs. This trend is revolutionizing the accessibility and scalability of bioprinting by decoupling the site of design from the site of manufacture. Cloud-based bioprinting ecosystems typically integrate computer-aided design (CAD) interfaces with cloud computing resources that allow multiple userso ften from different institutions to co-develop, edit, and validate construct blueprints in real time [20]. These blueprints can then be transmitted to remote bioprinters for localized fabrication, effectively creating a distributed manufacturing network. Such platforms also support real-time data analytics, enabling researchers to monitor print progress, adjust parameters, and access historical datasets to refine protocols. Integration with AI tools can facilitate predictive maintenance of printers, automate calibration, and ensure quality control across geographically separated labs. A particularly promising application of cloud-based systems is in educational and low-resource settings. Institutions lacking advanced bioprinters can access validated construct files and remotely print them through service providers. This model democratizes access to bioprinting, enabling participation from a wider scientific community. Despite these benefits, cybersecurity and data privacy are major concerns, especially when handling patient-specific constructs or clinical blueprints. There is also a need for standardized file formats, metadata tags, and regulatory oversight to ensure consistency and traceability across platforms. Nonetheless, cloud-connected bioprinting is anticipated to be a key enabler of the next-generation biofabrication economy.

CONCLUSION

Chapter 12 underscores that the future of 3D bioprinting is being shaped by a convergence of advanced technologies that go far beyond traditional fabrication methods. Emerging trends such as smart bioinks, 4D bioprinting, microfluidic integration, organoid and spheroid printing, artificial intelligence (AI), and cloud-based platforms are collectively redefining the boundaries of tissue engineering and regenerative medicine. Smart bioinks, responsive to environmental stimuli, allow dynamic tissue behavior and improved biological mimicry. The fusion of microfluidics with organ-on-chip systems enables precise control over microenvironments, while organoid and spheroid printing enhances the physiological relevance of printed constructs. The advent of 4D bioprinting introduces a temporal evolution in printed tissues, opening new avenues for self-assembling and adaptive implants. AI and machine learning are increasingly being used to automate design, monitor quality, and optimize biological outcomes. Wearable and point-of-care bioprinters are enabling decentralized, on-demand tissue fabrication in clinical and emergency settings. Meanwhile, cloud-based platforms are democratizing access to bioprinting by allowing remote collaboration and distributed manufacturing. Despite the exciting potential of these innovations, significant challenges remain including regulatory ambiguity, material limitations, and integration complexity. Nonetheless, these forward-looking trends mark a paradigm shift, positioning 3D bioprinting as a transformative tool in personalized and precision healthcare.

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