Bio-Design and Manufacturing (2026) 9:32–62
https://doi.org/10.1631/bdm.2400354

REVIEW

Artificial intelligence-enabled Bioprinting 5.0

Long Bai[1,4,5,7] · Yi Zhang[2] · Sicheng Wang[1,4,6] · Jinlong Liu[1,4] · Yuanyuan Liu[2,4,5] · Jiacan Su[1,3,4]

Received: 3 September 2024 / Accepted: 18 December 2024 / Published online: 6 October 2025

Abstract

With the rapid advancements in biomedical engineering, bioprinting has emerged as a pivotal solution to address the shortage of organ transplants and advance disease model research. The evolution of bioprinting has progressed from the fabrication of simple models (1.0) to the fabrication of permanent implants (2.0), tissue engineering scaffolds (3.0), and complex biostructures utilizing living cells (4.0). Nevertheless, significant challenges remain, particularly in accurately replicating the structure and function of host tissues, selecting appropriate materials, and optimizing printing parameters. The integration of artificial intelligence (AI), especially machine learning, provides promising novel opportunities in bioprinting (5.0). This review systematically summarizes the current applications of AI in bioprinting, discussing both construction strategies and application scenarios. It also explores the potential of AI to improve bioprinting in the preparation of complex functional tissues and in situ tissue repair. Overall, the synergy between AI and bioprinting is poised to drive the development of personalized medicine, facilitate high-throughput preparation of in vitro models, and provide robust tools for regenerative medicine and precision healthcare.

Long Bai and Yi Zhang have contributed equally to this work.

✉ Jinlong Liu
jlliu5049@163.com

✉ Yuanyuan Liu
yuanyuan_liu@shu.edu.cn

✉ Jiacan Su
drsujiacan@163.com

[1] Organoid Research Center, Institute of Translational Medicine, Shanghai University, Shanghai 200444, China

[2] School of Mechatronic Engineering and Automation, Shanghai University, Shanghai 200444, China

[3] Department of Orthopedics, Xinhua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai 200092, China

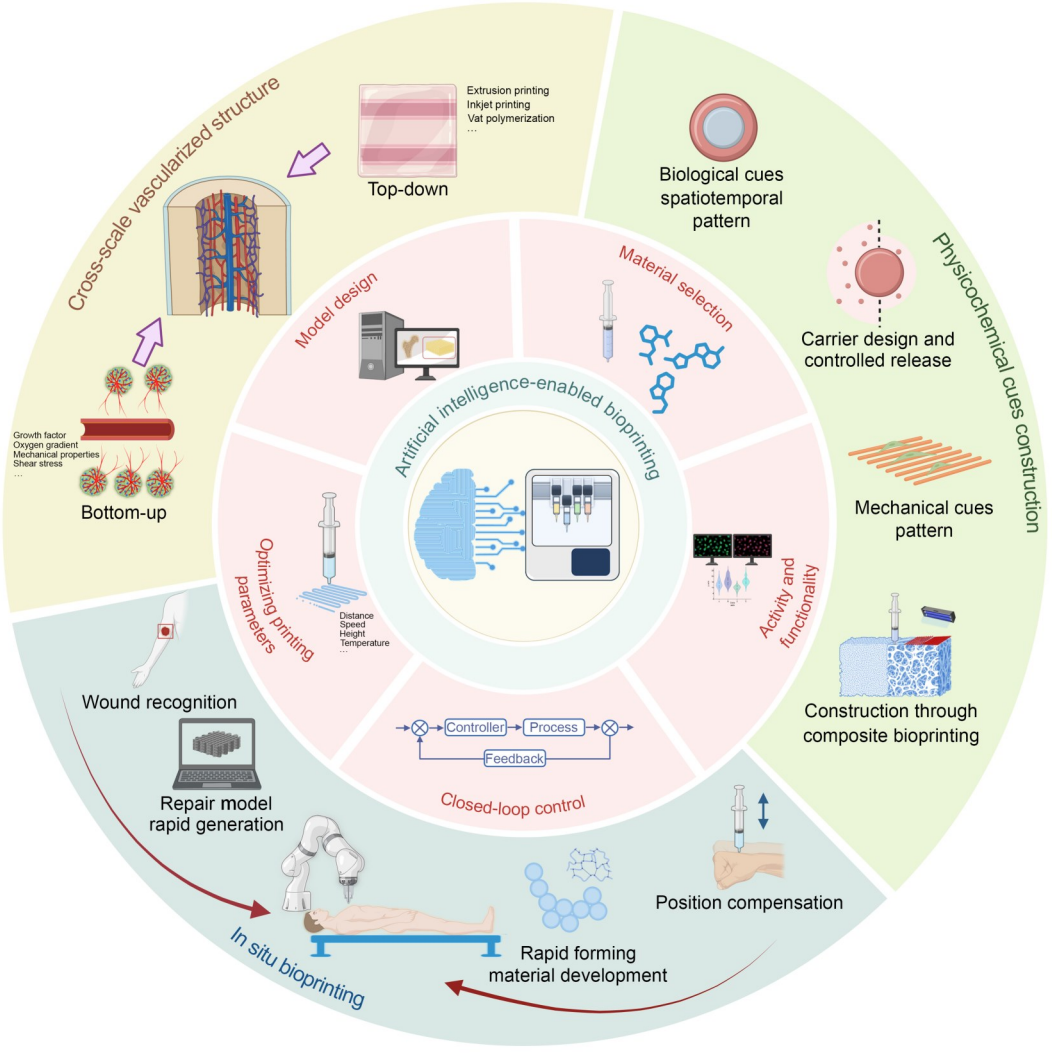
[4] National Center for Translational Medicine (Shanghai) SHU Branch, Shanghai University, Shanghai 200444, China

[5] Wenzhou Institute of Shanghai University, Wenzhou 325035, China

[6] Department of Orthopedics, Shanghai Zhongye Hospital, Shanghai 200444, China

[7] State Key Laboratory of Molecular Engineering of Polymers, Department of Macromolecular Science, Fudan University, Shanghai 200438, China

Graphical abstract



Keywords Artificial intelligence · Bioprinting · Tissue engineering · Machine learning

1 Introduction

Organ transplantation remains the definitive treatment for end-stage organ diseases; however, the chronic shortage of donor organs severely limits its availability [1, 2]. This shortage has driven the search for alternative solutions, particularly through bioprinting technologies such as three-dimensional (3D) bioprinting [3, 4]. Simultaneously, there is an increasing demand in biomedical research for reliable disease models that accurately mimic human physiological and pathological conditions [5]. Traditional two-dimensional (2D) cell cultures and animal models often fail to accurately replicate human disease mechanisms, resulting in inefficiencies in drug development and therapeutic interventions [6–8]. Consequently, advanced bioprinting techniques aim to create complex, multicellular 3D tissue models that provide more physiologically relevant environments for disease modeling and drug testing.

Bioprinting emerged as an extension of additive manufacturing within the biomedical sector, adhering to principles such as layered manufacturing and stacked assembly [9]. This field is distinguished by its use of a diverse array of components—including biomaterials, drugs, growth factors, cells, and even active tissues [10–15]—to fabricate complex tissue structures or organs. The manufacturing process not only replicates the structural and componential biomimicry but also ensures the viability and functionality of these prefabricated structures through their developmental stages

post-manufacturing [16]. This necessitates addressing both existing and novel scientific and technical challenges inherent to bioprinting processes. Currently, bioprinting predominantly utilizes an open-loop, prefabricated approach. Typically, biological constructs are produced and then subjected to biological testing and clinical validation to refine and iterate the manufacturing process. This approach often prolongs technology development cycles due to the intricate and interconnected nature of living systems and the internal microenvironments of tissues and organs, which are complex to replicate and standardize. These complexities frequently result in extensive trial-and-error efforts for identifying suitable bioinks and optimizing manufacturing processes to fulfill specific clinical requirements [17, 18].

Since the widespread adoption of ChatGPT in 2022 and the launch of AlphaFold 3, artificial intelligence (AI) has demonstrated its transformative impact across both humanities and technical sciences [19, 20]. Machine learning (ML), a subdiscipline of AI, has become pivotal in optimizing systems for a more efficient use of products, materials, and services, particularly in the 3D printing industry. ML significantly reduces fabrication time and costs, and improves the quality of standard 3D printing processes through improvements in process optimization, dimensional accuracy, defect detection, and material property prediction. In bioprinting, AI integration is refining the precision and efficiency of bioprinting processes. The capacity of AI to process large datasets enables optimization of bioprinting parameters, predictive modeling of tissue growth, and real-time adaptive responses during printing, thereby improving the accuracy and functionality of bioprinted organs and tissues. Unlike traditional physics-based models, which often struggle with nonlinearities and uncertainties, ML models are highly adaptable and excel at making data-driven predictions. These models autonomously learn, predict, and improve, significantly benefiting the production of precise biological structures. This capability is crucial for advancing drug testing, reducing animal testing, and improving regenerative medicine. For instance, Datta et al. demonstrated how ML algorithms could optimize bioprinting parameters to mitigate light scattering by cells in bioink, thus simplifying the calibration process for various structures in digital light-processing-based bioprinting methods [21]. The synergy between AI and bioprinting not only augments the capabilities of existing technologies but also opens novel avenues for innovative disease models and personalized therapeutic interventions, marking a substantial advancement in regenerative medicine and tissue engineering.

This review delves into how AI-enabled bioprinting, beginning with the historical development of bioprinting techniques and the foundational principles and functions of AI, has catalyzed groundbreaking scientific advancements. The discussion will encompass the specific applications of AI in the bioprinting of artificial tissues and organs, including its critical role in improving the precision and functionality of bioprinting, as well as predicting tissue adaptation postimplantation. Moreover, this review explores the contributions of AI to the construction of cross-scale vascularized tissues, arrangement of physicochemical cues in spatiotemporal distribution to guide controllable tissue growth, and in situ printing for tissue repair. These advancements will push bioprinting to a new phase, enabling the creation of tissues that more closely resemble natural tissues in both form and function, with greater convenience, reproducibility, and efficiency. By advancing algorithm development and fostering interdisciplinary collaboration, AI is poised to significantly propel life sciences and medical research forward, encouraging more researchers to engage with AI in bioprinting to accelerate progress in human health sciences (Fig. 1).

2 Overview of bioprinting

2.1 Historical development of bioprinting

The development of bioprinting technology has made remarkable strides over the decades, in terms of both technical systems and innovative applications, as depicted in Fig. 2. Initially, the focus was on boosting the capabilities of forming technologies, diversifying material choices, and advancing manufacturing systems. Concerning forming capabilities, the technology has evolved from producing homogeneous structures at a single scale to fabricating heterogeneous biological structures across multiple scales. Material choices have expanded from synthetic materials to active components such as cells and proteins. Manufacturing systems have advanced from conventional three-axis motion platforms to more complex systems with multiple degrees of freedom, incorporating multidegree robotic arms for in situ printing—a technique that has shown impressive results.

Innovative applications of bioprinting have progressed from creating models for surgical planning to using living tissues and organs as printing materials. These biologically inspired and functional structures are currently playing an increasingly vital role in areas such as new drug development and repair of tissue and organ defects. The narrative will next focus on reviewing the evolution of bioprinting technology through four representative stages, emphasizing both technical systems and innovative applications.

The first phase of bioprinting (Bioprinting 1.0) involved producing models without the requirement for biological compatibility, such as biomedical models and surgical aids. This phase allowed the use of standard additive manufacturing equipment and materials to create structures, often using extrusion-based techniques such as fused deposition modeling for orthopedic applications, where thermoplastic

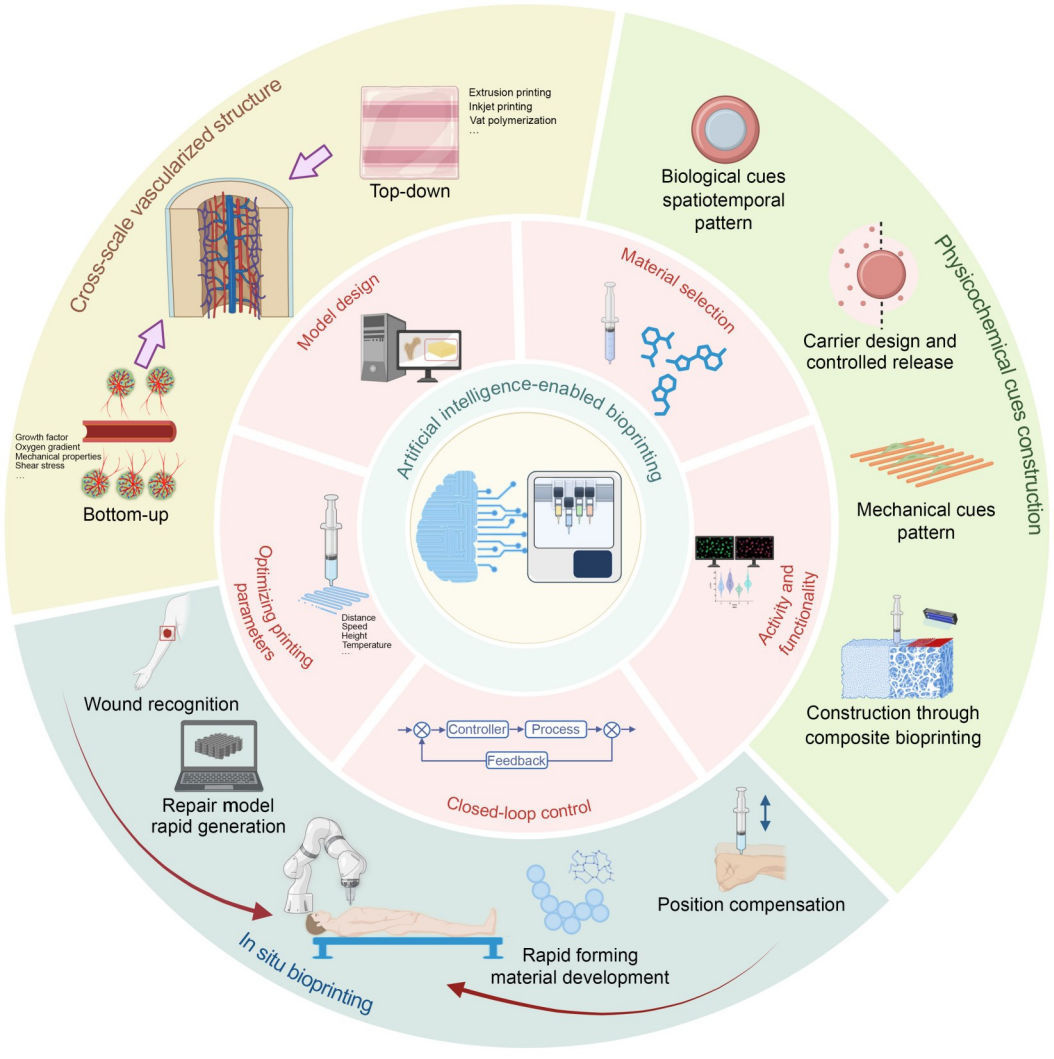


Fig. 1 Schematic of the current applications of AI in bioprinting and the role AI plays in enabling bioprinting of the next phase. Created with BioRender.com

filaments are extruded along predetermined paths to construct parts layer by layer [22, 23]. More complex solid organ models required higher precision, material diversity, and transparency, resulting in the adoption of multimaterial photopolymerization techniques such as PolyJet, which can print up to seven resins simultaneously, enabling customized textures, transparency, and hardness [24–26].

The second phase (Bioprinting 2.0) moved toward the fabrication of permanent implants that were biocompatible but not biodegradable. These structures had to mimic anatomical shapes and match the physical properties of existing bodily structures. Clinically used materials such as biocompatible ceramics and titanium were shaped using selective laser sintering, which sinters layers of metal or ceramic powder with a laser to achieve high-precision 3D structures [27, 28].

The third phase (Bioprinting 3.0) focused on tissue engineering scaffolds designed to maintain, repair, or improve tissue functions. These scaffolds are biocompatible and often biodegradable, designed to work synergistically with cells and tissues within the body or provide temporary mechanical support as new tissues grow. The materials used for designing these scaffolds range from synthetic polymers such as polylactic acid [29, 30] and polycaprolactone [31, 32] to natural biomaterials such as hyaluronic acid and collagen. Techniques such as extrusion printing [33–38], electrohydrodynamic (EHD) printing [39–43], laser sintering [44–47], and vat polymerization [48–53] are commonly used, with extrusion printing being the most widespread due to its versatility with various materials.

The fourth phase (Bioprinting 4.0) represents a significant advancement, using living cells, microtissues, and organ-like structures as printing materials. This phase includes the fabrication of in vitro tissue organ models, organ chips, and therapeutic implants [54], wherein techniques such as extrusion printing, inkjet printing, and light-based curing

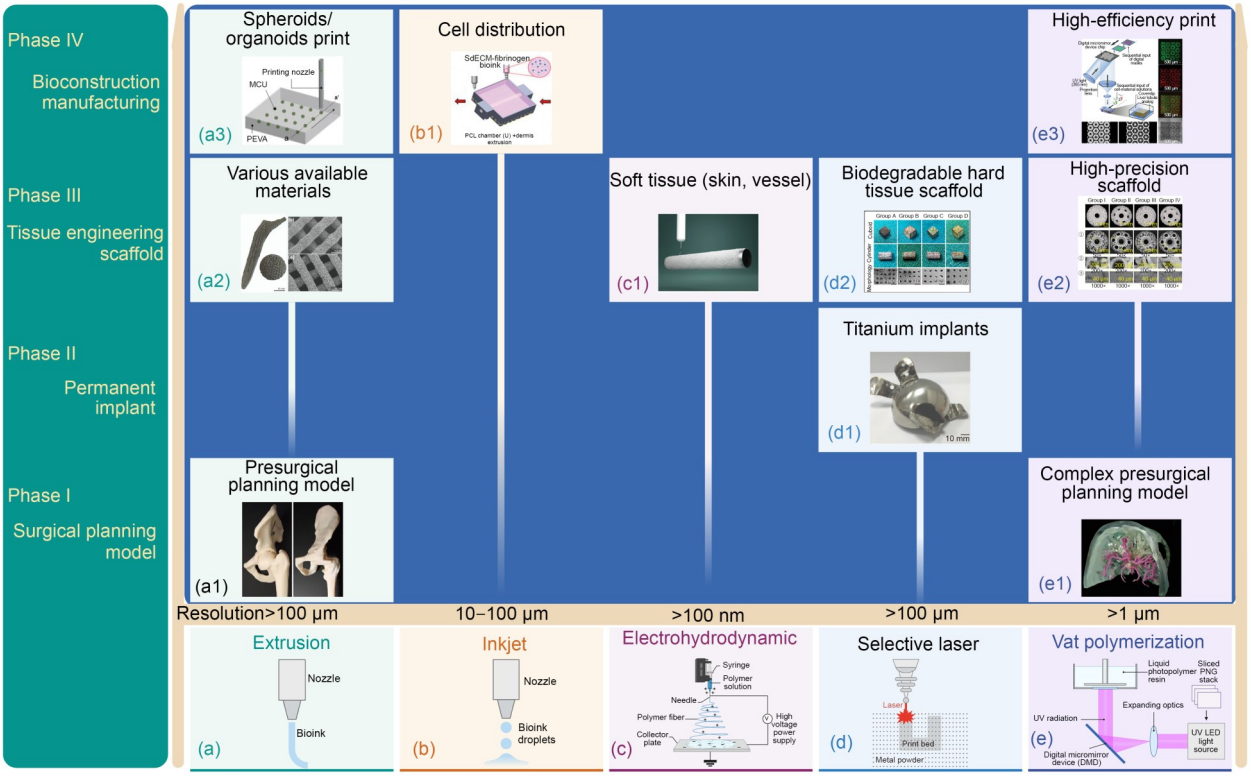


Fig. 2 Different bioprinting technologies used in different application phases. Created using BioRender.com. (a) Application of extrusion printing: (a1) presurgical planning model (reproduced from [23], Copyright 2011, with permission from Springer-Verlag); (a2) biodegradable scaffold with various available materials (reproduced from [35], Copyright 2023, with permission from the authors, licensed under CC BY 4.0); (a3) spheroids and organoids printing (reproduced from [75], Copyright 2021, with permission from Wiley-VCH GmbH). (b) Inkjet printing: (b1) inkjet printing used in cell distribution (reproduced from [72], Copyright 2018, with permission from WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim). (c) Application of EHD printing: (c1) soft scaffold preparation based on EHD technologies (reproduced from [40], Copyright 2019, with permission from the authors, licensed under CC-BY-NC). (d) Selective laser printing: (d1) hip joint prepared by selective laser melting (SLM) (polished) (reproduced from [27], Copyright 2023, with permission from the authors. licensed under CC BY-NC-ND); (d2) SLM-prepared porous biodegradable scaffolds (reproduced from [44], Copyright 2020, with permission from Acta Materialia Inc.). (e) Application of vat polymerization: (e1) complex presurgical planning model printed by PolyJet (reproduced from [26], Copyright 2019, with permission from Elsevier Inc.); (e2) DLP-based high-resolution scaffold preparation (reproduced from [53], Copyright 2024, with permission from the authors, licensed under CC BY-NC-ND); (e3) high-efficiency tissue construction printed by vat polymerization (reproduced from [66], Copyright 2024, with permission from Wiley-VCH GmbH)

are commonly used. Inkjet technology is particularly effective in providing high precision for cell placement [55–59]. The introduction of biologically active photosensitive materials such as gelatin methacryloyl (GelMA) has enabled the printing of cell-laden structures using high-precision, cell-friendly photocuring techniques such as digital light processing (DLP) and continuous liquid interface production (CLIP) [60–67]. Extrusion printing remains popular in this phase due to its adaptability in handling a wide range of materials and ease of integration with other manufacturing processes or external physical fields, making it ideal for constructing complex multimaterial structures [68–75].

2.2 Challenges and limitations of bioprinting

Despite significant advancements in biomanufacturing, several critical challenges remain that hinder its full realization in clinical and therapeutic applications. The complexity of biological systems presents a major obstacle; accurately replicating the mechanical properties and biological functions of native tissues requires precise control over both biomaterials and manufacturing processes. The inherent heterogeneity of tissues, characterized by diverse cell types and intricate structural configurations, further complicates the fabrication process. Furthermore, selecting suitable materials that are both biocompatible and possess the requisite mechanical and biological properties is immensely challenging. These materials must not only support cell growth and integrate seamlessly with the human body but also emulate the mechanical strength and flexibility of the tissues they aim to replace. In addition, the biodegradation rates of these materials must be precisely synchronized with tissue regeneration to maintain structural integrity and functionality over time.

Another set of challenges involves scalability and reproducibility, which are crucial for transitioning biomanufacturing processes from the laboratory to clinical settings. Ensuring consistency and maintaining high-quality standards across different production batches and setups are essential for medical applications. Variations in raw materials, environmental conditions, and operational techniques can cause reproducibility issues, affecting the overall efficacy and safety of bioprinted products. These challenges emphasize the need for advanced solutions that can streamline manufacturing processes, improve material properties, and ensure the scalability and reproducibility of bioprinted tissues and organs. Addressing these issues is vital not only for advancing the field but also for ensuring that biomanufacturing fulfills the stringent requirements of clinical applications, paving the way for broader adoption and implementation in healthcare.

3 Overview of AI

3.1 Definition and historical development

AI is a branch of computer science that aims to generate computational systems capable of performing tasks typically associated with human intelligence, including visual perception, speech recognition, decision-making, and natural language processing [76]. AI is a multidisciplinary field, drawing insights from computer science, mathematics, psychology, linguistics, and philosophy. In recent years, AI has gained prominence due to its potential to drive innovation across diverse sectors such as healthcare, finance, transportation, and manufacturing.

The inception of AI dates back to the 1950s, with the term "artificial intelligence" first coined by John McCarthy, a computer scientist at Dartmouth College, in 1955 [77]. A pivotal workshop organized by McCarthy and a group of computer scientists and cognitive psychologists laid the foundation for AI as an academic discipline. Early AI research primarily focused on developing rule-based systems, known as artificial expert systems, which used a defined set of rules and knowledge to make decisions. A landmark in the early history of AI was the creation of the Logic Theorist by Allen Newell and Herbert Simon in 1956, a program that could prove mathematical theorems and is considered an early milestone in AI [78].

The 1970s and 1980s witnessed a paradigm shift in AI research toward more complex systems capable of experiential learning. This era saw the emergence of ML algorithms such as decision trees, neural networks, and support vector machines (SVMs), which facilitated data-driven learning [79]. The 1990s and early 21st century brought a resurgence of interest in AI, with significant advances in ML, natural language processing, and computer vision, all spurred by the advent of the World Wide Web and the vast amounts of data it generated.

Over the past decade, the field of AI has experienced a series of significant developments and transformations. These advancements have not only propelled the progress of technology but also brought profound impacts on human society. In 2012, deep learning achieved a breakthrough in the field of visual recognition, during which the deep convolutional neural network (CNN) AlexNet achieved unprecedented results in the ImageNet competition. Subsequently, in 2014, the proposal of generative adversarial networks brought revolutionary changes to areas such as image generation and artistic creation. In 2016, DeepMind's AlphaGo defeated the world champion of Go, Lee Sedol. This event not only demonstrated the ability of AI in complex strategic games but also marked a significant progress of AI in the field of strategic decision-making. In 2017, natural language processing technology witnessed remarkable development. Deep learning-based language models began to emerge, significantly improving the ability of language understanding and generation and opening up novel possibilities for the interaction between AI and humans. In the same year, OpenAI released the GPT-1 model, which was the debut of pretrained language models and laid the foundation for subsequent language model research. In November 2022, OpenAI launched the AI conversation application service ChatGPT based on the GPT model. ChatGPT demonstrated the tremendous progress of natural language processing technology. Based on large-scale data training and deep learning algorithms, it can generate high-quality, logically coherent text responses, providing novel ideas and methods for the further development of AI technology and prompting researchers to continuously explore more advanced algorithms and model architectures [19]. During this period, a major breakthrough of AI in the field of biology was the emergence and development of AlphaFold, which can predict the structures and interactions of biomacromolecules with atomic precision. The development of this technology not only represents a scientific breakthrough but also indicates the immeasurable potential of AI in changing the way life science research is conducted. These key developments and progress together constitute the glorious course of AI in the past decade. They not only promoted the continuous advancement of AI technology but also depicted a future full of infinite possibilities for us. We should continuously focus on and deeply investigate these developments to better promote the continuous progress of AI and bring more benefits and development opportunities to human society.

3.2 Varieties of ML

AI involves developing computational agents that simulate human cognitive functions such as problem-solving, learning,

and strategic planning. The primary objective of AI is to engineer systems capable of performing tasks that typically require human intelligence, such as interpreting language, recognizing patterns, and making decisions. ML, a critical subset of AI, focuses on training algorithms to learn from data and make decisions or predictions based on these data. These algorithms improve their accuracy in predicting outcomes or identifying patterns through iterative learning, without being explicitly programmed for specific tasks, thereby forming the foundation of most practical AI applications today.

ML can be categorized into several distinct types, each suited to different problem-solving scenarios, thereby improving the flexibility and applicability of AI across various domains [80]. Supervised learning involves training an algorithm on a labeled dataset, where the correct outcomes are already known. The model learns to predict these outcomes on new, unseen data, making it ideal for applications such as spam detection and image classification. In contrast, unsupervised learning does not rely on labeled data; it identifies hidden patterns and relationships within the dataset, which is useful in applications such as market basket analysis and anomaly detection [81]. Reinforcement learning is distinguished by training algorithms through trial-and-error, guided primarily by rewards and penalties [82]. This method is particularly effective in dynamic environments such as robotics and gaming, where the algorithm must make a series of decisions to maximize a cumulative reward.

Together, these ML methods emphasize the robust versatility of AI, contributing to its transformative impact across industries and its ability to augment human capabilities in increasingly sophisticated manners.

3.3 Prominent ML models

In the rapidly evolving landscape of ML, various models have emerged, each tailored for specific tasks and data types, significantly improving the capabilities of computational analysis across numerous fields [79, 83, 84]. Random forests leverage the collective power of multiple decision trees to improve predictive accuracy and prevent overfitting, rendering them invaluable for ensemble learning. SVMs excel in high-dimensional data, adeptly handling both regression and classification tasks, and are particularly effective in scenarios requiring clear margins of separation. Logistic regression, though traditionally used for binary classification, effectively estimates the probability that an input belongs to a certain category, thereby facilitating applications such as medical diagnoses and other binary outcomes.

Neural networks represent a more complex class of ML models, capable of managing and interpreting intricate, structured data, rendering them particularly valuable in deep learning applications involving large volumes of data [85–87]. Recurrent neural networks are specifically designed to recognize patterns in sequential data, maintaining a flow of information across network loops, which is essential for processing text or speech where context and sequence are critical. CNNs are predominantly used in image processing and tasks requiring the recognition of spatial hierarchies, such as facial recognition and autonomous driving systems.

Graph neural networks are specialized for analyzing data formatted as graphs and examining the interdependencies between nodes, which is crucial for applications such as social network analysis and chemical structure analysis. Finally, transformers, utilizing self-attention mechanisms, excel in tasks requiring an understanding of the sequence of input data, such as language translation and text summarization. These models leverage large datasets to learn and are particularly effective in tasks where contextual relationships within the data are essential for generating accurate predictions or insights. Altogether, these diverse ML models facilitate a wide range of applications, driving innovation and efficiency in fields ranging from healthcare to autonomous vehicle navigation.

3.4 Benefits and limitations

The potential of AI to transform the biomedical field is profound, providing benefits that could significantly improve healthcare and research. Nevertheless, AI also faces challenges, including data requirements, potential biases, overreliance risks, and ethical dilemmas surrounding privacy and consent. The implementation of AI in the biomedical sector must be approached with cautious consideration.

3.4.1 Benefits of AI in biomedical fields

AI is revolutionizing biomedicine, providing numerous benefits that improve the quality and accessibility of healthcare services [88]. The ability of AI to customize treatments based on individual genetic profiles significantly improves the management and efficacy of therapies. In drug discovery, AI accelerates the identification and development of new drugs, reducing both time and the associated costs [89]. Furthermore, AI extends the reach of quality healthcare to underserved regions, potentially reducing the incidence of medical errors. For instance, using mobile health (mHealth) to collect residents' health data in relatively remote areas can enable local residents to receive timely health monitoring. The large amount of data collected can be analyzed with the assistance of AI to achieve rapid disease screening and provide effective strategies for promoting the development of local medical and health levels [90, 91]. By streamlining operations, AI also alleviates the administrative

burdens and costs associated with healthcare delivery. Similarly, AI has significant potential in reducing healthcare costs. The use of AI to analyze patient hospitalization records enables disease predictions for patients and the provision of early intervention treatments, thereby reducing possible future treatment costs [92]. For clinicians, AI serves as a powerful decision-support tool, augmenting their capacity to make informed decisions and thereby improving patient outcomes. By acquiring large amounts of real-time data from electronic health records (EHRs), AI can rapidly create patient-specific clinical prediction models, such as predicting whether a patient with a blood disease will develop a multidrug-resistant infection during neutropenia, so that appropriate treatment options can be recommended in a timely manner [93]. The advanced image recognition capabilities of AI are critical in fields such as radiology and pathology, enabling the detailed analysis required for accurate diagnoses. In the analysis of children's metacarpal bones, AI uses deep learning models to achieve efficient and accurate automated bone age evaluation in medical image analysis. Its accuracy is equivalent to that of expert radiologists, significantly reducing human errors and time costs [94]. To summarize, AI is comprehensively improving the efficiency, accuracy, and accessibility of the medical and health field through its excellent analytical capabilities, personalized medical support, and a wide range of application scenarios, providing strong technical support for the development of global medical services.

3.4.2 Limitations of AI in biomedical fields

Despite its substantial benefits, the application of AI in biomedicine comes with several challenges and limitations that must be carefully managed. The effectiveness of AI heavily depends on the quality and availability of training data, which must be comprehensive and free from biases to ensure reliability. When the data used in training an AI system are inconsistent with the data or environment in which it actually operates, it may result in incorrect predictions. For instance, different devices or individual differences between patients may cause errors in AI analysis. This problem can be significantly improved by increasing the quality and quantity of data used for training [95]. The inherent complexity of AI models, particularly those based on deep learning, poses challenges in terms of explainability and trust, making it difficult for users to fully understand and trust the decision-making processes of AI. For instance, AI is used to determine whether a patient will benefit from an antidepressant drug. Nevertheless, the use of a large amount of clinical data (such as age, region, and genetic information) in the training process results in an exceedingly complex reasoning model. The logic behind its decisions remains opaque, making it a so-called "black box" model. The possible misdiagnosis rate and the lack of transparency make it impossible for clinicians to trust the conclusions drawn by the model [96]. The performance of AI can also vary across different populations due to genetic, lifestyle, and environmental differences, thereby emphasizing issues with generalizability. Furthermore, integrating AI into healthcare raises significant regulatory and ethical concerns, including issues of responsibility, fairness, and the potential to exacerbate existing health disparities. When real patient data are used to train AI, there are problems with patient privacy and data leakage. How to ensure that the data are not used for other profit-making purposes has also become an urgent problem to be solved [97]. It is essential to address these challenges to maximize the positive impacts of AI in biomedicine and ensure equitable benefits across all sectors of society.

To summarize, although AI presents vast opportunities in biomedical fields, it is imperative to address the challenges related to data quality, model interpretability, and the ethical and regulatory aspects of its deployment. Overcoming these hurdles is essential to unlock the complete potential of AI in this domain.

4 Current status of AI applications in bioprinting

4.1 AI applications in structure design and performance prediction

The anisotropic microstructures of natural tissues and organs play a vital role in the effective reconstruction of biological functions [76]. This presents significant challenges for the artificial construction of tissue organs. To replicate the complex microstructures of natural tissues and organs in vitro, it is essential to consider the interrelationships among the design models, matrix materials, and forming processes. Moreover, potential manufacturing defects that may develop during the specific manufacturing process must be accounted for, making this a multiobjective analysis and optimization task. Considering the multidimensional and complex information involved in the manufacturing process of tissue organs, traditional mechanical design and finite element methods are often inadequate for predicting the design and manufacturing functions of natural tissues and organs. AI, particularly in the form of ML methods, provides transformative technical support for bioprinting.

4.1.1 AI-assisted model structure design

In model design, the macroscopic and microscopic structural characteristics of tissues are crucial for replicating their physical properties. Currently, tissue structure characteristics can be effectively captured using technologies such

as computed tomography (CT) and magnetic resonance imaging (MRI), followed by manual optimization of the structural design. With the development of bioprinting technologies, the construction of tissues has shifted from fabricating structures that macroscopically resemble natural tissues to pursuing the replication of microscopic structures, thereby fabricating biomimetic structures. Natural tissues feature complex and diverse microstructures, and the forming process involves the use of multiple material structural gradients and a combination of various processes. Therefore, manual design of tissue organ models is often inadequate to meet the requirements of model design under conditions involving multiple variables, objectives, and multifield coupling. In this context, AI-assisted model design has emerged as a feasible solution for overcoming these challenges.

Preliminary investigations have been conducted by researchers in this field. For instance, Li et al. developed a stepwise algorithm-assisted bioprinting technology that uses an adaptive mesh generation algorithm combined with a mechanical equilibrium mechanism to efficiently generate anisotropic mesh patterns with optimized topological structures within a designated space. These mesh patterns are then encoded into effective printing paths using a greedy search algorithm. The effectiveness of this method was validated using models of anisotropic femoral head units and femoral units featuring biomimetic osteon microstructures and biological properties. This design method effectively addresses the structural deformations caused by the accumulation of multiple materials and also shortens the printing time (Fig. 3a) [98]. AI can also be used to predict the final performance of the design model. Barrera et al. utilized hierarchical 2D images as input, with Young's modulus, shear modulus, and porosity as outputs, to train a 3D CNN, ultimately achieving the prediction of the mechanical properties of scaffolds [99].

4.1.2 AI-assisted bioink development

Material selection is a key factor determining the successful preparation and functionality of biological structures. In additive bioprinting, the selection of materials must consider both printability and fidelity postprinting, as well as

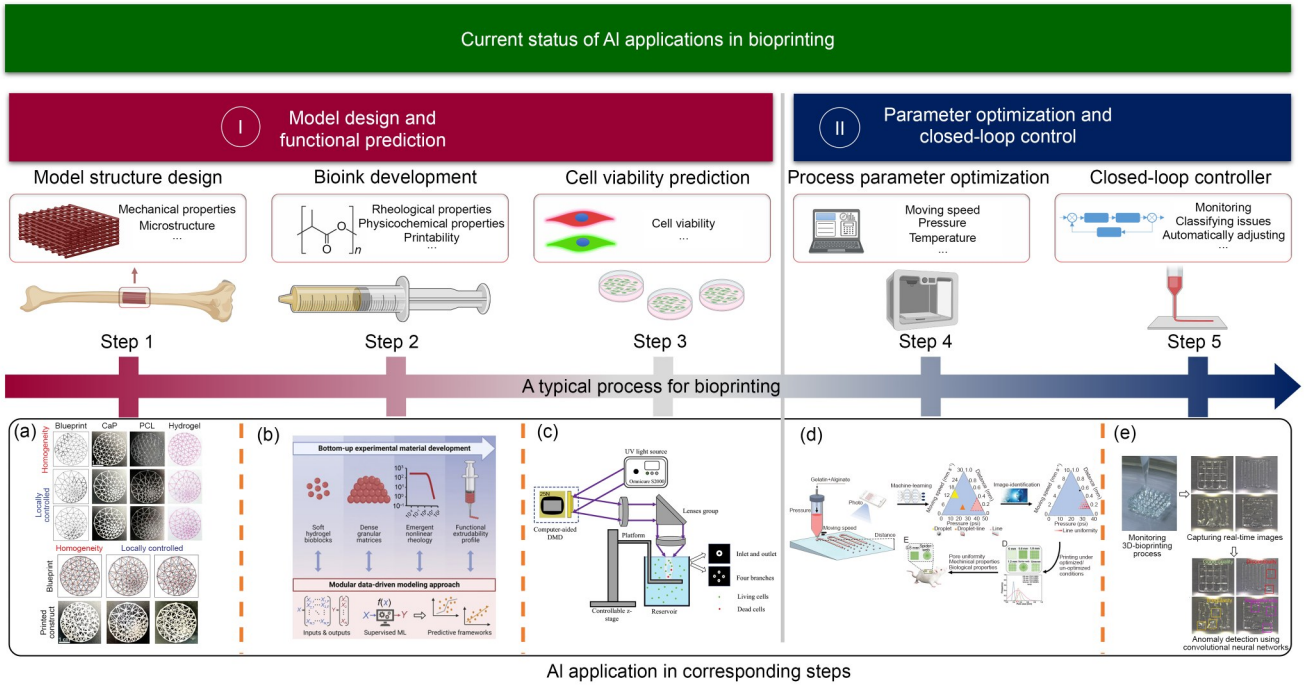


Fig. 3 AI-assisted biological additive manufacturing enabled through two paths: (I) model design and functional prediction; (II) parameter optimization and closed-loop control. Created using BioRender.com. (a) AI-assisted structure design: AI generates anisotropic mesh patterns with optimized topology and encodes them into efficient print paths (reproduced from [98], Copyright 2022, with permission from Wiley-VCH GmbH). (b) AI-assisted bioink development: machine learning predicts the structure, rheological properties, and printability of granular bioinks (reproduced from [106], Copyright 2023, with permission from the authors, licensed under CC BY-NC-ND). (c) AI-assisted viability prediction: ensemble algorithms combining neural networks, ridge regression, *K*-nearest neighbors, and random forests (RF) predict cell survival under various bioprinting conditions (reproduced from [110], Copyright 2020, with permission from Springer Science Business Media, LLC, part of Springer Nature). (d) AI-assisted optimized parameters: an AI-assisted high-throughput printing condition screening system (AI-HTPCSS) optimizes parameters by recognizing subregions of hydrogel pattern images via machine learning (reproduced from [113], Copyright 2022, with permission from Wiley-VCH GmbH). (e) AI-based closed-loop controller: anomalies in the printing process are monitored using a system based on layer-by-layer images and machine learning algorithms (reprinted from [116], Copyright 2021, with permission from the American Chemical Society)

biological requirements. Materials with high polymer content and viscosity typically exhibit good fidelity in terms of structural similarity to the original design. Nevertheless, such materials may adversely impact the function of active tissues such as cells. In extrusion printing, the matrix materials used in cell printing must possess sufficient mechanical properties to ensure appropriate shaping while also being conducive to subsequent cell survival, migration, and biological activity. This conflicting requirement requires comprehensive consideration of the application functions, forming effects, and other aspects in the selection of materials for bioprinting, resulting in adjustments in material printability and printing conditions that often require extensive time and cost for experimentation.

In recent years, researchers have begun using ML methods to address these issues through two primary approaches. The first approach involves integrating AI technology with bioink development, allowing researchers to simulate and predict the physical and chemical properties, bioactivity, and other characteristics of materials. For instance, AI methods such as artificial neural networks (ANNs), SVMs, and support vector regression can predict material properties under different pH, temperature, and other environmental conditions, thereby accelerating the design of materials with specific drug release requirements [100, 101]. In the field of nanomedicine design, AI can utilize computer vision or natural language processing to rapidly mine existing data and predict new datasets through model training, thus enabling the predictive analysis of nanomedicine properties [102]. Techniques such as quantitative structure–activity relationship (QSAR), which combine nanotechnology and computational methods, can link the structures of chemical compounds to their biological properties, predicting both their activity and potential toxic effects [103]. By combining AI technologies such as deep learning and reinforcement learning with QSAR, researchers can perform ultralarge-scale docking molecule screening, rapidly selecting potential material components and synthesis conditions [104].

The second approach involves using AI to predict the printability of materials before preparing structures. With improvements in computational power, it is possible to predict printing results with multiple material components and use these results as feedback to further optimize the material ratios. This iterative process ultimately yields optimized values concerning functionality and formability. In this regard, Ruberu et al. used ML based on Bayesian optimization to quantitatively evaluate the printability of materials, establishing a scoring system that includes fiber formation and layered stacking effects to assess the printability of GelMA and hyaluronic acid methacrylate (HAMA) bioinks. This method significantly reduces the number of experiments required [105]. Furthermore, Verheyen et al. developed an additive manufacturing ML model for the design and optimization of granular hydrogel matrix bioinks, which can predict the structural volume, rheological properties, and extrudability of granules, thus enabling the rapid design and manufacture of granule-based matrices with controllable structures and performance (Fig. 3b) [106]. Chen et al. used decision trees, random forests (RF), and deep learning to predict the printability of biomaterials, with accuracy, precision, recall, and F1 score used as metrics to evaluate predictive capabilities. Their results demonstrated that all three methods could predict material printability, with random forests achieving the best accuracy, precision, and F1 score, whereas deep learning had the highest recall rate. Moreover, the ML model can predict the printable window of biomaterials, providing guidance for material development [107]. Lee et al. used ML to examine the printability of collagen, hyaluronic acid, and fibrinogen composite inks. Their results revealed that printable inks should possess a high storage modulus (G') and low yield stress (τ_y). Subsequently, multivariate regression analysis was used to derive various natural biomaterial ink formulations that provide high shape fidelity. Finally, this framework of high-shape-fidelity biomaterial inks was used to fabricate a gelatinous 3D structure containing cells, confirming high cell survival and proliferation within the 3D structure [108].

4.1.3 AI-assisted prediction of cell viability

Maintaining the activity and functionality of cells and organoids is another critical consideration in bioprinting. Optimal process parameters for preserving cell activity typically depend on the size and shape of the specific cell type and its sensitivity to external mechanical forces. Nevertheless, current methods for evaluating cell viability often involve repeated experiments, which are both time-consuming and expensive [109]. To address this problem, researchers have investigated AI technology to predict cell survival rates under specific process parameters, thereby reducing the need for extensive experimentation.

Mohammadrezaei et al. developed an ML model for predicting cell viability based on various bioprinting variables. They further used a Bayesian optimization model combined with a regression neural network to optimize bioprinting parameters, maximizing cell viability while minimizing trial-and-error experiments [109]. Xu et al. used ML to develop a prediction model for cell viability by integrating neural networks, ridge regression, *K*-nearest neighbors, and RF. They investigated the performance of the model using three error metrics and used RF to determine the importance of each process parameter on cell viability. Their results indicated that the model could accurately predict cell viability and identify the critical process parameters in stereolithography (SLA) printing (Fig. 3c) [110].

4.2 AI applications in the optimization of bioprinting quality

In bioprinting, the selection and optimization of process parameters for printing structures and materials, as well as the real-time monitoring and feedback of these parameters during the printing process, are crucial for achieving accuracy and fidelity in the formed structures. These factors also impact the functionality of materials, growth factors, cells, and other components contained within the structures.

4.2.1 AI-assisted optimization of process parameters

Real-time monitoring and feedback optimization of process parameters are essential for ensuring the precision and fidelity of printed structures and the functionality of the incorporated active factors and cellular components. Currently, setting process parameters often depends on operators' previous knowledge and laborious optimization experiments [111, 112]. Several bioinks require repeated experimentation to optimize printing parameters such as nozzle movement speed, extrusion pressure, and printing distance, ensuring that the printed structures closely resemble the original digital model [113]. Furthermore, with the rapid increase in the types of biomaterial inks, particularly multicomponent bioinks, the added components can alter the rheological properties, potentially resulting in nonlinear relationships between input and output parameters [114]. The increasing complexity of the scaffold structures further escalates the cost and effort required for exploring and optimizing the printing parameters through extensive experimentation.

As AI technology advances, utilizing AI to obtain optimized printing parameters and improve print quality is emerging as a viable technical solution. For instance, Nguyen et al. used a deep neural network system in selective laser sintering processes to obtain the optimal laser power, scanning speed, powder layer thickness, and hatch distance, significantly enhancing the quality of printed structures [112]. Furthermore, Fu et al. identified critical material and process parameters that affect the printability of extrusion printing and developed a preliminary ML model for optimizing these parameters. They considered rheological properties, nozzle gauge, nozzle temperature, path height, and the effects of ink composition on the printability of Pluronic F127, generating a process map through an SVM model to help select the best printing parameters, achieving high-quality prints with a probability >75% [115]. Chen et al. also proposed an AI-assisted high-throughput printing condition screening system (AI-HTPCSS), comprising a programmable pneumatic extrusion (bio)printer and an AI-assisted image analysis algorithm. This method divided the extruded hydrogel images into 94 subregions and used ML to identify and mark the pattern state of each subregion, thus enabling the high-throughput screening of printing conditions for uniform hydrogel structures. The optimized scaffolds exhibited satisfactory mechanical and in vitro biological performance and accelerated in vivo diabetic wound healing (Fig. 3d) [113]. In addition, Sedigh et al. used a fuzzy model system for approximating and quantifying the accuracy and printability of common bioinks. The system approximated the line width under given printing speed, extrusion pressure, and media dilution percentage, identifying a set of printing parameters that could achieve the highest shaping accuracy. It also increased the shaping accuracy of Pluronic F127 by 68% and introduced a bioink precision index, which can rapidly generate bioink shaping accuracy without considering the printing technology or environmental parameters [114].

4.2.2 AI applications in the online regulation of bioprinting

Incorporating closed-loop control techniques into the bioprinting process is a critical strategy to improve the forming accuracy and ensure the repeatability of the prepared structures. As bioprinting technology expands its applications in tissue and organ repair, drug screening, and disease research, the need to explore process parameters for new functional materials becomes increasingly important. Conventionally, this exploration requires laborious trial-and-error by professionals. Even when optimal process parameters are identified, variations between different material batches can result in inconsistent outcomes, making closed-loop feedback systems a promising solution. Integrating AI-driven closed-loop controllers in additive manufacturing has become vital [111].

Current research attempts focus on the real-time evaluation of the material deposition morphology to adjust the printing parameters dynamically. For instance, Bonatti et al. proposed a deep learning-based robust control loop that optimizes the printing parameters and monitors the printing process in real time. This system uses a high-resolution network camera to record the printing process, generating a comprehensive dataset of the extruded prints. This dataset is used to train a CNN architecture for classifying the forming quality. Combined with a mathematical model of the extrusion printing process, the system can monitor and automatically adjust specific parameters during continuous printing [18]. Jin et al. developed an anomaly detection system for the bioprinting process using image-based ML algorithms to classify issues such as discontinuity, nonuniformity, and irregularity in transparent hydrogel prints. By applying CNN methods and advanced image processing techniques to small block images, the system achieved high accuracy in detecting anomalies, thereby predicting various

anomalies and simultaneously accurately identifying the category and location of the defects within the image blocks (Fig. 3e) [116].

For fine fiber or droplet-forming processes, monitoring the ink shape as it exits the nozzle is another method of evaluating the effectiveness of printing. Sun et al. used digital microscopic imaging technology to monitor the Taylor cone in the EHD printing process. They used image processing algorithms to extract relevant features and recognition algorithms for evaluating the suitability of the Taylor cone for manufacturing the electrohydrodynamically printed scaffold. A CNN recognition model was established and implemented for the morphological classification of the Taylor cone, achieving an accuracy >90% [117]. Huang et al. proposed an unsupervised learning approach using a deep recurrent neural network (DRNN) to examine droplet flow patterns in inkjet printing. Their experimental results demonstrated that this method could learn the hidden representations of the droplet ejection process video data and infer the key parameters of droplet formation. This approach is particularly useful to understand the process dynamics and achieve real-time in situ monitoring and control of droplet deposition quality [118].

In conclusion, bioprinting is rapidly emerging as a technology with vast application prospects in the biomedical field, finding applications in surgical models, permanent implants, tissue engineering scaffolds, and biostructured preparations. The various bioprinting methods address structural preparation requirements across scales from nanoscale to millimeter, utilizing materials that range from traditional 3D printing thermoplastics and metals to biologically active bioinks designed for functional tissue and organ repair. Integrating AI into bioprinting is an emerging field that provides substantial benefits. The combination of AI with bioprinting not only provides critical data support for bioink component design, topological structure optimization, process parameter optimization, and improved cell survival rates, thereby reducing both the number of trial-and-error experiments and the material, labor, and time costs, but also significantly improves forming accuracy. During bioprinting, AI technology provides essential process monitoring and feedback, enabling timely identification of anomalies and automatic optimization of process parameters (Table 1). The incorporation of AI improves the efficiency and quality of bioprinting, thereby enabling additive biotechnology to more effectively fulfill the demands of practical applications.

5 Role of AI in advancing bioprinting to the next phase

As discussed in the previous section, some research attempts have already combined AI with bioprinting technology to address the coupling relationships between design models, matrix materials, and forming processes. These advancements have enabled the improvement of printing capabilities through multiobjective analysis, optimization, performance prediction, and online intelligent control of manufacturing processes. Nevertheless, natural tissues and organs possess complex multiscale structures and intricate functions, such as vascular networks, anisotropic mechanical properties, and the highly organized orchestration of cells and the extracellular matrix (ECM) [119, 120]. Therefore, in the construction of artificial tissues and organs, it is imperative to replicate tissue-specific physicochemical cues and cross-scale vascular networks to effectively approximate the biological functions of natural tissues and organs. This results in more complex and challenging problems.

Furthermore, the integration of multi-degree-of-freedom robotic arms for direct in situ printing aimed at repairing tissue defects is demonstrating significant potential. However, this development also presents researchers with increasingly complex tasks related to system modeling, analysis, and evaluation. The in situ printing process involves intricate material–tissue interfaces and microenvironment control, which urgently require novel technological interventions to explore these uncharted domains.

The capability of AI to process vast amounts of data and learn from complex patterns provides more efficient and accurate methods for model design, material development, parameter prediction, and process control in bioprinting. This capability is vital for overcoming the abovementioned challenges, thereby advancing the bioprinting technology required to fabricate artificial tissues and organs that closely resemble their natural counterparts in both shape and function. Such advancements are essential for promoting further developments in tissue engineering and regenerative medicine.

5.1 AI-assisted construction of cross-scale vascularized structure

Achieving vascularization is critical in the construction of artificial tissues and organs because vascular networks play a fundamental role in nutrient exchange, selective substance passage, and the formation of pathological microenvironments [121, 122]. Current methods for constructing vascular channels in vitro include coaxial extrusion printing [75, 123], vat polymerization [124], and hybrid additive/subtractive manufacturing [125–127]. Although bioprinting has demonstrated promise in creating complex vascular networks, challenges remain in the controlled construction of cross-scale hierarchical vascular networks, particularly those involving capillaries. A promising approach involves integrating both bottom-up and top-down printing strategies, incorporating principles from developmental biology into the model design, and achieving capillary network

Table 1 Current status of AI used in bioprinting

Algorithm and model	Application	Function	Reference
Stepwise	Model design	Generating anisotropic mesh patterns with optimized topological structures	[98]
3D CNN	Model design	Predicting Young's modulus, shear modulus, and porosity from input layered 2D images of the porous structure	[99]
Bayesian optimization	Bioink development	Evaluating the printability of bioinks according to filament morphology and architecture in extrusion printing and providing the best parameters	[105]
Random forest and gradient boosting	Bioink development	Rapid design of granule-based matrices with controllable structures and performance	[106]
Decision trees, random forests, and deep learning	Bioink development	Outputting shape fidelity based on different input ink formulations; predicting the printability window to guide ink formulations	[107]
ML and multiple regression	Bioink development	Determining relationships between rheological properties and printability and predicting the printability of different ink compositions	[108]
Neural network-based Bayesian optimization model	Cell viability prediction	Analyzing different parameters' impact on cell viability; predicting optimal bioprinting parameters without experiments	[109]
Ensemble learning algorithm	Cell viability prediction	Predicting cell viability under various ultraviolet intensities, exposure times, concentrations, and layer thicknesses in SLA	[110]
Deep neural networks	Parameter optimization	Obtaining the optimal laser power, scanning speed, powder layer thickness, and hatch distance	[112]
Support vector machine	Parameter optimization	Selecting the best printing parameters based on rheological properties, nozzle gauge, nozzle temperature, path height, and ink composition	[115]
ML-assisted image analysis	Parameter optimization	High-throughput screening of printing conditions for uniform hydrogel structures	[113]
Fuzzy model system	Parameter optimization	Approximated line width under given printing speed, extrusion pressure, and media dilution percentage	[114]
Deep learning	Closed-loop controller	Monitoring and automatically adjusting specific parameters during continuous printing	[18]
Image-based machine learning	Closed-loop controller	Predicting various anomalies and identifying the category and location of the defects	[116]
CNN	Closed-loop controller	Morphological classification of the Taylor cone	[117]
DRNN	Closed-loop controller	Examining droplet flow patterns in inkjet printing and inferring key parameters of droplet formation	[118]

formation through guided angiogenesis rather than solely depending on manufacturing techniques. This strategy could enable the creation of vascularized structures as described earlier.

Nonetheless, integrating these two processes remains a challenge. Although bottom-up cell self-assembly can form capillary networks, it is hindered by prolonged formation times and the typically disorganized structure of the resulting vessels. Moreover, the capillary density and tissue patterns vary across different tissues, necessitating careful consideration of spatial distribution characteristics when constructing the capillary networks. Ensuring stable morphology and density in vascular networks is essential for obtaining consistent results in drug screening. Incorporating key regulatory information for capillary generation into the design and fabrication of macrostructures may address these issues, guiding capillaries to form as required. AI technologies can play a vital role in predicting and analyzing these aspects, selecting optimal strategies for preparing vascularized bioconstructions, and evaluating the function of vascular networks for further optimization (Fig. 4).

In the top-down approach, AI can assist in establishing structural models for preparing meso-sized channel networks. For instance, Wang et al. used a decision-tree-based method to extract key parameters—such as total vascular volume, average vessel diameter, total vessel length, and average vessel curvature—from patient data on hepatic veins, portal veins, the aorta, and inferior vena cava to construct geometric models of vascular networks. Clinical tests demonstrated good repeatability of this method, with intragroup correlation coefficients ranging from 0.81 to 1.00 [128]. Similarly, Takahashi et al. used ML to classify the images

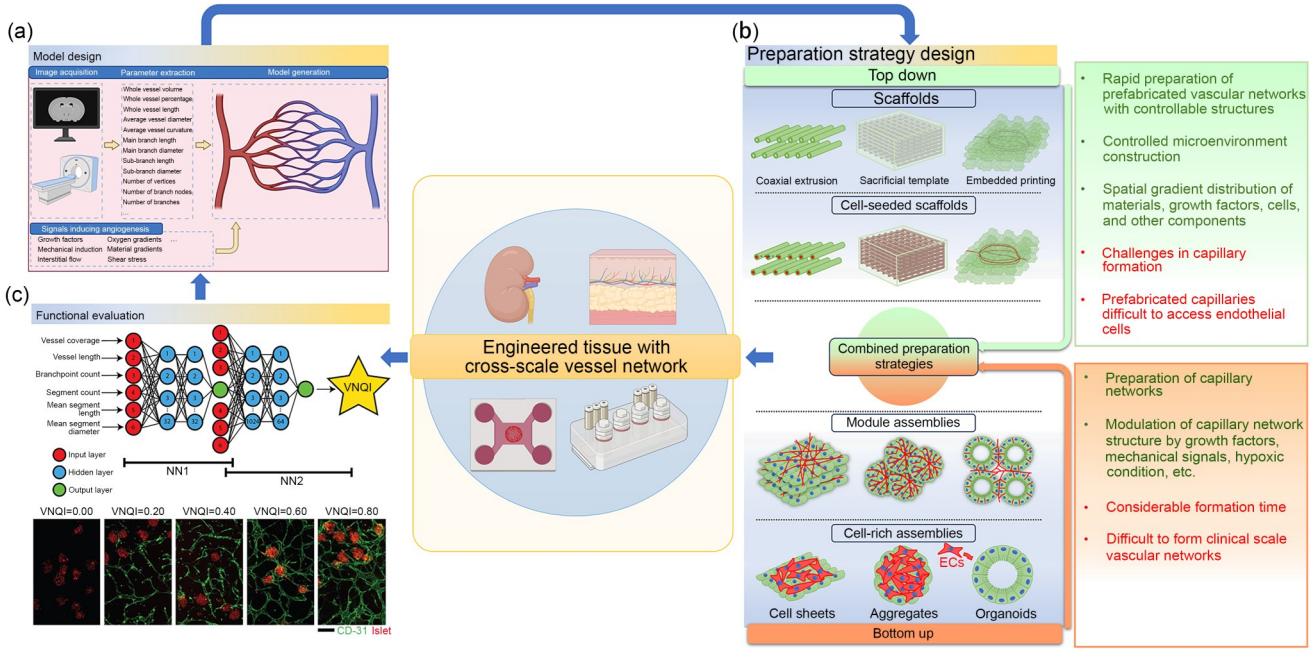


Fig. 4 AI-enabled vascularized structure preparation. (a) Design of vessel network morphology and spatiotemporal distribution of signals to guide vascularization based on AI technology. Created with BioRender.com. (b) Design of cross-scale vascular network construction strategies. Created with BioRender.com. (c) Prediction of oxygen delivery performance in vascular networks based on neural network algorithms (reproduced from [142], Copyright 2023, with permission from the authors, licensed under CC BY). VNQI: vascular network quality index

of organs. By combining topological data analysis with non-homogeneous Poisson process (NHPP) methods, they extracted high-resolution 3D geometric features of whole-organ vascular networks in mice [129].

At the bottom-up level, AI can also play an active role in generating capillary networks between printed channels in a controlled manner. Current research indicates that vascular endothelial growth factor (VEGF) significantly influences endothelial cell behavior. Endothelial cell filopodia preferentially extend toward increasing VEGF gradients, forming vascular sprouts, whereas negative gradients lead to sheet-like migration resembling vascular dilation [130]. Hence, guiding directional vascular growth through the spatiotemporal distribution of VEGF is a crucial method for constructing controlled capillary networks [131]. Although there has been no report that AI regulates VEGF distribution to control angiogenesis, it has been applied in the design of drug delivery systems in the biomedical field. For instance, Nemati et al. used inputs such as drug loading, pore-forming agent type, and concentration to predict the dexamethasone release curve from porous carriers [132]. Xu et al. synthesized 126 hydrogels with various compositional ratios using high-throughput robotics, characterized their swelling, mechanical properties, degradation rates, transparency, and protein release profiles, and used dynamic regression models and partial least squares regression to predict hydrogel compositions with specific protein release profiles [133].

The oxygen concentration gradient also plays a role in directing capillary growth, because hypoxic conditions reduce endothelial cell contact, promoting cell migration and vascular sprouting. Tronolone et al. developed regression models of vascular network morphology and oxygen delivery function using ML. They evaluated oxygen delivery capability within vascular networks in microfluidic chips using six metrics—vascular coverage, length, number of branches, number of segments, average segment length, and average segment diameter—as regression inputs. Their study found that vascular coverage showed the highest correlation with oxygen delivery capability, and combining other metrics improved prediction accuracy. Among regression models, random forests demonstrated the highest accuracy in predicting oxygen delivery capability [134].

The mechanical properties of the ECM are crucial factors that affect and regulate cell migration and vascular sprouting [135]. Recent advancements in bioadditive manufacturing technology, such as adjusting crosslinking density [136] and using multimaterial composite printing [137, 138], have enabled the preliminary development of gradient mechanical structures. AI technology provides a more efficient solution for selecting external matrix materials and structural preparation. AI can optimize printing model designs to achieve the spatial distribution of material gradients, facilitating the development of controlled microvascular networks at specific locations. AI can also determine the printable range of materials, optimizing material design through

methods such as Bayesian analysis, decision trees, and random forests. AI can also be used in the optimized design of printing systems. For instance, AI can optimize system design in multimaterial composite extrusion printing by reducing the need for experimental tests and addressing issues such as rapid material switching, feed rate control, and compatibility with different rheological properties and channel resistances.

Shear stress within blood vessels promotes the formation of endothelial cell adhesion plaques and improves cell migration along the flow direction [139], thereby accelerating capillary channel growth and extensive vascular network formation [131]. Currently, computational fluid dynamics (CFD) software can simulate fluid shear stress throughout the designed vascular networks using the Navier–Stokes equations. Nevertheless, fluid calculations in complex channel networks are challenging and time-consuming, limiting further biomedical applications. AI provides a promising solution to this problem. Kochkov et al. developed a numerical solver using end-to-end deep learning methods. By replacing lost variables affected by lower resolution with discrete equation-based pointwise accurate solutions on unsolved grids, they achieved comparable accuracy with coarser grid simulations, achieving a 40- to 80-fold increase in computational speed [140]. Liang et al. trained deep neural networks using CFD-simulated hemodynamic data to estimate intravascular pressure and flow velocity, achieving hemodynamic distribution predictions within 1 s with an average error <2% [141].

In addition, AI technologies provide robust support for accurately and rapidly evaluating vascularization quality and functionality, optimizing vascular network design, and improving the controllability and reproducibility of vascularized tissue and organ constructs. These advancements are essential for clinical translation and high-throughput in vitro drug testing and pathological studies. AI-driven approaches have already been applied to optimize vascular system models within the body. For instance, Tronolone et al. developed a neural network chain algorithm trained with indicators from vascularized microphysiological systems, effectively predicting the effects of matrix characteristics, cell density, types, and growth factors on vascular network oxygen transport, aiding in vascular network design and optimization within tissues (Fig. 4c) [142]. Furthermore, Lee et al. used an improved graph convolutional network (GCN) to analyze vasculature morphologies in microfluidic chips, describing vascular network structures through mesoskeleton extraction and segmenting skeletons into components using GCNs. This method accurately quantified the changes in vascular morphology [143].

Integrating top-down and bottom-up strategies provides feasible technological solutions for constructing hierarchical, multiscale vascular networks. However, linking vascular networks from top-down construction with those from bottom-up development to achieve controllable morphology and density remains a challenge. AI can predict conditions for vascular network formation, model design, top-down process selection, and printing path planning, simultaneously providing suitable component gradients for bottom-up methods, promoting the development of controlled capillary networks. Moreover, AI can evaluate the functionality of formed vascular networks, refine model designs, and adjust printing strategies. Overall, AI technology promises to improve the controllability and reproducibility of biomimetic vascularized tissues and organ constructs, enabling the advancement of tissue constructs with cross-scale vessel networks in clinical applications and in vitro high-throughput drug testing and pathological research.

5.2 AI applications in constructing physicochemical cues

Natural tissue organs, such as the heart, muscles, and blood vessels, possess unique anisotropic structures and complex internal components [144]. These physicochemical elements guide cells in forming orderly geometric structures in vivo and interact with the surrounding matrix to perform specific tissue functions, making the construction of such cues critical in fabricating in vitro organ models [145]. Currently, bioprinting involves the construction of both static [145–147] and dynamic cues [148, 149], including tissue-specific microstructures and biochemical components (Fig. 5a).

The biochemical cues within structures fabricated through bioprinting play a vital role in the growth and maturation of tissues. Freeman et al. demonstrated that creating gradients of bone morphogenetic protein-2 (BMP-2) and VEGF, both inside and outside structures, significantly improves angiogenesis and new bone formation. The timing and gradient of growth factor release can critically influence tissue growth, with inappropriate release rates and concentrations potentially weakening or negating their stimulatory effects [150]. Kilian et al. proposed a method for constructing osteochondral substitutes using coaxial printing, enabling the localized delivery of multiple factors and cells. By designing the core–shell layer's loaded factors and cell types, this method addresses the distinct growth requirements of cartilage and bone, with the release rate of factors controlled by the Laponite concentration in the core layer material. Their experimental results demonstrated that this method could induce directional differentiation of cells in different regions simultaneously while minimizing the impact of factors on cells in other areas [151]. These findings emphasize the importance of biochemical cue gradients and their spatial distribution in influencing cellular and tissue behavior.

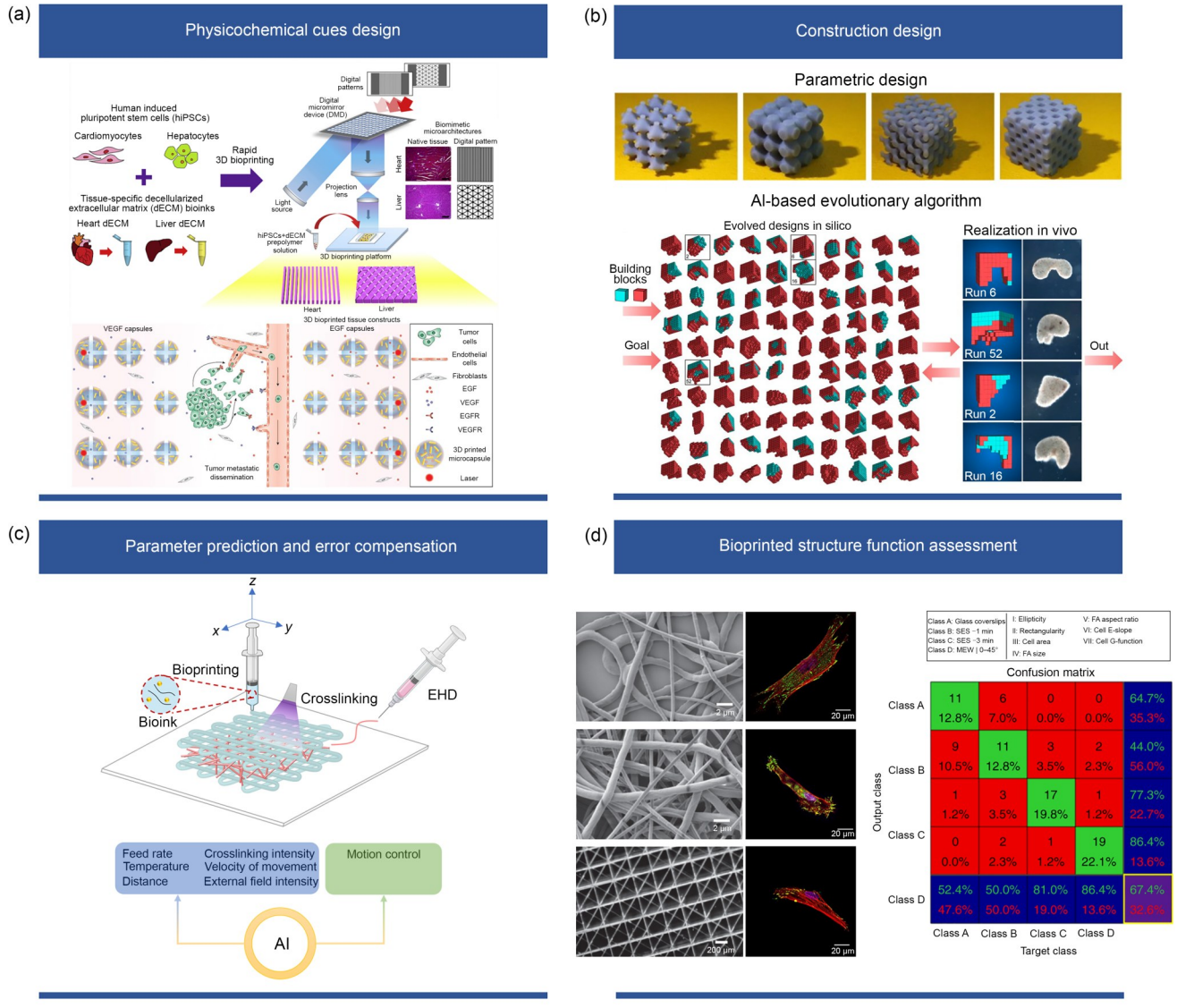


Fig. 5 Possible applications of AI in constructing physicochemical cues in artificial tissues and organs. (a) Physicochemical cues designed to guide cell behaviors (reproduced from [145] (Copyright 2018, with permission from Elsevier Ltd.) and [149] (Copyright 2019, with permission from WILEY-VCH Verlag GmbH & Co. KGaA, Weinheim)). (b) AI-based design methods for modeling structures with macrostructure and microstructure features (reproduced from [155], Copyright 2021, with permission from Zhejiang University Press). (c) AI-assisted parameter prediction and error compensation. Created with BioRender.com. (d) AI evaluation of the impact of substrate size and porous microstructure on cell behavior (reproduced from [158], Copyright 2019, with permission from the authors, licensed under CC BY 4.0)

Bioprinting provides an excellent platform for the precise, controllable, and reproducible arrangement of biochemical cues within complex tissue structures. Nevertheless, embedded drugs and factors can face challenges such as rapid clearance, degradation, and inappropriate release rates, which can undermine their effectiveness [152]. Using delivery carriers such as exosomes, liposomes, and polymers can effectively address these issues. AI can analyze the compatibility of different carriers with their payloads, predict release rates, and synchronize them with cell proliferation and migration behaviors, thereby achieving controlled tissue growth. Furthermore, the material properties and structural characteristics directly affect the diffusion of embedded components [153, 154]. AI can predict the diffusion performance of components in specific materials and structures, allowing for the incorporation of specific diffusion pathways in model designs to create gradient distributions. AI research on the dynamic behavior of biochemical cue carriers under various material component ratios and active–passive conditions is crucial. The complexity of multi-physical fields and fluid–solid interactions increases the difficulty of analyzing and predicting the dynamic behaviors of biochemical cue carriers, exponentially increasing the variables and coupled mechanisms involved. Using

AI for design optimization can significantly reduce the required testing time and costs, thereby improving the efficiency of developing functional tissue-engineered constructs.

Microstructural cues within biological organisms significantly influence the behavior of cells and tissues. Current fabrication technologies, such as multiphoton fabrication and EHD printing, provide micron- and submicron-level precision but struggle to efficiently produce the centimeter-scale 3D structures required for clinical applications. Although extrusion printing can create larger structures, its precision is typically >100 μm, which is inadequate for some internal microstructures. An effective solution is integrating multiple fabrication techniques to achieve controllable cross-scale structure assembly. However, manufacturing-induced structural size errors can affect the efficacy of physicochemical cues or even eliminate their benefits. For instance, in fused deposition modeling (FDM) and electrospinning, nozzle temperature, movement speed, and platform distance critically affect the interfacial structures. Inappropriate parameters can weaken interfacial bonding or erase fiber microstructures. Combining photolithography and EHD writing requires optimizing the structure to reduce light attenuation due to the opacity of electrohydrodynamically written structures. These issues reveal that integrating multi-fabrication techniques introduces numerous variables from multi-physical fields and fluid–solid coupling effects, thereby increasing the complexity. AI can optimize structural designs and process parameters tailored to composite fabrication structures, reducing test time and costs, as well as providing real-time correction of print errors, thereby achieving superior manufacturing precision and quality (Fig. 5c).

AI can significantly augment the understanding and optimization of physicochemical cues through spatial and temporal distribution and dynamic change analysis. This enables better design optimization and real-time monitoring and adjustment during the manufacturing process of artificial tissue organs. For instance, in the formation of biostructures, the surface and 3D morphology of matrix materials, as well as the geometry and size of pores, influence cellular behavior through contact guidance, cytoskeletal reorganization, and mechanotransduction. These complex physical cues present challenges in the model design using traditional computer-aided design (CAD) methods. To address these challenges, some researchers have integrated AI with CAD design methods. For instance, Wang et al. proposed using parametric design derived from CAD for the macro-design of models when using evolutionary algorithms for modeling local models and microstructures. This approach not only reduces the design costs but also minimizes the high computational demands solely on AI (Fig. 5b) [155].

AI can also be used to detect the effects of physicochemical cues on cellular behavior. Beyond functional predictions, AI can also monitor the induction effects of biochemical cues on cells in real time. For instance, Choi et al. developed a deep learning-based cell nucleus segmentation and image skeletonization algorithm that uses 16 metrics, including the length, number, and distribution of nuclei, to quantitatively evaluate angiogenesis responses under growth factor gradients [156]. Coupled with active physicochemical cues, this system can adjust tissue growth states online, providing a solid foundation for cultivating organ-on-chips with physiological and pathological characteristics or for creating tissue repair constructs and substitutes. Park et al. used a deep learning-based method to analyze the migration speed, travel distance, and orientation of L929 and HT22 cells on periodically nano-wrinkled surfaces by detecting and classifying cell boundaries, elongation rates, and directions. This approach helps determine the impact of the wrinkle geometric characteristics on cellular behavior [157]. Tourlomousis et al. investigated the effects of melt electrospinning writing fibers on cell morphology and focal adhesions using ML. In their study, fibroblasts served as model cells, and they used confocal fluorescence microscopy combined with automated single-cell bioimaging data analysis to quantify cells and their adhesions for model training. This technology revealed that substrate size and porous microstructures significantly influence the cell morphology, producing more uniform cell shapes than those produced using nonwoven fiber substrates (Fig. 5d) [158]. This method helps optimize the structure and spatial distribution of physicochemical cues during the model design phase.

The effectiveness of physicochemical cues is closely related to their topological structure, scale, concentration, and gradient. Integrating the design of these cues into bioprinting and constructing biological structures with macroscale and microscale features through multi-technique composite additive manufacturing significantly expand the capabilities of bioprinting, especially in the fabrication of complex tissues and organs. Nevertheless, incorporating various physicochemical cues, dynamically coordinating multi-cue interactions, and managing the complexity of multi-technique composites drastically increase the number of variables requiring analysis and optimization. These multifactorial coupling problems present significant challenges to traditional, manually driven experimental methods. AI technology provides solutions by improving fabrication precision, optimizing interface bonding, and improving the rational design and spatiotemporal distribution of physicochemical cues. Through real-time efficacy feedback monitoring, AI can achieve closed-loop iteration of the manufacturing process and products, thereby increasing the reliability and reproducibility of physicochemical cues, simultaneously constructing complex tissues and organs and in vitro models.

5.3 AI-enabled in situ bioprinting

In tissue repair, additive bioprinting is playing an increasingly vital role, particularly in in situ molding repair, which is gaining attention due to several advantages as follows: (1) better conformity to the complex contours of defective tissue surfaces, (2) improved alignment with the edges of damaged organs, (3) elimination of the need for an implantation process, thereby avoiding issues such as swelling and shrinkage during ex vivo preparation, and (4) reduced mechanical performance requirements for implants during ex vivo preparation [159, 160]. Unlike conventional bioprinting platforms, the forming platform in in situ bioprinting is the damaged tissue or organ itself, which features uneven contours and a complex, dynamic environment. This requires careful consideration of model design, material selection, process parameter optimization, and process supervision to ensure controlled and reliable formation that fulfills the intended functions. These demands require large-scale, high-speed data processing. Moreover, unlike conventional 3D printing, in situ printing involves the direct deposition of materials on the surface or inside tissues. If a print fails, the deposited structure must be corrected or removed rather than simply discarded, resulting in a lower tolerance for errors than standard bioprinting. Consequently, in situ molding places higher demands on process reliability, rendering the integration of AI a promising solution for overcoming these challenges. Current research in this field primarily focuses on injury site identification, geometric data acquisition, model construction, and in-process parameter compensation.

A crucial early step in in situ bioprinting for disease treatment is identifying the wound site. Traditional manual methods for image processing require significant labor and expertise, which is time-consuming and susceptible to errors. AI technology can extract extensive information from images, identifying subtle features that the human eye might miss. This improves disease recognition, thereby increasing accuracy and simultaneously reducing time and costs [161, 162]. For instance, Wang et al. proposed a wound area measurement method based on the MobileNetsV2 neural network. By training the model with 1109 images of foot wounds from 889 patients, they achieved quantitative measurement of the wound area. Their results demonstrated precision, recall, and Dice scores of 91.01%, 89.97%, and 90.47%, respectively, exceeding those obtained from the commonly used FCN-VGG-16 architecture for wound image measurement [163]. Curti et al. trained a regression model using a dataset of 612 wound images for wound segmentation and extraction of quantitative information, such as the color and morphology of the wound and surrounding areas (photographic wound assessment tool (PWAT)). The PWAT predictions demonstrated a strong correlation with clinical PWAT values [164]. Chen et al. developed a portable robotic device that integrates AI with near-infrared and ultrasound imaging technologies to acquire vascular images. These images serve as a training set for a deep convolutional network, enabling the identification of vascular positions within surrounding tissues and dynamically tracking and compensating for position changes caused by pulsation. Their test results confirmed that the system could accurately guide needles and catheters into submillimeter-sized blood vessels (Fig. 6a) [165].

In in situ bioprinting, after identifying the tissue to be repaired, the process typically involves 3D reconstruction, repair, and optimization to convert the data into 3D model files commonly used in bioadditive technology. For instance, Albanna et al. used a 3D laser scanner to capture wound data using markers placed around the wound as reference points, generated wound models using Geomagic Studio, and created the printing path using Artcam [166]. Similarly, Zhao et al. used a structured light scanner to obtain point cloud data of wounds, processed the data using Geomagic Studio, and used Boolean operations to generate models of skin defects [167]. For internal tissue defect repair, micro-CT was used to reconstruct the 3D geometry of liver defects, providing path data for subsequent in situ printing via minimally invasive surgical instruments [168]. In such applications, AI technology can efficiently and accurately model defect areas. For instance, Fuessinger et al. developed a statistical shape model (SSM) using the CT scans of 131 healthy skulls. By matching the SSM to defect areas, they reconstructed unilateral or bilateral skull defect models, reducing errors by 60% compared with those by traditional mirror-based manual reconstruction by surgeons [169]. Moreover, a fully automated 3D skull defect reconstruction method based on a cascaded CNN architecture was developed, achieving an average surface error of 0.59 mm and seamless integration with surrounding tissues without manual cleanup [170]. Some commercial software, such as Mimics, has already integrated AI algorithms to automatically recognize organ contours and internal structures from images, generating high-precision 3D models [161].

Unlike conventional bioprinting, the materials used in in situ bioprinting must consider the wound environment during formation. These materials should rapidly form within the body's environment, which involves considerations of body temperature, moisture, and dynamic conditions, distinct from traditional processes. The preparation must be rapid and simple to minimize treatment time and risk. In addition, material selection must ensure that components, preparation processes, solvents, and crosslinking agents do not harm normal tissues, narrowing the range of applicable materials and forming windows, thereby posing a significant challenge. AI technology can predict the forming windows and biocompatibility of different material

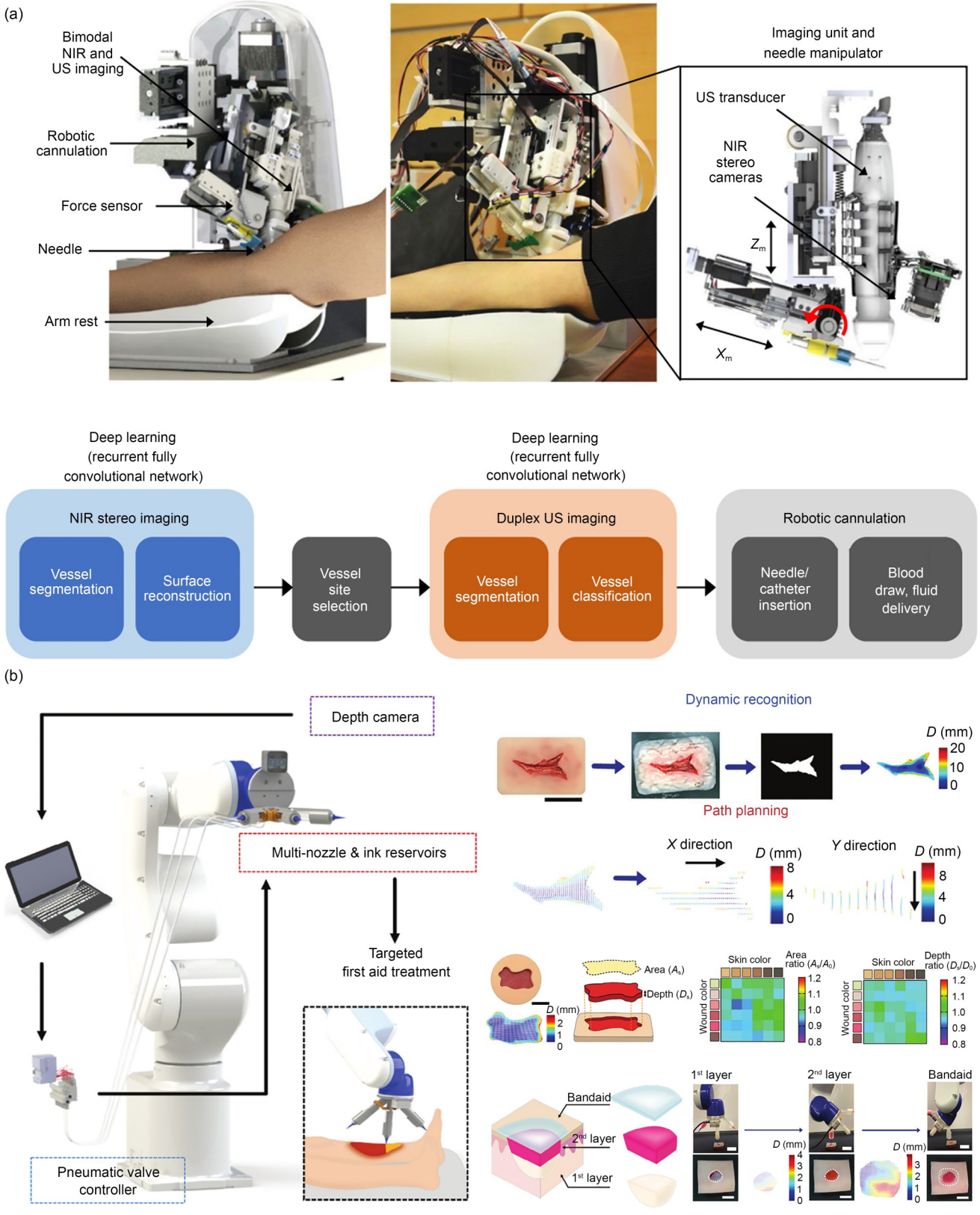


Fig. 6 Application of AI in in situ bioprinting for tissue repair. (a) Combining AI with near-infrared (NIR) and ultrasound (US) imaging technologies to identify the position of blood vessels from surrounding tissues and dynamically track and compensate for positional changes caused by pulsation (reproduced from [165], Copyright 2020, with permission from the authors, under exclusive licence to Springer Nature Limited). (b) AI-based in situ wound-repairing robot (reproduced from [175], Copyright 2024, with permission from Wiley-VCH GmbH)

compositions, facilitating material selection for in situ bioprinting. Moreover, improving in situ forming effects through material structure design is another effective approach. For instance, Xie et al. developed a bioconcrete hydrogel consisting of cell-laden microgels prepared by electrospray and a GelMA gel precursor solution. The former possesses rheological properties similar to those of Bingham fluids and is suitable for complex environments, whereas the latter ensures ink flowability and printability. This bioconcrete resolves the contradiction between mechanical performance and cellular biocompatibility in printed structures [171]. Upon photocrosslinking, strong interfacial bonding forms between the hydrogel and tissue. AI can pre-evaluate material printability, accelerate microunit structure design in the ink, and optimize printing processes and platform design. Sarmadi et al. constructed a model for microparticle extrudability, including parameters such as particle shape, size, concentration, initial distribution, nozzle diameter, and solution viscosity. A trained neural network predicted the performance of particle extrusion, improving the extrusion performance by six times [172].

Compared with the fixed-distance receiving platforms used in traditional bioprinting methods, in situ bioprinting prints components directly on the surface of tissues and organs. This direct approach results in positional deviations between the dynamic, deforming surface of tissues/organs and the preset forming surface, significantly affecting the quality of the formed structures and potentially causing complete failure. This issue can be addressed by implementing dynamic compensation to correct positional changes on the forming surface. Currently, some researchers have integrated dynamic compensation into in situ additive systems. For instance, Zhao et al. used a binocular camera to track wound positions. This method uses a color filter to identify the color of the wound, ultimately determining its contour and centroid coordinates. The binocular camera captures two simultaneous frames to obtain the spatial position of the wound, achieving a positioning error <0.8 mm. By incorporating the detected wound position changes into the preset path, this approach enables extrusion printing on moving surfaces [167]. Zhu et al. used a computer vision-based target tracking method, which tracks the position of the reference markers on the target surface using a camera to estimate the postural information of the target. Combined with point cloud data obtained from a structured light scanner, this information is fed back to the motion controller for compensation, allowing for extrusion printing on moving surfaces with a tracking error <1.5 mm. Nevertheless, the tracking effectiveness is related to the movement speed of the target, with higher speeds reducing the tracking stability that affects the forming outcome [173]. In addition, because human soft tissues are not rigid bodies, it is important to consider the complexities of expansion and contraction. Zhu et al. addressed this problem by optimizing parameters for the prior speed range of the target using AI technology, providing reliable and accurate tracking solutions for complex deforming surfaces and improving target tracking and forming outcomes. This method adopted a two-stage approach to track deformed lung surfaces, combining offline and online stages. Initially, they used a structured light scanner to collect multiple lung point clouds for training sets offline and applied ML to derive a linear shape model of the deforming surface. During online tracking, they used a stereo camera system to track reference markers on the target surface, deriving a deforming surface model from these marker positions, which generates real-time printing paths with temporal characteristics [174]. Furthermore, Jeong et al. proposed an INTIGHT computer recognition system, integrated with a six-degree-of-freedom robotic arm, which can recognize wounds from various angles and accurately allocate bioinks to multiple wounds in different positions using a method that also facilitates the rapid switching and printing of different bioinks across large wound areas, using an extrusion and inkjet multinozzle system (Fig. 6b) [175].

Currently, the application of AI in in situ molding is still in its infancy. Further integration of AI technology into in situ molding techniques is required to advance this technology toward clinical application. This integration is crucial for improving the precision and adaptability of in situ bioprinting methods, potentially transforming the manner through which surgical interventions and tissue repairs are conducted in medical settings.

The intricate heterogeneity of natural tissues, characterized by their complex physicochemical cues and hierarchical, multiscale vascular systems, presents significant challenges in constructing tissue repair structures or drug screening platforms through in vitro bioprinting techniques. The advancement of AI technologies provides promising solutions to these challenges (Fig. 7). AI-assisted model design and material selection optimization, coupled with the prediction of printability, enable precise control over the distribution and density of physicochemical cues to induce cell growth, differentiation, and migration. This approach integrates appropriate material and structural gradients within the design to facilitate the directional release of components, resulting in highly controlled and reproducible tissue growth. By rationalizing the integration of both bottom-up and top-down manufacturing strategies and effectively replacing certain experimental processes, exploring and optimizing parameters for composite-forming techniques, AI-enabled bioprinting will ultimately achieve the efficient fabrication of artificial tissues and organs with both macroscale and microscale characteristics.

Moreover, in situ printing has emerged as a promising research direction in tissue repair, providing advantages in

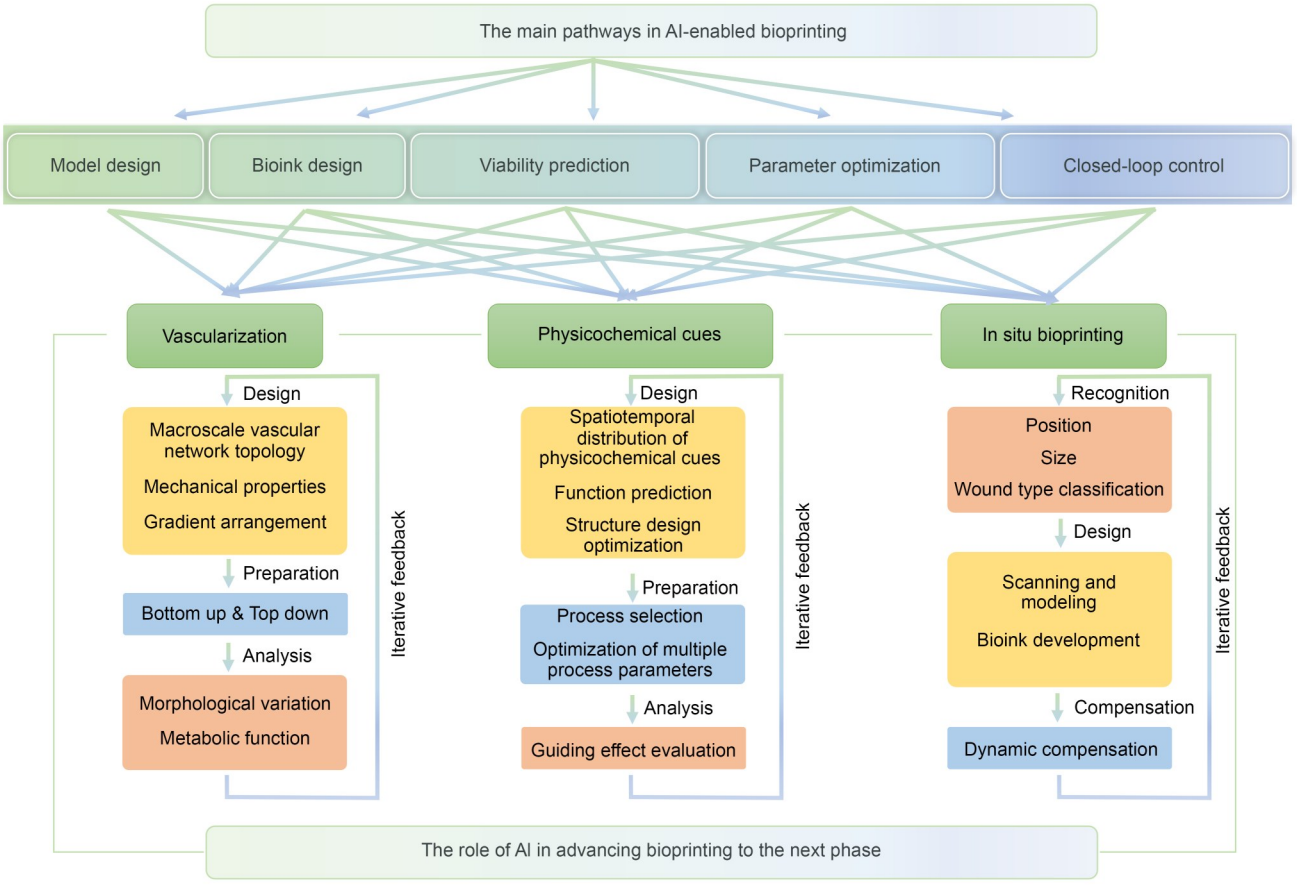


Fig. 7 Role of AI in addressing urgent challenges in bioprinting to advance it to the next phase

conformity and adaptability. The precise fabrication of repair structures directly on wound surfaces remains a critical issue. Currently, AI has shown preliminary applications in wound recognition, modeling, and dynamic surface compensation during printing, thus improving both precision and robustness and simultaneously reducing the time and labor required in the preparatory stages. Despite these advancements, the integration of AI and in situ printing remains in its infancy. Addressing large-surface wounds or performing internal tissue repairs with minimally invasive surgical tools requires further investigation. Furthermore, the fabrication of complex tissue and organ repair structures often requires multiple steps and processes in vitro. The integration of AI to enable precise, editable modeling and in situ formation of these structures, along with improving forming reliability, remains an area for future research.

To summarize, AI technology has made remarkable progress in model design, material selection, process parameter optimization, and closed-loop control of forming processes. However, the combined application of AI and bioprinting is still in its early stages, which is partially due to the lack of relevant training data and the high technical barriers associated with AI technology, indicating the need for interdisciplinary expertise spanning computer science, materials science, mechanical engineering, biology, and medicine. It is also important to further improve our understanding of the complex functions and phenomena within tissue and organ systems. Addressing these challenges is vital for advancing the application of AI in designing and fabricating complex, heterogeneous biological structures.

6 Future perspectives

Further integration of AI and bioprinting technology results in improved design of bionic macrostructures and microenvironments, more convenient material design and selection, more efficient exploration of material printing window and process parameter setting, improved forming accuracy and control, and a higher printing success rate. These benefits will augment the role of bioprinted structures in fields such as tissue engineering, drug screening, and disease research. Nevertheless, creating biological structures with specific functions is only the initial step in the application of bioprinting technology in biomedical research. A crucial area for future development is achieving the rapid and highly reproducible construction of these structures, leveraging the capabilities of AI.

The discovery and development of drugs depend heavily on high-throughput screening methods. However, the use of overly simplistic models, such as 2D culture dishes, often results in outcomes that deviate significantly from real-life scenarios [176]. This limitation has driven the growing interest in bioprinting for generating 3D in vitro tissue and organ models, marking a significant advancement in the manufacturing of artificial tissues. Nonetheless, the current industrial demand for throughput, such as the need for 10,000 drug screenings per day [177], emphasizes that the throughput of bioprinting for drug screening models is still relatively low, thereby limiting its further development and application in this field.

In recent years, researchers have recognized the need for the high-throughput fabrication of in vitro tissue and organ models and have sought to improve the throughput of bioprinting through various methods. For instance, Derman et al. used droplet-based bioprinting to efficiently generate nasal epithelial tissue models, requiring only a fraction of the cell density required by traditional methods (Fig. 8a) [178]. Moreover, Gong et al. used acoustofluidic technology to rapidly deposit cell-laden solutions, forming uniformly sized organ-like structures (Fig. 8b) [179]. In addition, the system developed by Shin et al. efficiently arranges organ precursors in a short time [180], whereas Lawlor et al. used extrusion printing to rapidly place cells with high repeatability in

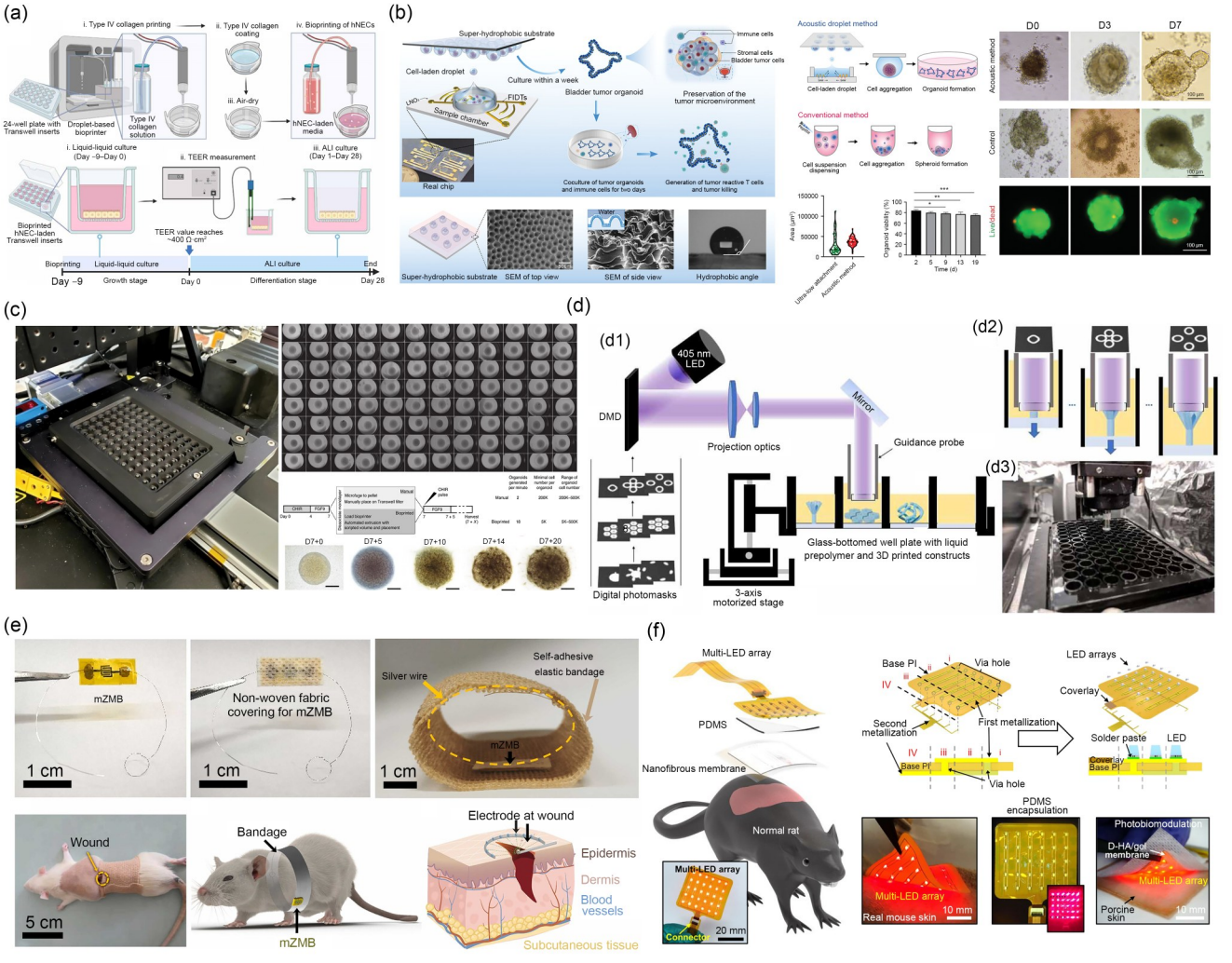


Fig. 8 Prospects for AI-empowered bioprinting of artificial tissues and organs. (a) High-throughput construction of a skin tissue model using droplet-based bioprinting (DBB) technology (reproduced from [178], Copyright 2023, with permission from the authors, licensed under CC BY 4.0). (b) High-throughput organoid preparation by acoustic field printing (reproduced from [179], Copyright 2021, with permission from Wiley-VCH GmbH). (c) High-throughput preparation of kidney organoids based on extrusion printing technology (reproduced from [181], Copyright 2020, with permission from the authors, under exclusive licence to Springer Nature Limited). (d) High-throughput preparation of in vitro models and organoids based on DLP technology (reproduced from [182], Copyright 2021, with permission from IOP Publishing Ltd.). (e) Exogenous electric field promotes cell migration and accelerates wound healing (reproduced from [185], Copyright 2024, with permission from Elsevier Ltd.). (f) Near infrared (NIR) irradiation affects cell migration and proliferation (reproduced from [187], Copyright 2022, with permission from the authors, licensed under CC BY-NC)

organ diameters (Fig. 8c) [181]. Furthermore, DLP technology has demonstrated efficiency and repeatability in preparing in vitro models and organoid structures, particularly in Chen's research, where it not only rapidly constructed samples but also improved the functional characteristics of biological structures (Fig. 8d) [182].

Despite significant progress in the high-throughput preparation of structured organ models and organoids, challenges remain that include not only the technical issues of mimicking natural tissue organs, as discussed in previous sections, but also those related to the success rate, stability, consistency, and repeatability of high-throughput preparations. Such aspects present new challenges for model design, process control, and the prediction and evaluation of sample performance. For instance, variations in matrix material types and component concentrations in different parts of the same organ model complicate the formulation of bioinks, which must consider shear thinning, viscoelasticity, yield stress, and crosslinking methods to ensure reliable molding along with considering the impact of material microproperties on cell behavior [183]. The high costs associated with the use of biological materials and growth factors in post-fabrication cultures also pose significant barriers to the rapid clinical translation of this field. Using AI to replace current labor-intensive and iterative trial-and-error methods could reduce human, time, and material costs. AI can play a vital role in investigating the optimal extracellular matrix materials, growth factor gradients, cell concentrations, and arrangements of different cell types to improve the efficiency of organ preparation. Particularly for patient-specific in vitro models using cells or tissues derived from patients, AI could enable inexpensive, high-throughput construction of personalized and specific organ models, providing technical support for clinical applications.

In constructing tissue constructs, incorporating external environmental information into the bioprinting process allows for the application of mechanical [184], electrical (Fig. 8e) [185], magnetic [186], optical (Fig. 8f) [187], and ultrasonic [74] stimuli, which can regulate the migration, proliferation, and differentiation of tissues. This, in turn, may accelerate the construction speed of biological structures and improve the functional development of organisms and tissue maturity in the high-throughput preparation of bioconstructions. Nevertheless, a single environmental stimulus may not suffice for tissue growth and repair. The synergistic action of various environmental stimuli with the components of the structure may provide a more favorable microenvironment for tissue growth [188]. The coupling effect between different external environmental stimuli and the structure itself on the microenvironment should be further analyzed using AI technology. Based on this analysis, functional prediction and synergistic optimization of environmental stimuli and structural components are potential future directions for AI-empowered bioprinting. Furthermore, the intensity of local environmental stimuli required within tissues and organs varies, and the deviations in the structures or materials produced during the preparation process can result in actual applied stimuli differing from the design. AI technology can provide real-time feedback on the local stimulation conditions at different positions of the bioprinted structures, enabling adjustments and compensation to the external environmental sources, thereby better regulating the cellular microenvironment [189].

Assessing the maturity of cultured tissues allows for the evaluation and optimization of process methods during the early developmental stages of bioprinted structures and helps determine the developmental level of the tissues. This is essential for providing quantitative indicators for the high-throughput cultivation of tissue and organ grafts and in vitro models, as well as for reducing costs through the timely elimination of substandard samples. Manually analyzing cell and tissue behaviors is time-consuming, labor-intensive, and often inconsistent. For instance, Andrion et al. reported only 70% consistency among five pathology experts when evaluating 88 cases of pleural malignant mesothelioma, emphasizing the challenges in evaluating preparation samples under high-throughput conditions [190]. Furthermore, some detection methods can cause irreversible damage to tissue cells, inadvertently increasing the preparation workload. Recently, computer vision technology based on deep learning has achieved capabilities such as monitoring cell viability [191], identifying cell differentiation [192], and tracking and monitoring organoids [193]. Further development of these technologies will enable the high-throughput, non-destructive identification of cell and tissue growth states from the perspective of image recognition. Moreover, applying AI technology to electrochemical analysis and other detection methods of cell tissues or their secretions can provide quantitative feedback for cell and tissue culture, achieving precise control over the cultivation process [194]. In the future, leveraging AI technology to integrate and analyze multiomics data from imaging, proteins, and metabolites, combined with robotic automation platforms [195, 196], is expected to provide robust technical support for the high-throughput preparation of personalized tissue constructs, thereby expanding further applications of bioprinting in medical applications such as translational tissue engineering, drug discovery, and disease model research.

Furthermore, in the field of AI, the integration of various resources is crucial for propelling technological advancement. Software and toolkits such as TensorFlow, PyTorch, and Scikit-learn are commonly used as open-source software for tasks including image recognition, parameter optimization, and ML [197]. These toolkits support a multitude of ML and deep learning algorithms, significantly accelerating

the processes of model training and performance optimization. Moreover, databases for biomaterials and printing parameters, such as MaterialHub and BioPrintDB, provide a data-driven basis for material selection and parameter optimization in the field of bioprinting [198, 199]. These databases meticulously document the physicochemical properties and biocompatibility parameters of materials, which are essential for improving printing accuracy and cell viability. In addition, biomedical datasets, such as ImageNet and MedMNIST, play a significant role in training image recognition algorithms and validating the efficacy of AI models [200, 201]. These standardized datasets not only provide a common benchmark for researchers but also facilitate the comparison and refinement of algorithms. Beyond these general datasets, there are specific cell image databases and 3D tissue image datasets for drug screening, which are vital for achieving automated analysis and high-throughput applications. By comprehensively leveraging these resources, the application of AI in the biomedical field will become more precise and efficient.

The complexity of the biological structure preparation also poses higher requirements for AI technology to better adapt to the requirements of bioprinting technology. Although the application of AI in bioprinting holds vast potential, there are inherent risks and challenges. The primary challenge that AI faces in bioprinting applications is the complexity and uncertainty inherent in biomedical systems. These systems are nonlinear and heterogeneous, with parameters that are highly complex and uncertain, including gene expression levels, protein–protein interactions, and metabolic levels, which are difficult to predict and are often influenced by a multitude of factors, several of which are unknown. Moreover, physiological parameters are not static; they are dynamic and change over time in response to environmental conditions and due to shifts in the internal state of the organism, further adding to the uncertainty of physiological parameters and functions. Studies have demonstrated that when analyzing complex systems with uncertain distribution functions, such as quantitative physiology, morphogenesis, and gene regulation, AI models may not yield significant benefits. Traditional statistical models, such as logistic regression, can cause biased estimations of treatment effects, especially in complex data that include nonlinear and nonadditive terms [202]. This is because parametric models require assumptions regarding the functional form and distribution of covariates [203], which is particularly pronounced in biomedical systems with multiple covariates [204]. In addition, although some studies have achieved success in contexts where the functional relationship of parameters is clearly defined, such as Catalanotti using bootstrap and Bayesian uncertainty quantification to address high-dimensional challenges in composite material damage modeling [205], the application of mathematics in the biomedical field is often questioned due to irreversible processes and black box models in biomedicine. The complexity of biomedicine, with its algorithms and information processing differing from simple laws, increases the difficulty of mathematical modeling and inevitably introduces errors [206]. Therefore, in the field of bioprinting, the theoretical foundation of AI models remains insufficient, and the application of existing engineering models such as finite element models [207], phase space methods [208], and minimax methods [209] is limited. Therefore, it is believed that this field requires more theoretical support and innovative methods to ensure that the application of AI in bioprinting is safe and effective.

7 Summary

Bioprinting provides precise spatial control over the distribution of cells and matrix components, providing an effective method for creating complex in vitro organ models and repairing intricate tissue defects. Nevertheless, the complexity of tissue organs poses significant challenges to bioprinting technologies. Several research initiatives have integrated AI with bioprinting to address the interconnectedness of design models, matrix materials, and forming processes. These efforts have focused on improving technological capabilities through multiobjective optimization, performance prediction, and intelligent closed-loop control during the manufacturing process. AI has helped achieve promising developments in innovative applications in constructing artificial tissue organs. These achievements emphasize the feasibility and importance of combining AI with bioprinting technologies. Observing the current research landscape and technological advances, the construction of in vitro organ models with cross-scale vascular networks and controllable spatiotemporal distribution of physicochemical cues, as well as the in situ repair of tissue and organ injuries through in situ bioprinting, is becoming the focus of the development of bioprinting technology, which is not only of considerable potential but also in great demand for innovative applications of AI. It is anticipated that the deep fusion of AI technology with top-down and bottom-up construction strategies, composite bioprinting and in situ printing technologies, and other manufacturing methods can elevate bioprinting technology to an entirely new phase, realizing the further application progress of bioprinting in human health sciences.

Acknowledgements This work was financially supported by the National Natural Science Foundation of China (Nos. 32471396, 82230071, 82172098, 82201716, and 61973206), the National Key R&D Program of China (No. 2023YFC2411303), the Integrated Project of Major Research Plan of the National Natural Science Foundation of

China (No. 92249303), the Shanghai Committee of Science and Technology (No. 23141900600, Laboratory Animal Research Project), the Shanghai Clinical Research Plan of SHDC2023CRT01, the Young Elite Scientist Sponsorship Program by the China Association for Science and Technology (No. YESS20230049), and the Baoshan District Health Commission Talents (Excellent Academic Leaders) Program (No. BSWSYX-2024-05). Figures 1 and 2, and part of Figs. 3–5 were generated using BioRender.

Author contributions LB and YZ investigated and summarized the literature, and wrote the original manuscript. SCW conducted deep review and editing. JLL edited the images. YYL and JCS helped revise the paper, supervised the work, and applied for funds. All authors have read and approved this manuscript for publication.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human or animal subjects performed by any of the authors.

References

1. Black CK, Termanini KM, Aguirre O et al (2018) Solid organ transplantation in the 21st century. Ann Transl Med 6(20):409. https://doi.org/10.21037/atm.2018.09.68
2. Wang BR, Zhou AW, Pan Q et al (2024) Adenosinergic metabolism pathway: an emerging target for improving outcomes of solid organ transplantation. Transl Res 263:93–101. https://doi.org/10.1016/j.trsl.2023.09.002
3. Ambhorkar P, Rakin RH, Wang ZJ et al (2020) Biofabrication strategies for engineering heterogeneous artificial tissues. Addit Manuf 36:101459. https://doi.org/10.1016/j.addma.2020.101459
4. Huang GB, Zhao YY, Chen D et al (2024) Applications, advancements, and challenges of 3D bioprinting in organ transplantation. Biomater Sci 12(6):1425–1448. https://doi.org/10.1039/d3bm01934a
5. Matai I, Kaur G, Seyedsalehi A et al (2020) Progress in 3D bioprinting technology for tissue/organ regenerative engineering. Biomaterials 226:119536. https://doi.org/10.1016/j.biomaterials.2019.119536
6. Jubelin C, Muñoz-Garcia J, Griscom L et al (2022) Three-dimensional in vitro culture models in oncology research. Cell Biosci 12(1):155. https://doi.org/10.1186/s13578-022-00887-3
7. Rodrigues J, Heinrich MA, Teixeira LM et al (2021) 3D in vitro model revolution: unveiling tumor-stroma interactions. Trends Cancer 7(3):249–264. https://doi.org/10.1016/j.trecan.2020.10.009
8. Zhang YS, Alvarez MM, de Santiago GT (2023) Placing biofabrication into the context of human disease modeling. Biofabrication 15(3):030402. https://doi.org/10.1088/1758-5090/acd27b
9. Murphy SV, Atala A (2014) 3D bioprinting of tissues and organs. Nat Biotechnol 32(8):773–785. https://doi.org/10.1038/nbt.2958
10. Shahrezaie M, Zamanian A, Sahranavard M et al (2024) A critical review on the 3D bioprinting in large bone defects regeneration. Bioprinting 37:e00327. https://doi.org/10.1016/j.bprint.2023.e00327
11. Wolf KJ, Weiss JD, Uzel SGM et al (2022) Biomanufacturing human tissues via organ building blocks. Cell Stem Cell 29(5):667–677. https://doi.org/10.1016/j.stem.2022.04.012
12. Ma Y, Deng B, He RB et al (2024) Advancements of 3D bioprinting in regenerative medicine: exploring cell sources for organ fabrication. Heliyon 10(3):e24593. https://doi.org/10.1016/j.heliyon.2024.e24593
13. An C, Zhang S, Xu J et al (2024) The microparticulate inks for bioprinting applications. Mater Today Bio 24:100930. https://doi.org/10.1016/j.mtbio.2023.100930
14. Mekhileri NV, Lim KS, Brown GJ et al (2018) Automated 3D bioassembly of micro-tissues for biofabrication of hybrid tissue engineered constructs. Biofabrication 10(2):024103. https://doi.org/10.1088/1758-5090/aa9ef1
15. Scalzone A, Imparato G, Urciuolo F et al (2024) Bioprinting of human dermal microtissues precursors as building blocks for endogenous in vitro connective tissue manufacturing. Biofabrication 16:035009. https://doi.org/10.1088/1758-5090/ad3aa5
16. Levato R, Jungst T, Scheuring RG et al (2020) From shape to function: the next step in bioprinting. Adv Mater 32(12):e1906423. https://doi.org/10.1002/adma.201906423
17. Chae S, Cho DW (2023) Biomaterial-based 3D bioprinting strategy for orthopedic tissue engineering. Acta Biomater 156:4–20. https://doi.org/10.1016/j.actbio.2022.08.004
18. Bonatti AF, Vozzi G, Chua C et al (2022) A deep learning quality control loop of the extrusion-based bioprinting process. Int J Bioprint 8(4):620. http://doi.org/10.18063/ijb.v8i4.620
19. Bai L, Liu X, Su J (2023) ChatGPT: the cognitive effects on learning and memory. Brain-X 1:e30. https://doi.org/10.1002/brx2.30
20. Abramson J, Adler J, Dunger J et al (2024) Accurate structure prediction of biomolecular interactions with AlphaFold 3. Nature 630(8016):493–500. https://doi.org/10.1038/s41586-024-07487-w
21. Datta P, Barui A, Wu Y et al (2018) Essential steps in bioprinting: from pre- to post-bioprinting. Biotechnol Adv 36(5):1481–1504. https://doi.org/10.1016/j.biotechadv.2018.06.003
22. Dutta A, Singh M, Kumar K et al (2023) Accuracy of 3D printed spine models for pre-surgical planning of complex adolescent idiopathic scoliosis (AIS) in spinal surgeries: a case series. Ann 3D Print Med 11:100117. https://doi.org/10.1016/j.stlm.2023.100117
23. Dhakshyani R, Nukman Y, Osman NAA (2010) Rapid prototyping models for dysplastic hip surgeries in Malaysia. Eur J Orthop Surg Tr 22:41–46. https://doi.org/10.1007/s00590-011-0778-x
24. Lindquist EM, Gosnell JM, Khan SK et al (2021) 3D printing in cardiology: a review of applications and roles for advanced cardiac imaging. Ann 3D Print Med 4:100034. https://doi.org/10.1016/j.stlm.2021.100034
25. Vukicevic M, Mosadegh B, Min JK et al (2017) Cardiac 3D printing and its future directions. JACC Cardiovasc Imag 10(2):171–184. https://doi.org/10.1016/j.jcmg.2016.12.001
26. Lan Q, Zhu Q, Xu L et al (2020) Application of 3D-printed craniocerebral model in simulated surgery for complex intracranial lesions. World Neurosurg 134:e761–e770. https://doi.org/10.1016/j.wneu.2019.10.191
27. Wu YH, Liu JY, Kang L et al (2023) An overview of 3D printed

metal implants in orthopedic applications: present and future perspectives. Heliyon 9(7):e17718. https://doi.org/10.1016/j.heliyon.2023.e17718
28. Nouri A, Shirvan AR, Li YC et al (2021) Additive manufacturing of metallic and polymeric load-bearing biomaterials using laser powder bed fusion: a review. J Mater Sci Technol 94(35): 196–215. https://doi.org/10.1016/j.jmst.2021.03.058
29. Zhang BQ, Wang L, Song P et al (2021) 3D printed bone tissue regenerative PLA/HA scaffolds with comprehensive performance optimizations. Mater Des 201:109490. https://doi.org/10.1016/j.matdes.2021.109490
30. Wang WZ, Zhang BQ, Li MX et al (2021) 3D printing of PLA/n-HA composite scaffolds with customized mechanical properties and biological functions for bone tissue engineering. Compos Part B Eng 224:109192. https://doi.org/10.1016/j.compositesb.2021.109192
31. Shen YH, Tang CJ, Sun BB et al (2022) 3D printed personalized, heparinized and biodegradable coronary artery stents for rabbit abdominal aorta implantation. Chem Eng J 450:138202. https://doi.org/10.1016/j.cej.2022.138202
32. Yang C, Ma HS, Wang ZY et al (2021) 3D printed wesselsite nanosheets functionalized scaffold facilitates NIR-II photothermal therapy and vascularized bone regeneration. Adv Sci 8(20): e2100894. https://doi.org/10.1002/advs.202100894
33. Wang LY, Pang YY, Tang YJ et al (2022) A biomimetic piezoelectric scaffold with sustained Mg^{2+} release promotes neurogenic and angiogenic differentiation for enhanced bone regeneration. Bioact Mater 25:399–414. https://doi.org/10.1016/j.bioactmat.2022.11.004
34. Sadeghianmaryan A, Naghieh S, Yazdanpanah Z et al (2022) Fabrication of chitosan/alginate/hydroxyapatite hybrid scaffolds using 3D printing and impregnating techniques for potential cartilage regeneration. Int J Biol Macromol 204:62–75. https://doi.org/10.1016/j.ijbiomac.2022.01.201
35. Putra NE, Leeflang MA, Klimopoulou M et al (2023) Extrusion-based 3D printing of biodegradable, osteogenic, paramagnetic, and porous FeMn-akermanite bone substitutes. Acta Biomater 162:182–198. https://doi.org/10.1016/j.actbio.2023.03.033
36. Yang JR, Chen ZG, Gao CJ et al (2024) A mechanical-assisted post-bioprinting strategy for challenging bone defects repair. Nat Commun 15:3565. https://doi.org/10.1038/s41467-024-48023-8
37. Li S, Liu YY, Liu LJ et al (2016) A versatile method for fabricating tissue engineering scaffolds with a three-dimensional channel for prevasculature networks. ACS Appl Mater Interfaces 8(38):25096–25103. https://doi.org/10.1021/acsami.6b07725
38. Camarero-Espinosa S, Moroni L (2021) Janus 3D printed dynamic scaffolds for nanovibration-driven bone regeneration. Nat Commun 12(1):1031. https://doi.org/10.1038/s41467-021-21325-x
39. Tang H, Sun W, Liu X et al (2023) A bioengineered trachea-like structure improves survival in a rabbit tracheal defect model. Sci Transl Med 15(714):eabo4272. https://doi.org/10.1126/scitranslmed.abo4272
40. Jungst T, Pennings I, Schmitz M et al (2019) Heterotypic scaffold design orchestrates primary cell organization and phenotypes in cocultured small diameter vascular grafts. Adv Funct Mater 29(43):1905987. https://doi.org/10.1002/adfm.201905987
41. Kim M, Yeo M, Kim M et al (2018) Biomimetic cellulose/calcium-deficient-hydroxyapatite composite scaffolds fabricated using an electric field for bone tissue engineering. RSC Adv 8(37):20637–20647. https://doi.org/10.1039/c8ra03657h
42. Smoak MM, Hogan KJ, Jane Grande-Allen K et al (2021) Bioinspired electrospun dECM scaffolds guide cell growth and control the formation of myotubes. Sci Adv 7(20):eabg4123. https://doi.org/10.1126/sciadv.abg4123
43. Fang YC, Wang CJ, Liu ZB et al (2023) 3D printed conductive multiscale nerve guidance conduit with hierarchical fibers for peripheral nerve regeneration. Adv Sci 10(12):e2205744. https://doi.org/10.1002/advs.202205744
44. Nie Y, Chen G, Peng HB et al (2021) In vitro and 48 weeks in vivo performances of 3D printed porous Fe-30Mn biodegradable scaffolds. Acta Biomater 121:724–740. https://doi.org/10.1016/j.actbio.2020.12.028
45. Shuai C, Shi XX, Yang F et al (2023) Oxygen vacancy boosting Fenton reaction in bone scaffold towards fighting bacterial infection. Int J Extreme Manuf 6:015101. https://doi.org/10.1088/2631-7990/ad01fd
46. Carluccio D, Xu C, Venezuela J et al (2020) Additively manufactured iron-manganese for biodegradable porous load-bearing bone scaffold applications. Acta Biomater 103:346–360. https://doi.org/10.1016/j.actbio.2019.12.018
47. Shuai CJ, Zan J, Deng F et al (2021) Core–shell-structured ZIF-8@PDA-HA with controllable zinc ion release and superior bioactivity for improving a poly-L-lactic acid scaffold. Acs Sustain Chem Eng 9(4):1814–1825. https://doi.org/10.1021/acssuschemeng.0c08009
48. Shao H, Nian ZH, Jing ZL et al (2022) Additive manufacturing of hydroxyapatite bioceramic scaffolds with projection based 3D printing. Chin J Mech Eng-En 1(2):100021. https://doi.org/10.1016/j.cjmeam.2022.100021
49. Gao XM, Yang JT, Gan XJ et al (2024) Optimized DLP 3D-printed high-resolution nano zirconia-hydroxyapatite scaffold with craniomaxillofacial soft tissue invasion resistance and pro-osteogenic properties via dectin-1/syk inflammatory axis. Chem Eng J 491:152044. https://doi.org/10.1016/j.cej.2024.152044
50. Jiang WB, Zhan YC, Zhang YF et al (2024) Synergistic large segmental bone repair by 3D printed bionic scaffolds and engineered ADSC nanovesicles: towards an optimized regenerative microenvironment. Biomaterials 308:122566. https://doi.org/10.1016/j.biomaterials.2024.122566
51. Mao RQ, Lai YX, Li DX et al (2023) Flow channel performance in 3D printed hydroxyapatite scaffolds to improve metabolism and tissue ingrowth in flat bone repair. Compos Part B Eng 259:110727. https://doi.org/10.1016/j.compositesb.2023.110727
52. Feng BS, Zhang M, Qin C et al (2022) 3D printing of conch-like scaffolds for guiding cell migration and directional bone growth. Bioact Mater 22:127–140. https://doi.org/10.1016/j.bioactmat.2022.09.014
53. Liu W, Zheng LL, Wang C et al (2024) Additively manufactured bioceramic scaffolds with 3D architecture for vertical bone augmentation: a proof-of-concept study. Mater Des 239: 112749. https://doi.org/10.1016/j.matdes.2024.112749
54. Gu ZM, Fu JZ, Lin H et al (2020) Development of 3D bioprinting: from printing methods to biomedical applications. Asian J Pharm Sci 15(5):529–557. https://doi.org/10.1016/j.ajps.2019.11.003
55. Kang D, Park JA, Kim W et al (2021) All-inkjet-printed 3D alveolar barrier model with physiologically relevant microarchitecture. Adv Sci 8(10):2004990. https://doi.org/10.1002/advs.202004990

56. Kim BS, Lee JS, Gao G et al (2017) Direct 3D cell-printing of human skin with functional transwell system. Biofabrication 9(2):025034. https://doi.org/10.1088/1758-5090/aa71c8
57. Park JA, Yoon S, Kwon J et al (2017) Freeform micropatterning of living cells into cell culture medium using direct inkjet printing. Sci Rep 7:14610. https://doi.org/10.1038/s41598-017-14726-w
58. Xu T, Zhao WX, Zhu JM et al (2013) Complex heterogeneous tissue constructs containing multiple cell types prepared by inkjet printing technology. Biomaterials 34(1):130–139. https://doi.org/10.1016/j.biomaterials.2012.09.035
59. Dufour A, Gallostra XB, O'Keeffe C et al (2022) Integrating melt electrowriting and inkjet bioprinting for engineering structurally organized articular cartilage. Biomaterials 283:121405. https://doi.org/10.1016/j.biomaterials.2022.121405
60. Qian Y, Gong JX, Lu KJ et al (2023) DLP printed hDPSC-loaded GelMA microsphere regenerates dental pulp and repairs spinal cord. Biomaterials 299:122137. https://doi.org/10.1016/j.biomaterials.2023.122137
61. Tao J, Zhu SY, Liao XY et al (2022) DLP-based bioprinting of void-forming hydrogels for enhanced stem-cell-mediated bone regeneration. Mater Today Bio 17:100487. https://doi.org/10.1016/j.mtbio.2022.100487
62. Mao QJ, Wang YF, Li Y et al (2020) Fabrication of liver microtissue with liver decellularized extracellular matrix (dECM) bioink by digital light processing (DLP) bioprinting. Mater Sci Eng C Mater Biol Appl 109:110625. https://doi.org/10.1016/j.msec.2020.110625
63. Hong H, Seo YB, Kim DY et al (2020) Digital light processing 3D printed silk fibroin hydrogel for cartilage tissue engineering. Biomaterials 232:119679. https://doi.org/10.1016/j.biomaterials.2019.119679
64. Kunwar P, Aryal U, Poudel A et al (2024) Droplet bioprinting of acellular and cell-laden structures at high-resolutions. Biofabrication 16:035019. https://doi.org/10.1088/1758-5090/ad4c09
65. Zhao HY, Xing HY, Lai QG et al (2022) Additive manufacturing of graphene oxide/hydroxyapatite bioceramic scaffolds with reinforced osteoinductivity based on digital light processing technology. Mater Des 223:111231. https://doi.org/10.1016/j.matdes.2022.111231
66. Fei GH, Parra-Cabrera C, Zhong K et al (2024) From grayscale photopolymerization 3D printing to functionally graded materials. Adv Funct Mater 34(32):2314635. https://doi.org/10.1002/adfm.202314635
67. Zhang M, Lin RC, Wang X et al (2020) 3D printing of Haversian bone-mimicking scaffolds for multicellular delivery in bone regeneration. Sci Adv 6(12):eaaz6725. https://doi.org/10.1126/sciadv.aaz6725
68. Ouyang LL, Highley CB, Sun W et al (2017) A generalizable strategy for the 3D bioprinting of hydrogels from nonviscous photo-crosslinkable inks. Adv Mater 29(8):1604983. https://doi.org/10.1002/adma.201604983
69. Jang J, Park HJ, Kim SW et al (2017) 3D printed complex tissue construct using stem cell-laden decellularized extracellular matrix bioinks for cardiac repair. Biomaterials 112:264–274. https://doi.org/10.1016/j.biomaterials.2016.10.026
70. Liu W, Zhang YS, Heinrich MA et al (2017) Rapid continuous multimaterial extrusion bioprinting. Adv Mater 29:1604630. https://doi.org/10.1002/adma.201604630
71. Kang HW, Lee SJ, Ko IK et al (2016) A 3D bioprinting system to produce human-scale tissue constructs with structural integrity. Nat Biotechnol 34(3):312–319. https://doi.org/10.1038/nbt.3413
72. Kim BS, Gao G, Kim JY et al (2019) 3D cell printing of perfusable vascularized human skin equivalent composed of epidermis, dermis, and hypodermis for better structural recapitulation of native skin. Adv Healthc Mater 8(7):e1801019. https://doi.org/10.1002/adhm.201801019
73. de Ruijter M, Ribeiro A, Dokter I et al (2019) Simultaneous micropatterning of fibrous meshes and bioinks for the fabrication of living tissue constructs. Adv Healthc Mater 8(7): e1800418. https://doi.org/10.1002/adhm.201800418
74. Deshmukh DV, Reichert P, Zvick J et al (2022) Continuous production of acoustically patterned cells within hydrogel fibers for musculoskeletal tissue engineering. Adv Funct Mater 32(30): 2113038. https://doi.org/10.1002/adfm.202113038
75. Kim BS, Cho WW, Gao G et al (2021) Construction of tissue-level cancer-vascular model with high-precision position control via in situ 3D cell printing. Small Methods 5(7):e2100072. https://doi.org/10.1002/smtd.202100072
76. Ertel W (2024) Introduction to Artificial Intelligence (3rd Ed.). Springer Wiesbaden, Germany. https://doi.org/10.1007/978-3-658-43102-0
77. McCarthy J, Minsky ML, Rochester N et al (2006) A proposal for the Dartmouth summer research project on artificial intelligence: August 31, 1955. AI Mag 27(4):12–14. https://doi.org/10.1609/aimag.v27i4.1904
78. Newell A, Simon H (1956) The logic theory machine: a complex information processing system. IRE Trans Inform Theory 2(3):61–79. https://doi.org/10.1109/TIT.1956.1056797
79. Mahesh B (2018) Machine learning algorithms - a review. Int J Sci Res 9(1):381–386. https://doi.org/10.21275/ART20203995
80. Jordan MI, Mitchell TM (2015) Machine learning: trends, perspectives, and prospects. Science 349(6245):255–260. https://doi.org/10.1126/science.aaa8415
81. Alloghani M, Al-Jumeily D, Mustafina J et al (2020) A systematic review on supervised and unsupervised machine learning algorithms for data science. In: Berry M, Mohamed A, Yap B (Eds.), Supervised and Unsupervised Learning for Data Science (1st Ed.). Springer Cham, Switzerland, p.3–21. https://doi.org/10.1007/978-3-030-22475-2_1
82. Ding ZH, Huang YH, Yuan H et al (2020) Introduction to reinforcement learning. In: Dong H, Ding Z, Zhang S (Eds.), Deep Reinforcement Learning. Springer, Singapore. https://doi.org/10.1007/978-981-15-4095-0_2
83. Sullivan E (2022) Understanding from machine learning models. Br J Philos Sci 73(1):109–133. https://doi.org/10.1093/bjps/axz035
84. Chen PC, Liu Y, Peng L (2019) How to develop machine learning models for healthcare. Nat Mater 18(5):410–414. https://doi.org/10.1038/s41563-019-0345-0
85. Wu YC, Feng JW (2018) Development and application of artificial neural network. Wirel Pers Commun 102(2):1645–1656. https://doi.org/10.1007/s11277-017-5224-x
86. Abiodun OI, Jantan A, Omolara AE et al (2018) State-of-the-art in artificial neural network applications: a survey. Heliyon 4(11):e00938. https://doi.org/10.1016/j.heliyon.2018.e00938
87. Zhang ZH (2017) Artificial neural network. In: Zhang ZH (Ed.), Multivariate Time Series Analysis in Climate and Environmental Research (1st Ed.). Springer Cham, Switzerland, p.1–35. https://doi.org/10.1007/978-3-319-67340-0_1
88. Wainberg M, Merico D, Delong A et al (2018) Deep learning in biomedicine. Nat Biotechnol 36(9):829–838.

https://doi.org/10.1038/nbt.4233
89. Stephen Chan HC, Shan HB, Dahoun T et al (2019) Advancing drug discovery via artificial intelligence. Trends Pharmacol Sci 40(10):801. https://doi.org/10.1016/j.tips.2019.06.004
90. Wahl B, Cossy-Gantner A, Germann S et al (2018) Artificial intelligence (AI) and global health: how can AI contribute to health in resource-poor settings? BMJ Glob Health 3(4): e000798. https://doi.org/10.1136/bmjgh-2018-000798
91. Rowland SP, Fitzgerald JE, Holme T et al (2020) What is the clinical value of mHealth for patients? NPJ Digit Med 3:4. https://doi.org/10.1038/s41746-019-0206-x
92. Prabhod KJ (2024) The role of artificial intelligence in reducing healthcare costs and improving operational efficiency. Q J Emerg Technol Innov 9(2):47–59. https://vectoral.org/index.php/QJETI/article/view/111
93. Garcia-Vidal C, Sanjuan G, Puerta-Alcalde P et al (2019) Artificial intelligence to support clinical decision-making processes. eBioMedicine 46:27–29. https://doi.org/10.1016/j.ebiom.2019.07.019
94. Larson DB, Chen MC, Lungren MP et al (2018) Performance of a deep-learning neural network model in assessing skeletal maturity on pediatric hand radiographs. Radiology 287(1):313–322. https://doi.org/10.1148/radiol.2017170236
95. Challen R, Denny J, Pitt M et al (2019) Artificial intelligence, bias and clinical safety. BMJ Qual Saf 28(3):231–237. https://doi.org/10.1136/bmjqs-2018-008370
96. Hassija V, Chamola V, Mahapatra A et al (2024) Interpreting black-box models: a review on explainable artificial intelligence. Cogn Comput 16(1):45–74. https://doi.org/10.1007/s12559-023-10179-8
97. Jaremko JL, Azar M, Bromwich R et al (2019) Canadian Association of Radiologists white paper on ethical and legal issues related to artificial intelligence in radiology. Can Assoc Radiol J 70(2):107–118. https://doi.org/10.1016/j.carj.2019.03.001
98. Li CD, Chen JL, Jie TY et al (2022) Construction of biomimetic tissues with anisotropic structures via stepwise algorithm-assisted bioprinting. Small 18(46):e2204316. https://doi.org/10.1002/smll.202204316
99. Barrera MDB, Franco-Martínez F, Lantada AD (2021) Artificial intelligence aided design of tissue engineering scaffolds employing virtual tomography and 3D convolutional neural networks. Materials 14(18):5278. https://doi.org/10.3390/ma14185278
100. Han SY, Wu J (2024) Artificial intelligence (AI) meets biomaterials and biomedicine. Smart Mater Med 5(2):251–255. https://doi.org/10.1016/j.smaim.2024.03.001
101. Boztepe C, Künkül A, Yüceer M (2020) Application of artificial intelligence in modeling of the doxorubicin release behavior of pH and temperature responsive poly(NIPAAm-co-AAc)-PEG IPN hydrogel. J Drug Deliv Sci Technol 57:101603. https://doi.org/10.1016/j.jddst.2020.101603
102. Mozafari N, Mozafari N, Dehshahri A et al (2023) Knowledge gaps in generating cell-based drug delivery systems and a possible meeting with artificial intelligence. Mol Pharm 20(8):3757–3778. https://doi.org/10.1021/acs.molpharmaceut.3c00162
103. Figueiró Longo JP, Narcizo de Souza PE, Morais PC (2023) Artificial intelligence and machine learning in nanomedicine. What do we expect for 2030? Nanomedicine 18(16):1041–1043. https://doi.org/10.2217/nnm-2023-0084
104. Tropsha A, Isayev O, Varnek A et al (2024) Integrating QSAR modelling and deep learning in drug discovery: the emergence of deep QSAR. Nat Rev Drug Discov 23(2):141–155. https://doi.org/10.1038/s41573-023-00832-0
105. Ruberu K, Senadeera M, Rana ST et al (2021) Coupling machine learning with 3D bioprinting to fast track optimisation of extrusion printing. Appl Mater Today 22:100914. https://doi.org/10.1016/j.apmt.2020.100914
106. Verheyen CA, Uzel SGM, Kurum A et al (2023) Integrated data-driven modeling and experimental optimization of granular hydrogel matrices. Matter 6(3):1015–1036. https://doi.org/10.1016/j.matt.2023.01.011
107. Chen H, Liu Y, Balabani S et al (2023) Machine learning in predicting printable biomaterial formulations for direct ink writing. Research 6:0197. https://doi.org/10.34133/research.0197
108. Lee J, Oh SJ, An SH et al (2020) Machine learning-based design strategy for 3D printable bioink: elastic modulus and yield stress determine printability. Biofabrication 12(3):035018. https://doi.org/10.1088/1758-5090/ab8707
109. Mohammadrezaei D, Podina L, De Silva J et al (2024) Cell viability prediction and optimization in extrusion-based bioprinting via neural network-based Bayesian optimization models. Biofabrication 16(2):025016. https://doi.org/10.1088/1758-5090/ad17cf
110. Xu HQ, Liu QY, Casillas J et al (2022) Prediction of cell viability in dynamic optical projection stereolithography-based bioprinting using machine learning. J Intell Manuf 33(4):995–1005. https://doi.org/10.1007/s10845-020-01708-5
111. Piovarči M, Foshey M, Xu J et al (2022) Closed-loop control of direct ink writing via reinforcement learning. ACM Trans Graph 41(4):112. https://doi.org/10.1145/3528223.3530144
112. Nguyen DS, Park HS, Lee CM (2020) Optimization of selective laser melting process parameters for Ti-6Al-4V alloy manufacturing using deep learning. J Manuf Process 55:230–235. https://doi.org/10.1016/j.jmapro.2020.04.014
113. Chen BQ, Dong JP, Ruelas M et al (2022) Artificial intelligence-assisted high-throughput screening of printing conditions of hydrogel architectures for accelerated diabetic wound healing. Adv Funct Mater 32(38):2201843. https://doi.org/10.1002/adfm.202201843
114. Sedigh A, DiPiero D, Shine KM et al (2022) Enhancing precision in bioprinting utilizing fuzzy systems. Bioprinting 25: e00190. https://doi.org/10.1016/j.bprint.2021.e00190
115. Fu Z, Angeline V, Sun W (2021) Evaluation of printing parameters on 3D extrusion printing of pluronic hydrogels and machine learning guided parameter recommendation. Int J Bioprint 7(4): 434. https://doi.org/10.18063/ijb.v7i4.434
116. Jin ZQ, Zhang ZZ, Shao XL et al (2023) Monitoring anomalies in 3D bioprinting with deep neural networks. ACS Biomater Sci Eng 9(7):3945–3952. https://doi.org/10.1021/acsbiomaterials.0c01761
117. Sun J, Jing LZ, Fan XT et al (2018) Electrohydrodynamic printing process monitoring by microscopic image identification. Int J Bioprint 5(1):164. https://doi.org/10.18063/ijb.v5i1.164
118. Huang JD, Segura LJ, Wang TJ et al (2020) Unsupervised learning for the droplet evolution prediction and process dynamics understanding in inkjet printing. Addit Manuf 35:101197. https://doi.org/10.1016/j.addma.2020.101197
119. Cui XL, Li J, Hartanto Y et al (2020) Advances in extrusion 3D bioprinting: a focus on multicomponent hydrogel-based bioinks. Adv Healthcare Mater 9(15):1901648.

https://doi.org/10.1002/adhm.201901648
120. Castilho M, de Ruijter M, Beirne S et al (2020) Multitechnology biofabrication: a new approach for the manufacturing of functional tissue structures? Trends Biotechnol 38(12):1316–1328. https://doi.org/10.1016/j.tibtech.2020.04.014
121. Han XY, Saiding Q, Cai XL et al (2023) Intelligent vascularized 3D/4D/5D/6D-printed tissue scaffolds. Nanomicro Lett 15(1): 239. https://doi.org/10.1007/s40820-023-01187-2
122. Xing F, Xu JW, Yu PY et al (2023) Recent advances in biofabrication strategies based on bioprinting for vascularized tissue repair and regeneration. Mater Des 229:111885. https://doi.org/10.1016/j.matdes.2023.111885
123. Cao X, Ashfaq R, Cheng F et al (2019) A tumor-on-a-chip system with bioprinted blood and lymphatic vessel pair. Adv Funct Mater 29(31):1807173. https://doi.org/10.1002/adfm.201807173
124. Grigoryan B, Paulsen SJ, Corbett DC et al (2019) Multivascular networks and functional intravascular topologies within biocompatible hydrogels. Science 364(6439):458–464. https://doi.org/10.1126/science.aav9750
125. Neufeld L, Yeini E, Reisman N et al (2021) Microengineered perfusable 3D-bioprinted glioblastoma model for in vivo mimicry of tumor microenvironment. Sci Adv 7(34):eabi9119. https://doi.org/10.1126/sciadv.abi9119
126. Noor N, Shapira A, Edri R et al (2019) 3D printing of personalized thick and perfusable cardiac patches and hearts. Adv Sci 6(11):1900344. https://doi.org/10.1002/advs.201900344
127. Ouyang LL, Armstrong JPK, Chen Q et al (2019) Void-free 3D bioprinting for in situ endothelialization and microfluidic perfusion. Adv Funct Mater 30(1):1908349. https://doi.org/10.1002/adfm.201908349
128. Wang CY, Huang YF, Liu CC et al (2023) Diagnosis of clinically significant portal hypertension using CT- and MRI-based vascular model. Radiology 307(2):e221648. https://doi.org/10.1148/radiol.221648
129. Takahashi K, Abe K, Kubota SI et al (2022) An analysis modality for vascular structures combining tissue-clearing technology and topological data analysis. Nat Commun 13(1):5239. https://doi.org/10.1038/s41467-022-32848-2
130. Song JW, Munn LL (2011) Fluid forces control endothelial sprouting. Proc Natl Acad Sci USA 108(37):15342–15347. https://doi.org/10.1073/pnas.1105316108
131. Kutikhin AG, Sinitsky MY, Yuzhalin AE et al (2018) Shear stress: an essential driver of endothelial progenitor cells. J Mol Cell Cardiol 118:46–69. https://doi.org/10.1016/j.yjmcc.2018.03.007
132. Nemati P, Imani M, Farahmandghavi F et al (2014) Artificial neural networks for bilateral prediction of formulation parameters and drug release profiles from cochlear implant coatings fabricated as porous monolithic devices based on silicone rubber. J Pharm Pharmacol 66(5):624–638. https://doi.org/10.1111/jphp.12187
133. Xu F, Corbett B, Bell S et al (2020) High-throughput synthesis, analysis, and optimization of injectable hydrogels for protein delivery. Biomacromolecules 21(1):214–229. https://doi.org/10.1021/acs.biomac.9b01132
134. Tronolone JJ, Mathur T, Chaftari CP et al (2023) Evaluation of the morphological and biological functions of vascularized microphysiological systems with supervised machine learning. Ann Biomed Eng 51:1723–1737. https://doi.org/10.1007/s10439-023-03177-2
135. Shamloo A, Mohammadaliha N, Heilshorn SC et al (2016) A comparative study of collagen matrix density effect on endothelial sprout formation using experimental and computational approaches. Ann Biomed Eng 44(4):929–941. https://doi.org/10.1007/s10439-015-1416-2
136. Yin H, Ding YH, Zhai Y et al (2018) Orthogonal programming of heterogeneous micro-mechano-environments and geometries in three-dimensional bio-stereolithography. Nat Commun 9(1): 4096. https://doi.org/10.1038/s41467-018-06685-1
137. Ober TJ, Foresti D, Lewis JA (2015) Active mixing of complex fluids at the microscale. Proc Natl Acad Sci USA 112(40):12293–12298. https://doi.org/10.1073/pnas.1509224112
138. Idaszek J, Costantini M, Karlsen TA et al (2019) 3D bioprinting of hydrogel constructs with cell and material gradients for the regeneration of full-thickness chondral defect using a microfluidic printing head. Biofabrication 11(4):044101. https://doi.org/10.1088/1758-5090/ab2622
139. Esch MB, Post DJ, Shuler ML et al (2011) Characterization of in vitro endothelial linings grown within microfluidic channels. Tissue Eng Part A 17(23–24):2965–2971. https://doi.org/10.1089/ten.tea.2010.0371
140. Kochkov D, Smith JA, Alieva A et al (2021) Machine learning-accelerated computational fluid dynamics. Proc Natl Acad Sci USA 118(21):e2101784118. https://doi.org/10.1073/pnas.2101784118
141. Liang L, Mao WB, Sun W (2020) A feasibility study of deep learning for predicting hemodynamics of human thoracic aorta. J Biomech 99:109544. https://doi.org/10.1016/j.jbiomech.2019.109544
142. Tronolone JJ, Mathur T, Chaftari CP et al (2023) Machine learning chained neural network analysis of oxygen transport amplifies the physiological relevance of vascularized microphysiological systems. Bioeng Transl Med 8(6):e10582. https://doi.org/10.1002/btm2.10582
143. Lee W, Yoon B, Lee J et al (2023) Machine learning-aided three-dimensional morphological quantification of angiogenic vasculature in the multiculture microfluidic platform. BioChip J 17(3):357–368. https://doi.org/10.1007/s13206-023-00114-2
144. Zhang Y, Wang B, Hu JC et al (2020) 3D composite bioprinting for fabrication of artificial biological tissues. Int J Bioprint 7(1): 299. https://doi.org/10.18063/ijb.v7i1.299
145. Yu C, Ma XY, Zhu W et al (2019) Scanningless and continuous 3D bioprinting of human tissues with decellularized extracellular matrix. Biomaterials 194:1–13. https://doi.org/10.1016/j.biomaterials.2018.12.009
146. Reynolds DS, de Lázaro I, Blache ML et al (2023) Microporogen-structured collagen matrices for embedded bioprinting of tumor models for immuno-oncology. Adv Mater 35(33):e2210748. https://doi.org/10.1002/adma.202210748
147. Zhao HM, Chen YS, Shao L et al (2018) Airflow-assisted 3D bioprinting of human heterogeneous microspheroidal organoids with microfluidic nozzle. Small 14(39):e1802630. https://doi.org/10.1002/smll.201802630
148. Soliman BG, Longoni A, Wang M et al (2023) Programming delayed dissolution into sacrificial bioinks for dynamic temporal control of architecture within 3D-bioprinted constructs. Adv Funct Mater 33(8):2210521. https://doi.org/10.1002/adfm.202210521
149. Meng FB, Meyer CM, Joung D et al (2019) 3D bioprinted in vitro metastatic models via reconstruction of tumor microenvironments. Adv Mater 31(10):e1806899. https://doi.org/10.1002/adma.201806899

150. Freeman FE, Pitacco P, van Dommelen LHA et al (2020) 3D bioprinting spatiotemporally defined patterns of growth factors to tightly control tissue regeneration. Sci Adv 6(33):eabb5093. https://doi.org/10.1126/sciadv.abb5093
151. Kilian D, Cometta S, Bernhardt A et al (2022) Core-shell bioprinting as a strategy to apply differentiation factors in a spatially defined manner inside osteochondral tissue substitutes. Biofabrication 14:014108. https://doi.org/10.1088/1758-5090/ac457b
152. Liao JH, Timoshenko AB, Cordova DJ et al (2024) Propelling minimally invasive tissue regeneration with next-era injectable pre-formed scaffolds. Adv Mater 36(33):2400700. https://doi.org/10.1002/adma.202400700
153. Smith BT, Bittner SM, Watson E et al (2020) Multimaterial dual gradient three-dimensional printing for osteogenic differentiation and spatial segregation. Tissue Eng Part A 26(5–6):239–252. https://doi.org/10.1089/ten.TEA.2019.0204
154. Cai B, Kilian D, Ramos Mejia D et al (2024) Diffusion-based 3D bioprinting strategies. Adv Sci 11(8):e2306470. https://doi.org/10.1002/advs.202306470
155. Wang PJ, Sun YZ, Shi XQ et al (2021) 3D printing of tissue engineering scaffolds: a focus on vascular regeneration. Bio-Des Manuf 4(2):344–378. https://doi.org/10.1007/s42242-020-00109-0
156. Choi DH, Liu HW, Jung YH et al (2023) Analyzing angiogenesis on a chip using deep learning-based image processing. Lab Chip 23(3):475–484. https://doi.org/10.1039/d2lc00983h
157. Park R, Kang MS, Heo G et al (2024) Regulated behavior in living cells with highly aligned configurations on nanowrinkled graphene oxide substrates: deep learning based on interplay of cellular contact guidance. ACS Nano 18(2):1325–1344. https://doi.org/10.1021/acsnano.2c09815
158. Tourlomousis F, Jia C, Karydis T et al (2019) Machine learning metrology of cell confinement in melt electrowritten three-dimensional biomaterial substrates. Microsyst Nanoeng 5:15. https://doi.org/10.1038/s41378-019-0055-4
159. Samandari M, Mostafavi A, Quint J et al (2022) In situ bioprinting: intraoperative implementation of regenerative medicine. Trends Biotechnol 40(10):1229–1247. https://doi.org/10.1016/j.tibtech.2022.03.009
160. Wu Y, Ravnic DJ, Ozbolat IT (2020) Intraoperative bioprinting: repairing tissues and organs in a surgical setting. Trends Biotechnol 38(6):594–605. https://doi.org/10.1016/j.tibtech.2020.01.004
161. Ma L, Yu S, Xu X et al (2023) Application of artificial intelligence in 3D printing physical organ models. Mater Today Bio 23:100792. https://doi.org/10.1016/j.mtbio.2023.100792
162. Iacucci M, Santacroce G, Zammarchi I et al (2024) Artificial intelligence and endo-histo-omics: new dimensions of precision endoscopy and histology in inflammatory bowel disease. Lancet Gastroenterol Hepatol 9(8):758–772. https://doi.org/10.1016/s2468-1253(24)00053-0
163. Wang CB, Anisuzzaman DM, Williamson V et al (2020) Fully automatic wound segmentation with deep convolutional neural networks. Sci Rep 10(1):21897. https://doi.org/10.1038/s41598-020-78799-w
164. Curti N, Merli Y, Zengarini C et al (2024) Automated prediction of photographic wound assessment tool in chronic wound images. J Med Syst 48(1):14. https://doi.org/10.1007/s10916-023-02029-9
165. Chen AI, Balter ML, Maguire TJ et al (2020) Deep learning robotic guidance for autonomous vascular access. Nat Mach Intell 2(2):104–115. https://doi.org/10.1038/s42256-020-0148-7
166. Albanna M, Binder KW, Murphy SV et al (2019) In situ bioprinting of autologous skin cells accelerates wound healing of extensive excisional full-thickness wounds. Sci Rep 9(1):1856. https://doi.org/10.1038/s41598-018-38366-w
167. Zhao WX, Chen HY, Zhang Y et al (2022) Adaptive multi-degree-of-freedom in situ bioprinting robot for hair-follicle-inclusive skin repair: a preliminary study conducted in mice. Bioeng Transl Med 7(3):e10303. https://doi.org/10.1002/btm2.10303
168. Yang YY, Yu ZY, Lu XH et al (2023) Minimally invasive bioprinting for in situ liver regeneration. Bioact Mater 26:465–477. https://doi.org/10.1016/j.bioactmat.2023.03.011
169. Fuessinger MA, Schwarz S, Cornelius CP et al (2018) Planning of skull reconstruction based on a statistical shape model combined with geometric morphometrics. Int J Comput Assist Radiol Surg 13(4):519–529. https://doi.org/10.1007/s11548-017-1674-6
170. Kodym O, Španěl M, Herout A (2020) Skull shape reconstruction using cascaded convolutional networks. Comput Biol Med 123:103886. https://doi.org/10.1016/j.compbiomed.2020.103886
171. Xie MJ, Shi Y, Zhang C et al (2022) In situ 3D bioprinting with bioconcrete bioink. Nat Commun 13(1):3597. https://doi.org/10.1038/s41467-022-30997-y
172. Sarmadi M, Behrens AM, McHugh KJ et al (2020) Modeling, design, and machine learning-based framework for optimal injectability of microparticle-based drug formulations. Sci Adv 6(28):eabb6594. https://doi.org/10.1126/sciadv.abb6594
173. Zhu ZJ, Guo SZ, Hirdler T et al (2018) 3D printed functional and biological materials on moving freeform surfaces. Adv Mater 30(23):1707495. https://doi.org/10.1002/adma.201707495
174. Zhu Z, Park HS, McAlpine MC (2020) 3D printed deformable sensors. Sci Adv 6(25):eaba5575. https://doi.org/10.1126/sciadv.aba5575
175. Jeong SH, Kim J, Thibault BC et al (2024) Intelligent in situ printing of multimaterial bioinks for first-aid wound care guided by eye-in-hand robot technology. Adv Mater Technol 9(11):2400060. https://doi.org/10.1002/admt.202400060
176. Dennison NR, Fusenig M, Grönnert L et al (2024) Precision culture scaling to establish high-throughput vasculogenesis models. Adv Healthc Mater 13(18):e2400388. https://doi.org/10.1002/adhm.202400388
177. Huskin G, Chen J, Davis T et al (2023) Tissue-engineered 3D in vitro disease models for high-throughput drug screening. Tissue Eng Regen Med 20(4):523–538. https://doi.org/10.1007/s13770-023-00522-3
178. Derman ID, Yeo M, Castaneda DC et al (2023) High-throughput bioprinting of the nasal epithelium using patient-derived nasal epithelial cells. Biofabrication 15:044103. https://doi.org/10.1088/1758-5090/aced23
179. Gong ZY, Huang LX, Tang X et al (2021) Acoustic droplet printing tumor organoids for modeling bladder tumor immune microenvironment within a week. Adv Healthc Mater 10(22):e2101312. https://doi.org/10.1002/adhm.202101312
180. Shin J, Chung H, Kumar H et al (2024) 3D bioprinting of human iPSC-derived kidney organoids using a low-cost, high-throughput customizable 3D bioprinting system. Bioprinting 38:e00337. https://doi.org/10.1016/j.bprint.2024.e00337
181. Lawlor KT, Vanslambrouck JM, Higgins JW et al (2021) Cellular

extrusion bioprinting improves kidney organoid reproducibility and conformation. Nat Mater 20(2):260–271. https://doi.org/10.1038/s41563-020-00853-9
182. Hwang HH, You ST, Ma XY et al (2021) High throughput direct 3D bioprinting in multiwell plates. Biofabrication 13(2): 025007. https://doi.org/10.1088/1758-5090/ab89ca
183. Kolomenskaya E, Butova V, Poltavskiy A et al (2023) Application of artificial intelligence at all stages of bone tissue engineering. Biomedicines 12(1):76. https://doi.org/10.3390/biomedicines12010076
184. Abdel Fattah AR, Kolaitis N, Van Daele K et al (2023) Targeted mechanical stimulation via magnetic nanoparticles guides in vitro tissue development. Nat Commun 14(1):5281. https://doi.org/10.1038/s41467-023-41037-8
185. Sun XT, Yang YN, Liu QW et al (2024) Accelerating wound healing with flexible zinc ion microbatteries coupled with endogenous electrical fields. Nano Energy 123:109425. https://doi.org/10.1016/j.nanoen.2024.109425
186. Matos AM, Gonçalves AI, Rodrigues MT et al (2020) Remote triggering of TGF-β/Smad2/3 signaling in human adipose stem cells laden on magnetic scaffolds synergistically promotes tenogenic commitment. Acta Biomater 113:488–500. https://doi.org/10.1016/j.actbio.2020.07.009
187. Lee SY, Jeon S, Kwon YW et al (2022) Combinatorial wound healing therapy using adhesive nanofibrous membrane equipped with wearable LED patches for photobiomodulation. Sci Adv 8(15):eabn1646. https://doi.org/10.1126/sciadv.abn1646
188. Luo TY, Tan BW, Liao JF et al (2024) A review on external physical stimuli with biomaterials for bone repair. Chem Eng J 496:153749. https://doi.org/10.1016/j.cej.2024.153749
189. Wang NQ, Liu RX, Asmare N et al (2021) Closed-loop feedback control of microfluidic cell manipulation via deep-learning integrated sensor networks. Lab Chip 21(10):1916–1928. https://doi.org/10.1039/D1LC00076D
190. Andrion A, Magnani C, Betta PG et al (1995) Malignant mesothelioma of the pleura: interobserver variability. J Clin Pathol 48(9):856–860. https://doi.org/10.1136/jcp.48.9.856
191. Bian XS, Li G, Wang C et al (2021) OrgaNet: a deep learning approach for automated evaluation of organoids viability in drug screening. In: Wei Y, Li M, Skums P, Cai Z (Eds.), Bioinformatics Research and Applications (1st Ed.). Springer Cham, Switzerland, p.411–423. https://doi.org/10.1007/978-3-030-91415-8_35
192. Kegeles E, Naumov A, Karpulevich EA et al (2020) Convolutional neural networks can predict retinal differentiation in retinal organoids. Front Cell Neurosci 14:171. https://doi.org/10.3389/fncel.2020.00171
193. Bian XS, Li G, Wang C et al (2021) A deep learning model for detection and tracking in high-throughput images of organoid. Comput Biol Med 134:104490. https://doi.org/10.1016/j.compbiomed.2021.104490
194. Cao Y, Shi HH, Yi C et al (2024) Recent progress of non-invasive in vitro diagnosis using electrochemical analysis strategy and wearable microfluidic devices applied to exocrine secretion sampling. Trac Trends Anal Chem 172:117561. https://doi.org/10.1016/j.trac.2024.117561
195. Coley CW, Thomas DA III, Lummiss JAM et al (2019) A robotic platform for flow synthesis of organic compounds informed by AI planning. Science 365(6453):eaax1566. https://doi.org/10.1126/science.aax1566
196. Hamm J, Lim S, Park J et al (2024) A modular robotic platform for biological research: cell culture automation and remote experimentation. Adv Intell Syst 6(5):2300566. https://doi.org/10.1002/aisy.202300566
197. Gevorkyan MN, Demidova AV, Demidova TS et al (2019) Review and comparative analysis of machine learning libraries for machine learning. Discrete Contin Models Appl Comput Sci 27(4):305–315. https://doi.org/10.22363/2658-4670-2019-27-4-305-315
198. Wang ZL, Chen A, Tao KH et al (2023) AlphaMat: a material informatics hub connecting data, features, models and applications. NPJ Comput Mater 9:130. https://doi.org/10.1038/s41524-023-01086-5
199. Mahadik B, Margolis R, McLoughlin S et al (2022) An open-source bioink database for microextrusion 3D printing. Biofabrication 15(1):015008. https://doi.org/10.1088/1758-5090/ac933a
200. Krizhevsky A, Sutskever I, Hinton GE (2017) ImageNet classification with deep convolutional neural networks. Commun ACM 60(6):84–90. https://doi.org/10.1145/3065386
201. Yang JC, Shi R, Wei DL et al (2023) MedMNIST v2 - a large-scale lightweight benchmark for 2D and 3D biomedical image classification. Sci Data 10(1):41. https://doi.org/10.1038/s41597-022-01721-8
202. Cannas M, Arpino B (2019) A comparison of machine learning algorithms and covariate balance measures for propensity score matching and weighting. Biom J 61(4):1049–1072. https://doi.org/10.1002/bimj.201800132
203. Hill MJ, Kunz RF, Medvitz RB et al (2011) CFD analysis of gear windage losses: validation and parametric aerodynamic studies. J Fluids Eng 133(3):031103. https://doi.org/10.1115/1.4003681
204. Guzman-Alvarez A (2023) Deep Learning for Investigating Causal Effects with High-Dimensional Data: Analytic Tools and Applications to Educational Interventions. Doctoral Dissertation, University of Pittsburgh, USA. https://d-scholarship.pitt.edu/44666/ [Accessed on 21 July 2024]
205. Catalanotti G (2024) Navigating the unknown: tackling high-dimensional challenges in composite damage modeling with bootstrapping and Bayesian uncertainty quantification. Compos Sci Technol 248:110462. https://doi.org/10.1016/j.compscitech.2024.110462
206. Borovik A (2021) A mathematician's view of the unreasonable ineffectiveness of mathematics in biology. Biosystems 205: 104410. https://doi.org/10.1016/j.biosystems.2021.104410
207. Teixeira AM, Martins P (2023) A review of bioengineering techniques applied to breast tissue: mechanical properties, tissue engineering and finite element analysis. Front Bioeng Biotechnol 11:1161815. https://doi.org/10.3389/fbioe.2023.1161815
208. Klabukov I, Tenchurin T, Shepelev A et al (2023) Biomechanical behaviors and degradation properties of multilayered polymer scaffolds: the phase space method for bile duct design and bioengineering. Biomedicines 11(3):745. https://doi.org/10.3390/biomedicines11030745
209. Ginoux G, Vroman I, Alix S (2021) Influence of fused filament fabrication parameters on tensile properties of polylactide/layered silicate nanocomposite using response surface methodology. J Appl Polym Sci 138(14):50174. https://doi.org/10.1002/app.50174