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REVIEW ARTICLE

Artificial intelligence-augmented bioprinting systems: Data-driven optimization and future applications in pharmacological research

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Abstract

The high attrition rate of drug candidates in clinical trials is often attributed to the use of conventional two-dimensional cell cultures and animal models that fail to accurately recapitulate human physiology. Three-dimensional (3D) bioprinting has emerged as a transformative technology for creating sophisticated, patient-relevant tissue models for drug screening and toxicity assessment. Concurrently, machine learning (ML) offers a powerful paradigm for extracting insights from complex, multi-modal data and optimizing intricate processes. This review presents a comprehensive and critical overview of the convergence of 3D bioprinting and ML, with a focus on their integrated applications in drug development. We critically and comprehensively analyze the various data types generated throughout the bioprinting workflow, from process parameters and material properties to biological and "omics" data. We then discuss the application of diverse ML approaches, from statistical methods to deep learning, for optimizing bioprinting processes and enhancing the predictive accuracy of drug screening. By including specific quantitative outcomes and comparative analyses from recent studies, we provide an evidence-based perspective on the state of the field and highlight its potential to accelerate the drug discovery pipeline.

Keywords: 3D bioprinting; Deep learning; Drug discovery; Machine learning; Predictive modeling

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1. Introduction

Drug discovery and development remain lengthy, costly, and high-risk processes, with an average timeline exceeding a decade and costs reaching billions of dollars per approved drug.[1,2] A major bottleneck lies in the translation of preclinical findings into successful clinical outcomes, as conventional two-dimensional (2D) cell cultures and animal models often fail to replicate the complexity of human physiology.[3–5] This mismatch contributes to high attrition rates in late-stage clinical trials, particularly due to unforeseen toxicity or insufficient efficacy.[6–8]

Bioprinting has emerged as a transformative platform to address these challenges.[9–11] By enabling the automated fabrication of three-dimensional (3D) tissue constructs with precise control over architecture, cell composition, and microenvironment,[12–14] bioprinting offers physiologically relevant models for drug screening and toxicity testing.[15] These 3D models can more accurately mimic human tissue function, improving predictive power for pharmacological and toxicological assessments.[16–18] Furthermore, the scalability and reproducibility of bioprinting make it well-suited for experimental pipelines requiring standardized and reproducible tissue models.[13]

However, the full potential of bioprinting is hindered by the complexity of its workflows and the vast amount of heterogeneous data it generates.[19] Variations in bioprinting parameters, biomaterial properties, and biological responses create multidimensional datasets that are challenging to interpret using traditional statistical approaches.[20,21] Herein, machine learning (ML) offers powerful solutions.[22,23] By identifying hidden patterns, learning from complex datasets, and enabling predictive modeling, ML can be integrated into bioprinting systems to optimize printing parameters, automate quality control, and predict drug responses with higher accuracy.[24–26]

The integration of ML with bioprinting represents a paradigm shift toward more intelligent and automated biomedical research workflows.[12,23] In such systems, ML algorithms continuously process data from bioprinted constructs—ranging from imaging and viability assays to omics-based readouts—and feed back into the printing process in real time.[27] This closed-loop approach not only accelerates experimental cycles but also enhances the reproducibility, scalability, and predictive reliability of preclinical studies.[23] As a result, the convergence of ML and bioprinting holds significant promise for drug development, including potential benefits for shortening timelines, reducing costs, and improving patient safety.[26,28]

Despite this promise, direct research integrating ML and bioprinting specifically for drug discovery and pharmacological testing remains scarce. Most current efforts focus on print process optimization and quality assessment rather than end-to-end applications in drug pipelines. Addressing this gap is crucial for unlocking the full translational potential of ML-driven bioprinting. The organizational framework of this review is presented in Figure 1. It first provides foundational principles of bioprinting and the current applications of ML in biomedical research. The review then explores strategies for leveraging artificial intelligence (AI) to achieve the data-driven optimization of bioprinting workflows and create predictive models for drug screening and toxicity testing. It highlights recent advances in developing advanced models for disease and therapeutic screening before concluding with a discussion on the future outlook and translational roadmap for intelligent, data-driven drug discovery platforms.

2. Fundamentals of bioprinting

Bioprinting refers to the automated, layer-by-layer fabrication of 3D biological structures using living cells, biomaterials, and supporting factors.[14] This technology enables precise spatial control over cell placement and scaffold architecture, allowing researchers to recreate complex tissue microenvironments with high fidelity.[29] Unlike traditional tissue engineering approaches, bioprinting offers improved reproducibility, customization, and scalability, making it a powerful tool for building functional biological systems for a wide range of biomedical applications.

2.1. Core principles and workflow

The bioprinting workflow typically begins with the preparation of bioinks, which are biomaterial formulations designed for both printability and biological compatibility. These formulations may include cell-laden hydrogels, microparticles, and other components.[30–33] Automated bioprinting platforms then deposit these bioinks in a layer-by-layer fashion with precise spatial control, guided by computer-aided design models.[34] Post-printing, the constructs undergo processes such as crosslinking, maturation, and culture under controlled environmental conditions to achieve functional tissue properties.[35] The entire workflow is integrated with high-content analytical systems—including imaging platforms, viability assays, and biochemical sensors—that enable rapid and consistent data acquisition across large sample sets.[10,36] The core principles and stages of this workflow are illustrated in Figure 2.

2.2. Bioprinting technologies

Various bioprinting modalities have been adapted for high-throughput applications, each with distinct strengths.[37,38] Inkjet bioprinting enables rapid, droplet-based deposition of low-viscosity bioinks, ideal for miniaturized tissue constructs, and cost-efficient screening.[39] Microextrusion systems allow for continuous filament deposition of more viscous bioinks, supporting higher cell densities and better structural stability, though often at the expense of printing speed.[40,41] Light-based methods, such as stereolithography and digital light processing, use photopolymerization to achieve high resolution and complex architectures, making them valuable for creating intricate tissue microenvironments.[42–44] Increasingly, hybrid platforms combine these approaches to balance throughput, resolution, and biomaterial compatibility for different experimental needs.[10,45]

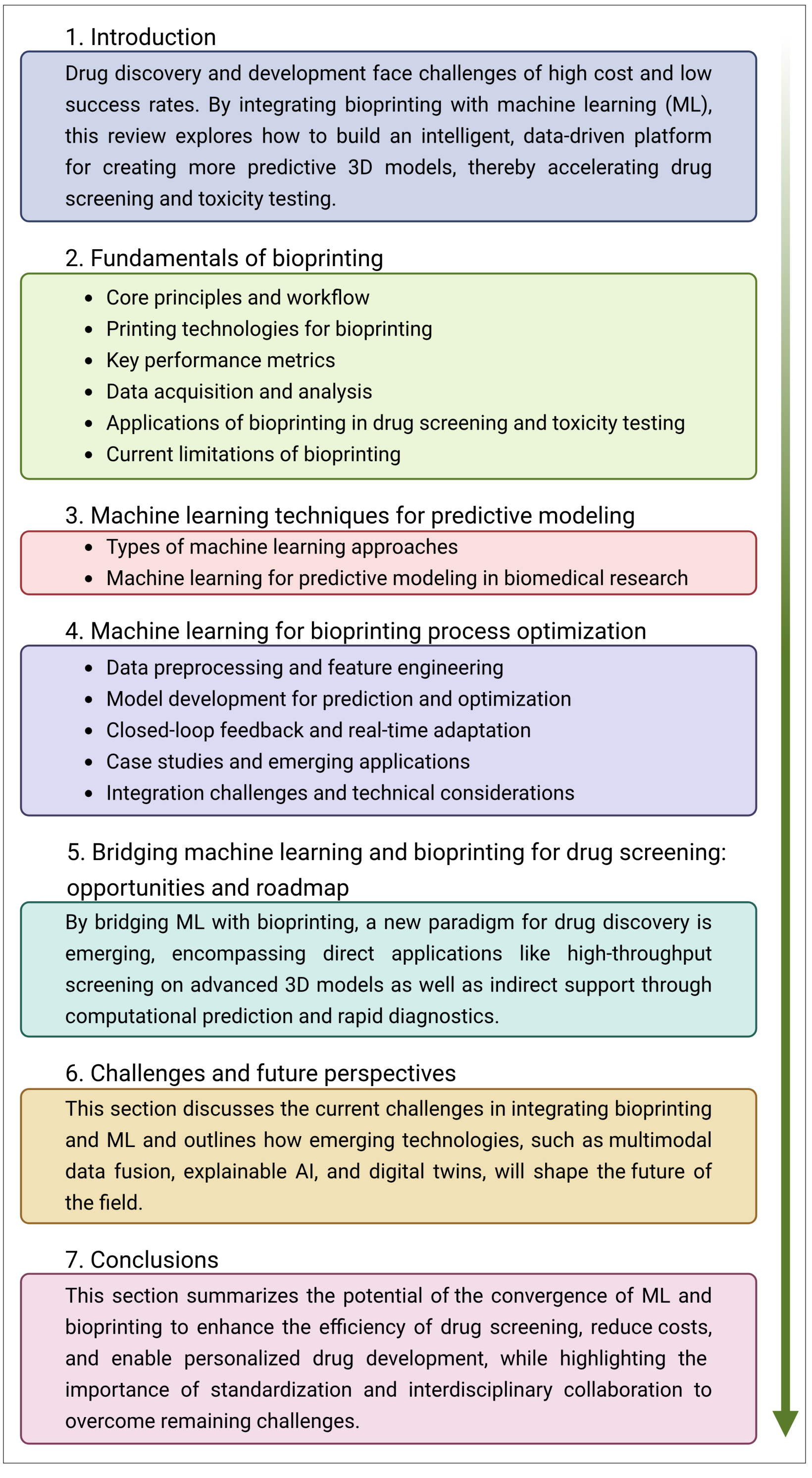

Figure 1. An overview of the organizational framework of this review. The framework first provides foundational principles of bioprinting and machine learning, then explores their synergistic applications in data-driven bioprinting workflows and drug discovery, and finally concludes with a discussion on the future outlook and translational roadmap.

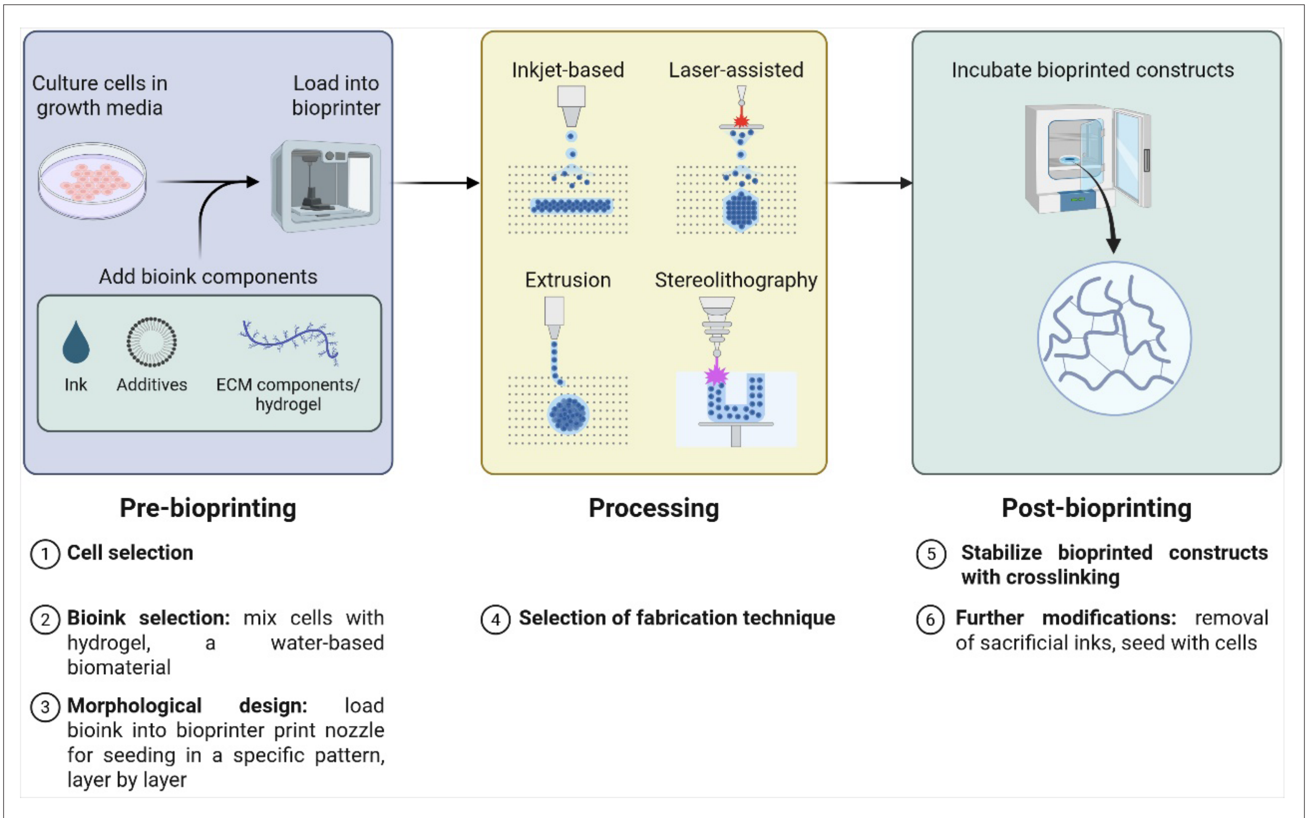

Figure 2. Bioprinting workflow. The process comprises three main stages: pre-bioprinting (cell cultures and bioink preparation, including cell selection and construct design), processing (layer-by-layer deposition of bioinks using different bioprinting technologies), and post-bioprinting (construct stabilization via crosslinking and maturation in controlled environments). Abbreviation: ECM, extracellular matrix.

2.3. Key performance metrics

For bioprinting to be impactful in drug discovery, several performance parameters are critical. Among them, throughput—defined as the number of tissue constructs produced per unit time—determines scalability.[46] Resolution influences how accurately microenvironmental features are reproduced, which can affect cell behaviors and drug responses.[30,47,48] Reproducibility ensures consistency in geometry, cell distribution, and viability across large batches, all of which are essential for generating reliable screening data.[49] Biological fidelity—the ability of printed constructs to replicate relevant *in vivo* functions—directly impacts the predictive value of assays.[47,50] Finally, integration compatibility with automated liquid handling, microfluidic systems, and high-content imaging is essential to streamline workflows in industrial and research settings.[51]

2.4. Data acquisition and analysis

Bioprinting platforms are a foundation for integrating with ML because they generate vast amounts of heterogeneous data. The first critical step is the systematic collection of these high-quality, multi-modal datasets. These data streams, which include those from fluorescence imaging, live–dead staining assays, metabolic activity measurements, and multi-omics profiling, provide critical information about the biological constructs.[46] This is complemented by detailed process parameters such as nozzle pressure, extrusion speed, and bioink rheology collected from embedded sensors.[52,53] The quality, diversity, and completeness of these datasets directly influence the accuracy and generalizability of downstream ML models.[54] Table 1 provides a comprehensive overview of the various data types generated throughout the bioprinting workflow, detailing their common processing methods and the associated ML models and tasks.

2.5. Applications of bioprinting in drug screening and toxicity testing

In practice, bioprinting has been applied to generate a diverse range of tissue models for both efficacy and toxicity studies.[64,65] Examples include liver spheroids for drug metabolism analysis, tumor organoids for cancer drug sensitivity profiling, and cardiac microtissues for cardiotoxicity evaluation.[16,66,67] These 3D constructs can be tailored to represent specific patient populations or

Table 1. Data types generated during bioprinting workflows and their integration with machine learning models

Data type	General data sources	Common processing methods	Associated ML models & tasks	Advantages	Limitations	References
Imaging data (microscopy, high-content screening)	Fluorescence microscopy, confocal imaging, high-content imaging systems in bioprinting setups	Image preprocessing (denoising, normalization), segmentation (cell/nuclei/organoid), feature extraction (morphology, intensity), DL-based classification	DL (especially CNNs) for real-time quality control, defect detection, cell counting, and morphological analysis; unsupervised learning for anomaly detection and morphological pattern recognition	Rich spatial and morphological information; enables phenotypic profiling and subcellular resolution	High data volume; requires complex preprocessing and large storage; sensitive to imaging artifacts	55
Bioprinter process data (print path, droplet size, temperature, pressure)	Real-time printer logs, embedded sensor arrays, nozzle monitoring systems	Time-series analysis, sensor fusion, anomaly detection, predictive maintenance modeling	Regression models for predicting print quality, cell viability, and mechanical properties; reinforcement learning for real-time parameter optimization and closed-loop control	Enables real-time quality control and process optimization	Requires specialized hardware; complex integration of heterogeneous signals	56,57
Mechanical property data (tissue stiffness, viscoelasticity)	Atomic force microscopy, compression testing, and rheology measurements	Curve fitting, stress–strain modeling, statistical comparison across conditions	Regression models for predicting mechanical properties and printability from process parameters	Provides functional readouts relevant to tissue physiology	Destructive testing may limit repeated measures; device calibration is needed	58,59
Viability and metabolic activity data	Live/dead staining, ATP-based luminescence assays, resazurin assays	Signal normalization, dose–response curve fitting, statistical analysis	Classification models for predicting toxicity or drug response (live vs. dead); regression models for predicting quantitative cell viability values	Rapid and widely used for cell health monitoring	Limited mechanistic insight; end-point only (non-real time)	8
Genomic/ transcriptomic/ proteomic/ metabolomic data	Bulk RNA-seq, LC–MS, GC–MS, NMR profiling from printed constructs or culture supernatants	Quality control, normalization, differential expression, pathway enrichment, peptide/metabolite identification	Clustering and classification models for predicting tissue states, cell phenotypes, or drug response	Comprehensive, systems-level view; detects complex relationships; non-invasive monitoring	High cost and complexity; requires specialized tools; challenging data integration	60,61
Bioink composition data	Rheological measurements, spectroscopic analysis of bioinks	Composition profiling, crosslinking efficiency testing, viscosity analysis	Regression models for predicting printability and viscosity; clustering models for grouping similar bioink formulations	Critical for reproducible printing; affects cell viability and construct integrity	Bioink variability between batches; sensitive to storage/handling	58,62,63

Abbreviations: CNN, convolutional neural network; DL, deep learning; GC, gas chromatography; LC, liquid chromatography; ML, machine learning; MS, mass spectrometry; NMR, nuclear magnetic resonance.

disease states, offering valuable platforms for personalized medicine research.[68,69] By enabling large-scale, physiologically relevant testing, bioprinting holds promise for improving early-stage decision-making and reducing the rate of costly late-stage clinical trial failures.[70] Table 2 provides a summary of relevant studies (since 2020) that highlight the application of bioprinting in drug screening and toxicity testing.

2.6. Current limitations of bioprinting

Despite its potential, bioprinting still faces challenges. The range of bioinks that combine printability with long-term biological functionality remains limited, constraining the diversity of tissue constructs.[94] Standardized metrics for assessing construct quality and performance are lacking, making it difficult to compare results across laboratories.[95] Biological complexity—such as multi-tissue interactions, immune responses, and long-term maturation—remains difficult to reproduce at scale.[96,97] Additionally, the sheer volume of heterogeneous data generated through bioprinting platforms creates a bottleneck in analysis and interpretation, underscoring the need for advanced computational approaches, including ML, to fully harness the technology's capabilities.

3. Machine learning techniques for predictive modeling

Machine learning, a subset of AI, has emerged as a powerful computational approach for uncovering patterns, making predictions, and optimizing processes in complex biomedical systems.[56,98] In drug discovery and development, ML algorithms are capable of analyzing vast, heterogeneous datasets, including chemical structures, molecular interaction profiles, genomic and proteomic data, imaging outputs, and clinical records.[99,100] Through learning from these diverse inputs, ML can predict compound efficacy, identify potential toxicity, and even suggest novel molecular designs with improved pharmacological properties.[101] This data-driven approach has the potential to accelerate early-stage research, reduce experimental costs, and increase the success rate of clinical translation.[102] The fundamental concepts of ML are illustrated in Figure 3.

3.1. Types of machine learning approaches

Different classes of ML methods are applied to biomedical problems, each suited to particular data types and research objectives.[103,104] Supervised learning methods, such as random forests (RFs)[105] and support vector machines,[106] are trained on labeled datasets to predict specific outcomes, such as drug responses and cell viability. A key subfield of supervised learning is deep learning (DL), which utilizes multi-layered neural networks to learn complex patterns. Deep neural networks and their specialized architectures, such as convolutional neural networks, have proven particularly effective in processing high-dimensional data, including images and time-series signals, enabling rapid, automated analysis of microscopy images and real-time quality control.[107,108] Unsupervised learning methods, including clustering algorithms and dimensionality reduction techniques, are used to reveal hidden structures in unlabeled datasets, for example, the identification of disease subtypes from patient omics profiles.[109] Reinforcement learning methods allow systems to improve decision-making through iterative trial-and-error processes, a strategy increasingly explored in automated experimental design.[110]

3.2. Machine learning for predictive modeling in biomedical research

In drug screening and toxicity testing, ML has been successfully used to predict off-target effects, model dose–response relationships, and stratify compounds based on their predicted therapeutic potential[111–113]. Algorithms trained on large public toxicity datasets can predict the safety profiles of novel molecules.[114,115] Furthermore, ML can optimize experimental workflows by selecting the most informative combinations of parameters to test, thereby reducing the number of experiments required without sacrificing predictive accuracy.[116,117]

While different ML methods can be broadly categorized, their practical application depends on the specific bioprinting data type and research goal.[118] Supervised learning is most suitable for bioprinting datasets with labeled outcomes, such as predicting the final cell viability from process parameters or anticipating drug response from omics data. Its strength lies in its ability to provide clear, quantifiable predictions, though it relies on the availability of large, high-quality labeled datasets. In contrast, unsupervised learning excels at exploring unlabeled data to uncover hidden patterns, making it invaluable for tasks such as identifying new tissue phenotypes or grouping similar bioink formulations without prior knowledge. Meanwhile, DL, the powerful subset of these methods, is particularly effective with high-dimensional data. For example, a standard deep neural network can be used to model complex, non-linear relationships in multi-modal datasets, and convolutional neural networks are the go-to choices for image-based data, enabling automated defect detection and morphological analysis.[119,120] Finally, reinforcement learning is suited for dynamic, real-time optimization, allowing the bioprinting system to learn and autonomously adjust parameters to achieve a desired outcome without direct human intervention.[121] This predictive capability is particularly relevant in bioprinting,

Table 2. Representative studies of bioprinting in drug screening and toxicity testing

Cell type/source	Bioprinting modality	Construct type/model	Main findings	References
Alveolar, bronchial, and intestinal epithelial cells	Inkjet-based bioprinting	Simple epithelial layers (alveolar, bronchial, intestinal)	Developed a protocol for the automated and reproducible printing of simple epithelial layers for respiratory and gastrointestinal models, useful for high-throughput toxicity screening.	71
HepaRG liver cells	Extrusion-based bioprinting	3D-bioprinted HepaRG cultures	3D models were more resistant to aflatoxin B1 and viable for longer (up to three weeks) than 2D cultures, providing a better model for chronic hepatotoxicity studies.	72
Cryopreserved primary human hepatocytes and hepatic stellate cells	Extrusion-based bioprinting	3D-bioprinted human liver tissues	3D tissue showed improved viability and enhanced drug-metabolism gene expression compared to controls. It can detect the toxicity of compounds undetected using 2D culture and conventional spheroids, offering high sensitivity for hepatotoxicity prediction.	73
Multiple cell types	Inkjet-based bioprinting	Stiffness-tunable collagen-alginate microgels	Developed a high-throughput, stiffness-tunable 3D culture platform with consistent reproducibility, which can be used to screen chemotherapeutics and study mechanobiology.	74
Human pluripotent stem cells	Extrusion-based bioprinting	Kidney organoids	Bioprinting improves organoid reproducibility, viability, and nephron yield compared to manual methods. It facilitates the generation of uniformly patterned kidney tissue sheets for drug testing and *in vitro*/*in vivo* applications.	75
Human liver-derived epithelial organoids	Extrusion-based bioprinting	Bioprinted liver organoids	Bioprinted organoids showed stable viability and increased expression of hepatic markers. They demonstrated the ability to detect toxicity from acetaminophen, indicating their potential for use as toxicology and disease models.	76
HepG2 cells	Extrusion-based bioprinting	Hexagonal bioprinted hepatic construct	A spinning culture condition enhanced proliferation and functionality, increasing the susceptibility of the model to acetaminophen-induced hepatotoxicity and better mimicking *in vivo* liver injury.	77
Unspecified cells for cartilage model	Extrusion-based bioprinting	Scaffold-free 3D-bioprinted cartilage model	Developed a scalable bioprinting method for creating cartilage constructs suitable for high-efficiency *in vitro* toxicology studies.	78
HepG2 cells	Extrusion-based bioprinting	3D HepG2 liver spheroid model in hydrogel constructs	Developed a platform for *in situ* quantitative evaluation of drug toxicity. Spheroids were more resistant to nefazodone-induced toxicity than 2D cells, and fluorescence intensities of markers could be used to determine EC50 values.	79
Lung cancer cell line	Extrusion-based bioprinting	3D-bioprinted tumor model with a multicomponent bioink	Developed and validated a novel bioink and a 3D tumor model suitable for anti-cancer drug screening, overcoming limitations of 2D monolayer models.	80
Renal epithelial cells	Inkjet-based bioprinting	Bioprinted renal spheroids	3D spheroids showed enhanced sensitivity to cisplatin compared to monolayers. A DL algorithm was developed for automatic toxicity readout from images with 78.7% accuracy.	81
SW480 cells, tumor-associated macrophages, and endothelial cells	Extrusion-based bioprinting	3D multicellular colorectal cancer model	The multicellular model showed improved tumor-related gene expression and higher resistance to chemotherapy than single-cell models, demonstrating its improved physiological relevance for drug screening.	82

(Continues....)

Table 2. Representative studies of bioprinting in drug screening and toxicity testing

Human pancreatic cancer cells and stromal fibroblasts	Extrusion-based bioprinting	Pancreatic tumor-stroma microtissues (hydrogel beads)	Engineered tumor-stroma microtissues recapitulated native features, demonstrated better resistance to anti-cancer drugs than mono-cultured spheroids, and served as a new drug screening platform.	83
Hepatocytes and human umbilical vein endothelial cells	Extrusion-based bioprinting	Endothelialized liver lobule-like constructs	The model successfully recreated liver lobule-like morphology and showed stronger drug resistance to sorafenib compared to other models, demonstrating its potential as a tumor-scale drug screening platform.	84
Cervical cancer cells from PDOs	Light-based bioprinting	3D-bioprinted PDOs	Higher expression of NSUN6 promotes radioresistance in the 3D PDOs model by activating a specific molecular pathway, while silencing *NSUN6* increases radiosensitivity.	85
Triple-negative breast cancer PDOs	Extrusion-based bioprinting	3D-bioprinted models from PDOs	Identified a new molecular glue (aurovertin B) that promotes the degradation of coronin 1A, resulting in robust antitumor effects in the 3D-bioprinted models.	86
HuH-7 cell line	Extrusion-based bioprinting	Xeno-free 3D-bioprinted liver model	Developed the first xeno-free 3D-bioprinted liver model, which showed high cell viability and required three-fold higher concentrations of a biotoxin to induce cytotoxicity compared to 2D cultures.	87
Dermal fibroblasts, adipose-derived stem cells, and human epidermal keratinocytes	Extrusion-based bioprinting	3D-bioprinted skin equivalent (tri-layer with an epidermal layer)	Developed a 3D skin model and confirmed permeation and cellular uptake of a drug-loaded nanocapsule. The combined nanocapsule and photodynamic therapy resulted in reduced cytokine levels, suggesting a new therapeutic approach for skin inflammation.	88
MCF-7 breast cancer cells	Inkjet-based bioprinting	Single spheroids	Developed a fast-crosslinking bioink for high-throughput and reproducible single spheroid formation, highlighting the importance of ink characterization for future drug screening applications.	89
Foregut cells differentiated from human iPSCs	Droplet-based printing	HLOs on a pillar plate platform	Achieved a high-throughput, reproducible generation of HLOs with superior function compared to conventional methods, demonstrating their utility for hepatotoxicity assays.	90
Primary hepatocytes	Light-based bioprinting	HCD liver model	An HCD model was fabricated with enhanced cell–cell interactions and metabolic functions. The model was more sensitive to drug treatments than lower-density models, demonstrating the importance of HCD for recapitulating physiological drug responses.	91
Neonatal mouse primary testicular cells	Light-based bioprinting	Testicular organoids	Bioprinted organoids recapitulated key testicular features and showed the loss of a tight junction protein and altered gene expression in response to a known toxicant, demonstrating a high-throughput platform for reproductive toxicity assessment.	92
E18 mouse fetus epidermal and dermal cells	Inkjet-based bioprinting	Skin organospheres	Developed a high-throughput, reproducible model to assess microplastic-induced skin toxicity, demonstrating a size-dependent uptake rate and increased oxidative stress in response to ultraviolet A-irradiated prevalence of microplastics.	93

Abbreviations: DL, deep learning; EC50, half-maximal effective concentration; HCD, high cell density; HLO, human liver organoid; iPSC, induced pluripotent stem cell; NSUN6, NOP2/Sun RNA methyltransferase family member 6; PDO, patient-derived organoid.

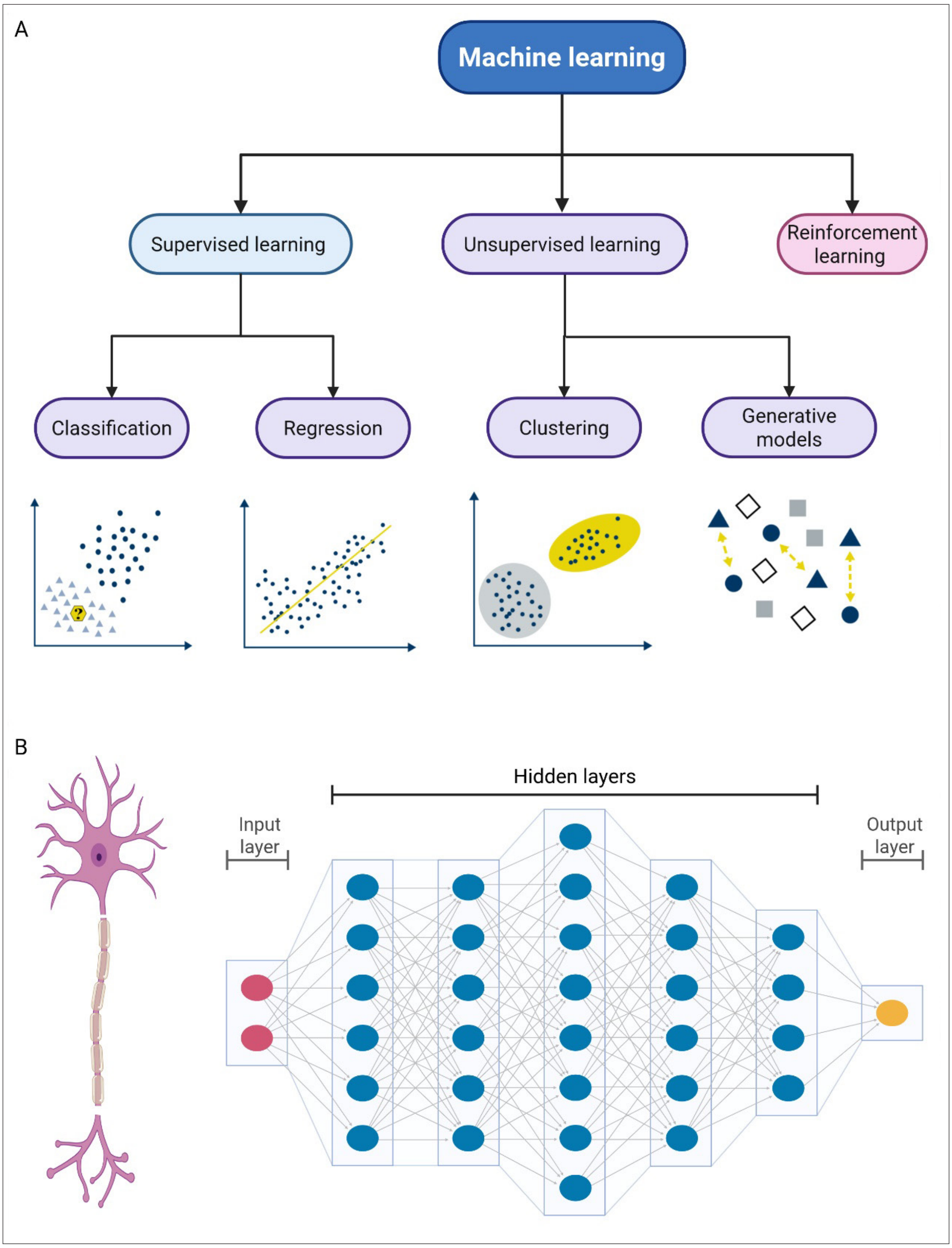

Figure 3. Machine learning (ML) techniques. (A) An overview of the main ML paradigms, illustrating the three primary types of ML: supervised learning, which uses labeled data for tasks such as classification (sorting data points into categories) and regression (predicting a continuous value); unsupervised learning, which discovers hidden structures in unlabeled data, as seen in clustering (grouping similar data points) and generative models (creating new data from learned patterns); and reinforcement learning, where an agent learns to make optimal decisions through a system of rewards and punishments. (B) The architecture of an artificial neural network is the basis of deep learning. It shows how information is processed from an input layer, through multiple hidden layers, to an output layer, mimicking the structure and function of a biological neuron.

where ML-driven approaches have been used to analyze bioprinted structures for drug response profiling[12,60,122] and to predict key biological outcomes, such as cell viability and tissue maturation.[22,23,123] For example, deep convolutional neural networks have been applied to analyze optical coherence tomography data to enable the automated detection and growth tracking of bioprinted organoid clusters.[123,124] This predictive capability extends to optimizing printing parameters to improve throughput and print fidelity in cellular droplet bioprinting.[125,126] These applications demonstrate the direct utility of ML in enhancing the precision of the bioprinting process.

4. Machine learning for bioprinting process optimization

As experimental technologies such as bioprinting continue to evolve, the application of ML becomes increasingly important. Bioprinting platforms generate multidimensional datasets encompassing imaging, viability metrics, molecular readouts, and environmental parameters, all of which can be integrated into ML models for more efficient and adaptive experimentation.[26,127] By enabling automated analysis, real-time feedback, and predictive modeling, ML provides the computational backbone needed to transform high-throughput experimental platforms into intelligent, closed-loop systems capable of continuously improving their performance.[128,129] A conceptual pipeline of how AI-driven multi-modal sensing can achieve comprehensive results in such a system is shown in Figure 4.

4.1. Data preprocessing and feature engineering

Before ML models can be trained, raw bioprinting data require preprocessing to remove noise, standardize formats, and extract relevant features.[12,23] While a summary of common methods has been provided in Table 1, the specific approach is highly dependent on the data type and research objective. For imaging data, which includes microscopy and high-content screening, the process often begins with image preprocessing steps, such as denoising, normalization, and artifact removal, to ensure data quality.[130,131] This is followed by segmentation to isolate biological entities, such as cells, nuclei, and organoids.

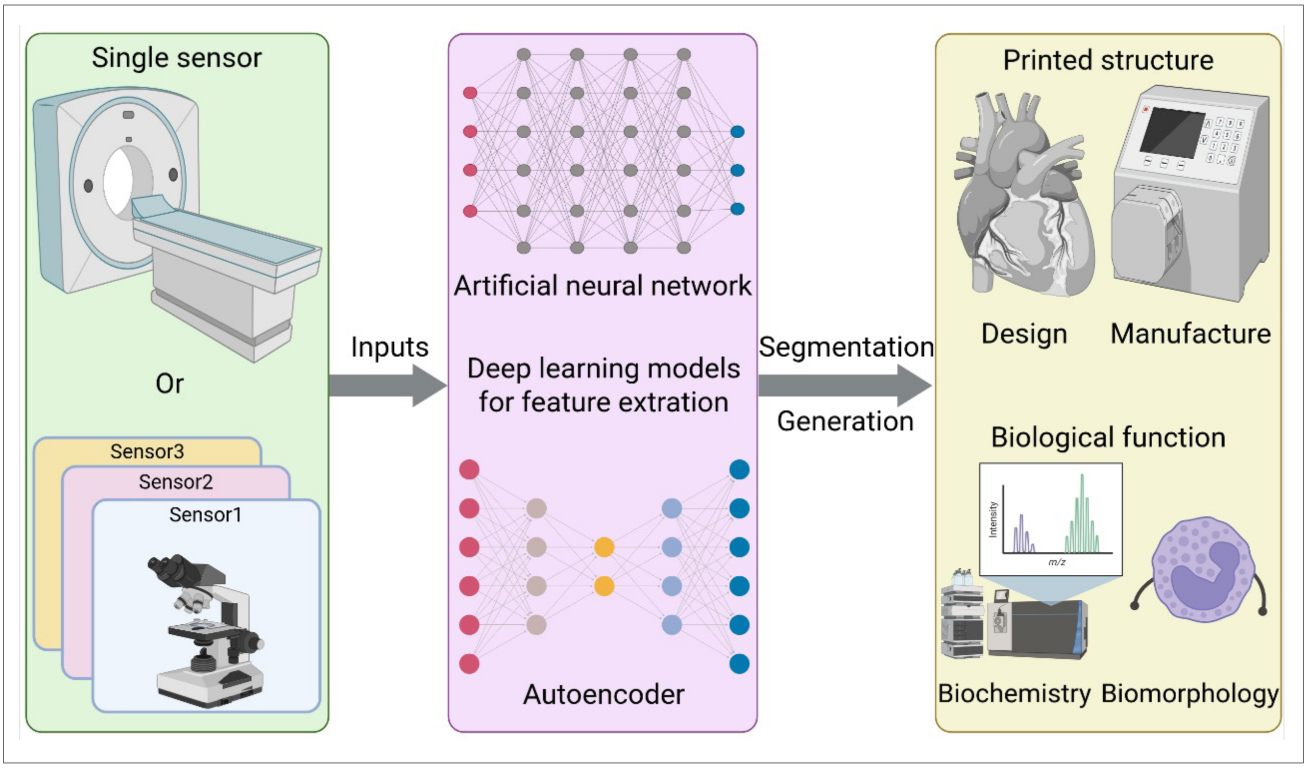

Figure 4. An artificial intelligence-driven multi-modal sensing pipeline for achieving comprehensive results in bioprinting. The workflow starts with data collection from diverse sensors and bioprinter logs. In data preprocessing and feature extraction, these data streams are processed by deep learning models to extract key features. The machine learning modeling step uses these features to predict important outcomes. Finally, in bioprinting process optimization, the model's predictions are used to provide real-time feedback for autonomous adjustments to the bioprinting process, ensuring a closed-loop system for continuous improvement.

Feature engineering then quantifies these elements into morphological descriptors, such as size, shape, porosity, and cellular distribution.

For sensor-based process data, such as time-series readouts of nozzle pressure and temperature, advanced techniques, including sensor fusion and time-series analysis, are used to integrate disparate signals.[132,133] These processed data streams are aligned with experimental metadata to enable the modeling of complex, non-linear relationships, and the detection of anomalies for predictive maintenance. Similarly, with omics datasets, which are often high-dimensional, specialized pipelines are required. After initial quality control and normalization, techniques like dimensionality reduction are crucial to mitigate redundancy and focus on the most informative genes or proteins.[134,135] Feature engineering—whether handcrafted or automatically learned through DL—plays a key role in transforming raw bioprinting data into informative representations that capture both biological and manufacturing variables.[136,137] These refined features form the basis for robust ML models that can accurately predict a wide range of outcomes.

4.2. Model development for prediction and optimization

Machine learning models can serve multiple purposes within bioprinting workflows.[138] Predictive models are trained to forecast biological responses, such as drug efficacy or toxicity, based on construct features and experimental parameters.[139,140] Optimization models, often employing reinforcement learning or Bayesian optimization, can identify optimal combinations of printing parameters, bioink compositions, and culture conditions to achieve desired outcomes.[128,141] In addition, generative models, such as variational autoencoders and generative adversarial networks, can be used to design novel tissue architectures with tailored functional properties.[136,142] The choice of algorithm depends on the prediction target, dataset size, and desired interpretability.

4.3. Closed-loop feedback and real-time adaptation

A defining feature of truly "smart" bioprinting systems is the implementation of closed-loop feedback, where ML models continuously analyze experimental data and adjust bioprinting parameters in real time.[143,144] For example, if imaging data indicate uneven cell distribution or structural collapse, the system can automatically recalibrate nozzle pressure, printing speed, or crosslinking intensity to correct the issue in subsequent prints.[25,145] This adaptive control reduces variability, improves reproducibility, and minimizes material waste. Real-time integration requires seamless communication among ML algorithms, printer control software, and data acquisition systems, supported by low-latency computation.[146]

4.4. Case studies and emerging applications

The integration of ML into bioprinting is moving beyond theoretical concepts and is being applied in concrete research to enhance the entire workflow. For example, ML models are now used to predict optimal printing parameters, such as extrusion pressure and laser power, to minimize trial-and-error and material waste.[147,148] Furthermore, AI-driven image analysis provides real-time feedback on construct fidelity and cell viability, allowing for immediate process adjustments to ensure quality control.[121] These advancements in process optimization are paving the way for fully automated and intelligent biomanufacturing. Table 3 provides a summary of representative studies, detailing the specific bioprinting modalities, constructs, and ML approaches used in these applications.

4.5. Integration challenges and technical considerations

While the potential benefits are substantial, several barriers hinder seamless ML–bioprinting integration. Data heterogeneity across imaging platforms, bioink formulations, and cell sources complicates model training and transferability.[26] The need for large, high-quality labeled datasets can be a bottleneck, particularly for rare disease models and patient-specific constructs. Additionally, ensuring that ML models are interpretable and compliant with regulatory standards is essential for eventual clinical translation.[152] Overcoming these challenges requires not only advances in algorithmic development but also the standardization of bioprinting protocols, improved interoperability between hardware and software, and the adoption of open data sharing practices.

5. Bridging machine learning and bioprinting for drug screening: opportunities and roadmap

The integration of ML with bioprinting offers transformative opportunities for drug screening by enabling data-driven, predictive, and automated experimentation. By combining the precise fabrication capabilities of bioprinting with ML's ability to extract patterns and make predictions from complex datasets, researchers can move beyond conventional trial-and-error approaches and establish more efficient and reproducible workflows. This synergy allows for not only the optimization of tissue construct design and printing parameters but also the anticipation of functional outcomes, such as drug response, toxicity, and phenotypic changes. As a conceptual roadmap for this integrated workflow, Figure 5 highlights the opportunities

Table 3. Representative studies on the integration of machine learning with bioprinting

Dataset source	ML method	Bioprinting modality	Construct type/ model	Main findings	References
A dataset of 48 prints with systematically varied print parameters	HML with LASSO	Extrusion-based bioprinting	3D alginate hydrogel features	Developed an HML framework to predict dominant build parameters for high-fidelity 3D prints, reducing the need for iterative testing and identifying process maps for optimization.	125
Data collected from 75 published papers on extrusion-based bioprinting	Supervised regression and classification models	Extrusion-based bioprinting	Cell-laden alginate and gelatin composite filaments	ML models trained on literature data can predict printing outcomes (cell viability, filament diameter, extrusion pressure) and show the potential for optimizing bioprinting experimental design.	149
Patient-derived glioblastomas and tumor-associated macrophages bioprinted into 3D models	Multi-algorithm ML, including a weighted ensemble model	Light-based bioprinting	3D-bioprinted patient-derived glioma tissues (complex multicellular models)	Developed an integrated workflow of 3D bioprinting and ML to predict glioma treatment responses, with the ensemble model outperforming individual algorithms and identifying promising compounds.	60
A dataset of cellular droplets (over 50 printed simultaneously)	Multilayer perceptron and decision tree	Droplet-based bioprinting	Cellular droplets	Developed an ML-enhanced platform to optimize five key printing parameters and predict cellular droplet size with high accuracy, enabling reproducible and scalable organoid production.	26
Experimental data from GelMA and HAMA bioinks	Bayesian optimization	Extrusion-based bioprinting	3D scaffolds from GelMA and HAMA bioinks	Bayesian optimization drastically reduced the number of experiments needed to identify optimal print parameters, enabling the quantitative assessment of printability for reproducible scaffold fabrication.	27
Experimental data from the development of a chitosan–gelatin–agarose ink	Bayesian optimization	Extrusion-based bioprinting	3D complex tissue constructs from an optimized chitosan–gelatin–agarose biomaterial ink	Employed ML to assist in developing an optimized biomaterial ink with suitable printability, rheological properties, and biocompatibility for fabricating 3D tissue constructs.	150
224 datapoints from 3D printing experiments; 9 CAD images; a self-designed "complexity index"	Gradient boosting regression and eight other ML algorithms	Extrusion-based bioprinting	Single-layer hydrogel filaments and multilayer lattice constructs	GBR achieved the best prediction accuracy for filament morphology; the application of eight ML methods facilitated parameter optimization; combining ML with extrusion printing reduced experimental iterations and improved reproducibility and fidelity.	147
Experimental dataset of extrusion-based bioprinting with NIH/3T3 fibroblasts, varying pressure, speed, and nozzle diameter	Support vector regression	Extrusion-based bioprinting	3D-printed objects based on CAD images	Developed an ML-embedded graphical user interface to optimize printing parameters and predict print outcome, reducing trial-and-error and waste.	151
High-throughput droplet images and an extensive dataset generated by the bioprinting platform	Supervised ML models, including RF, ANN, and others	Droplet-based bioprinting	Cellular droplets and 3D microtissues	Developed an ML-driven platform to predict and control cellular droplet volume, promising to advance the mass production of organoids and microtissues with precise volume control.	129

Abbreviations: ANN, artificial neural network; CAD, computer-aided design; GelMA, gelatin methacryloyl; GBR, gradient boosting regression; HAMA, hyaluronic acid methacrylate; HML, hierarchical machine learning; LASSO, least absolute shrinkage and selection operator; ML, machine learning; RF, random forest.

for combining bioprinting and ML to revolutionize drug screening.

In the short term, ML can be employed to optimize bioprinting experimental designs, improving both efficiency and data utilization. Predictive models, such as random forests, which are trained on historical bioprinting and assay data, can guide the selection of bioink formulations, printing parameters (e.g., pressure,

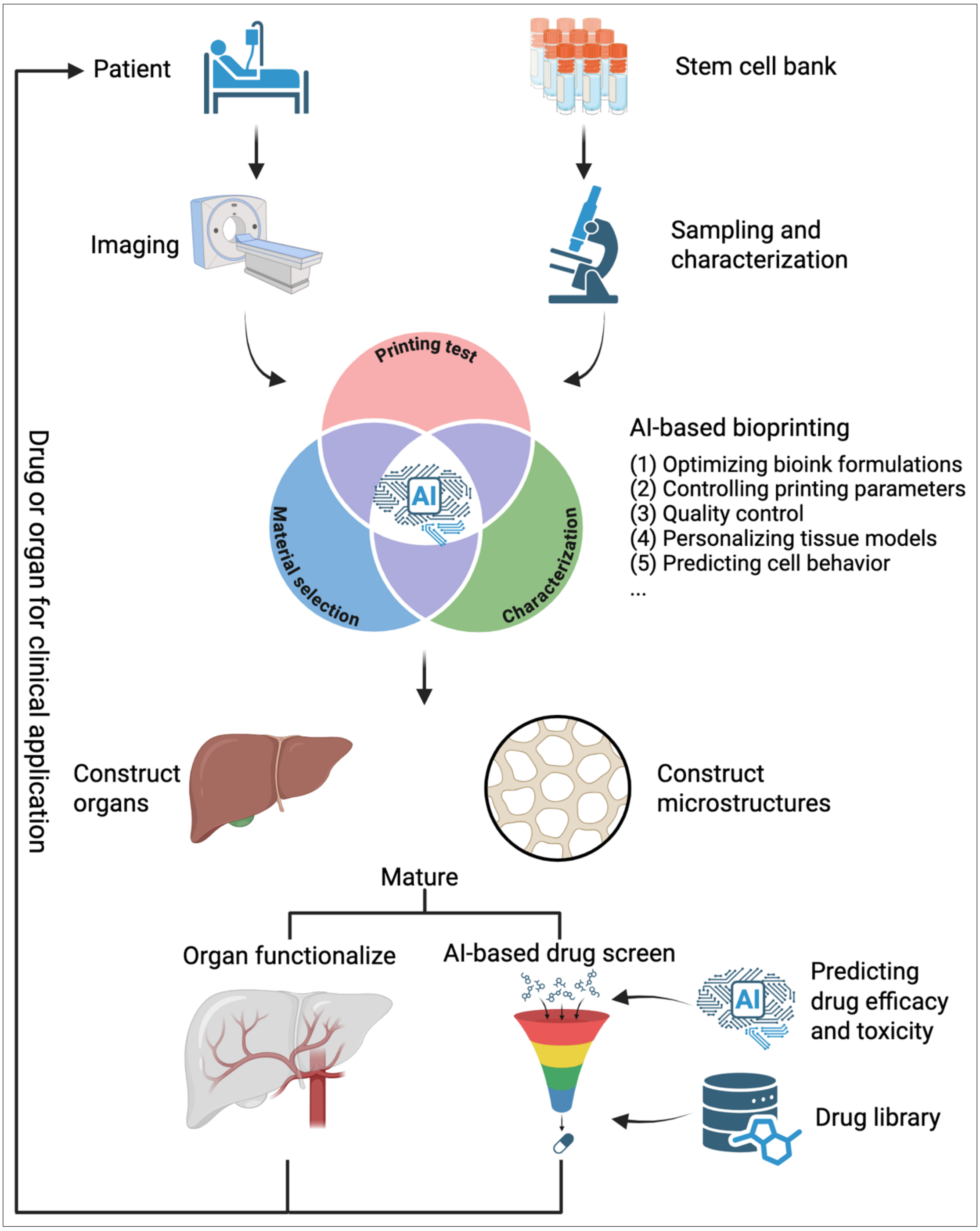

Figure 5. An artificial intelligence (AI)-powered drug screening workflow integrating bioprinting and machine learning (ML). This framework outlines a comprehensive data-driven approach, from generating multi-modal data with 3D bioprinting and high-throughput screening to using AI/ML models for predictive analysis. The workflow includes a feedback loop that informs new experimental designs, enabling efficient and iterative drug discovery.

speed, and nozzle diameter), and culture conditions, reducing the number of iterations needed to achieve high-quality constructs.[21] This approach maximizes the informational content of each experiment and supports the rapid generation of reproducible tissue models suitable for downstream drug screening applications.

In the medium term, closed-loop platforms can be developed in which ML algorithms continuously monitor data from in-line sensors (e.g., cameras for real-time image analysis and embedded pressure sensors), viability assays, and biochemical readouts, and then adjust printing parameters in real time.[150] By integrating predictive models for toxicity or drug response into this feedback system, bioprinting pipelines can be dynamically tuned to produce tissue constructs with consistent properties and functional readouts. Such adaptive systems will enhance reproducibility, enable multi-day experimental runs, and reduce variability in pharmacological testing. Additionally, the development of more interpretable AI models will be crucial to facilitate regulatory approval and clinical translation.

Looking toward the long term, the combination of ML and bioprinting could facilitate the development of truly personalized and disease-specific tissue constructs. Advances in bioink design informed by patient-derived data, along with AI-driven tissue modeling, can allow for the generation of "digital twins" or *in silico* models that recapitulate individual genetic or pathological contexts.[153,154] These approaches will support patient-specific drug testing, the identification of optimal therapeutic regimens, and the exploration of complex multi-tissue interactions. Ultimately, AI-guided bioprinting can enable the *in silico* design and *in vitro* fabrication of highly predictive tissue models, forming a new paradigm for preclinical drug development.

Several recent studies have demonstrated the feasibility of integrating ML into bioprinting workflows for drug screening and toxicity testing. For example, in a study on nephrotoxicity testing, researchers used bioprinted renal spheroids and a DL approach to automatically analyze microscopic images. The study found that the bioprinted spheroids showed enhanced sensitivity to cisplatin, with an inhibitory concentration leading to 50% cell death (IC_{50}) of 9 ± 3 μM compared to 17 ± 2 μM for conventional monolayers. Furthermore, the DL algorithm was able to distinguish between no, mild, and severe treatment effects with a balanced accuracy of 78.7%.[81] Similarly, in a study on glioma, researchers integrated 3D bioprinting and multi-algorithm ML to assess treatment responses. The bioprinted patient-derived glioma tissues successfully mimicked the molecular properties and drug responses of native tumors, with the GlioML ensemble model achieving a median R^2 value of 0.83 for World Health Organization grade IV gliomas, significantly outperforming individual algorithms. This model also showed high predictive accuracy for recurrent glioblastoma, with an R^2 value as high as 0.94, validating the use of bioprinted models and computational predictors for robust, gene-expression-based drug screening.[60] Another study showcased how to leverage bioprinting and ML for drug screening at the single-organoid level,[8] successfully identifying organoids that were transiently or persistently sensitive or resistant to specific therapies. The study's XGBoost classifier, used to filter organoid data, achieved a high cross-validation score of 93.1 ± 1.3% with an area under the curve of 0.966 ± 0.020. This approach successfully quantified drug responses, revealing, for example, that when treated with 10 μM neratinib, only 4.5% of MCF-7 cell clusters grew, while in another cell line (BT-474) treated with 10 μM lapatinib, 73.7% of cell clusters lost mass. This ability to quantify intra-sample heterogeneity highlights the platform's potential for robust drug screening.

Beyond these direct drug screening applications, the convergence of bioprinting and AI technology also enables other critical biomedical functions that indirectly support therapeutic development. In the early stages of drug discovery, AI plays a crucial role in predicting the absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties of drugs. For example, a study developed AI-based ADMET models that can rapidly and efficiently predict the properties of molecules using computational methods rather than physical bioprinting.[155] Moreover, this synergy opens up new avenues for diagnostics that inform therapeutic decisions. One study combined acoustic bioprinting with AI-assisted spectroscopy for the high-throughput identification of bacteria in blood.[156] This platform is indirectly linked to drug therapy by enabling rapid pathogen identification—a critical first step in guiding the selection of appropriate antimicrobial drugs and combating antibiotic resistance. This highlights the potential for this synergistic technology to streamline not only drug development but also the targeted application of existing treatments.

6. Challenges and future perspectives

Integrating ML with bioprinting offers significant promise for drug screening and toxicity testing, but several barriers remain. Data heterogeneity—arising from differences in imaging systems, bioink formulations, and cell sources—limits model generalizability, while the scarcity of large, high-quality labeled datasets hinders robust algorithm training. Technical integration requires custom interfaces and real-time processing pipelines, while biological complexity means that even advanced models struggle to replicate multi-tissue interactions or long-term drug effects.[14,157] Concerns over interpretability, reproducibility, and regulatory compliance further slow adoption. Notably, despite the conceptual synergy, there is still a lack of direct, systematic research focusing on the integration of ML with bioprinting specifically for drug discovery and preclinical testing; most studies remain either proof-of-concept or focused separately on each field.

Future advances can address these limitations. Multi-modal data fusion will allow the integration of imaging, omics, biomechanical, and environmental datasets into unified predictive frameworks, while explainable AI can enhance trust and regulatory acceptance. Edge computing and embedded AI may enable real-time, on-device analysis, improving closed-loop bioprinting control. Meanwhile, digital twin models can simulate and optimize experiments before printing, saving time and resources. Standardized protocols, shared databases, and interoperable software will be critical for scalability. Through sustained interdisciplinary collaboration, ML-enhanced bioprinting platforms can revolutionize preclinical testing by accelerating discovery, reducing costs, and enabling personalized predictive drug evaluation.

7. Conclusion

In conclusion, the convergence of ML and 3D bioprinting presents a transformative paradigm for drug discovery and toxicology testing. By enabling data-driven optimization of bioprinting processes and providing a powerful framework for analyzing complex biological readouts, ML-augmented bioprinting systems are poised to address key limitations of conventional preclinical models. This review has demonstrated how diverse ML methods can be applied across the entire bioprinting workflow, from predicting material printability and optimizing process parameters to enhancing the predictive accuracy of drug response in physiologically relevant 3D tissue models. The inclusion of specific quantitative results from recent case studies underscores the tangible benefits of this integration, moving the field beyond conceptual discussions and towards verifiable, evidence-based applications. While significant challenges remain, particularly in the standardization of data collection and the development of more robust, universal models, the rapid advancement in both fields points to a promising future. The continued synergy between ML and bioprinting holds the potential to accelerate the development of personalized, effective, and safer therapeutics, ultimately bridging the gap between preclinical research and clinical success.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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References

1. Schlander M, Hernandez-Villafuerte K, Cheng CY, Mestre-Ferrandiz J, Baumann M. How much does it cost to research and develop a new drug? A systematic review and assessment. *Pharmacoeconomics*. 2021;39(11): 1243-1269.
doi: 10.1007/s40273-021-01065-y
2. Rennane S, Baker L, Mulcahy A. Estimating the cost of industry investment in drug research and development: a review of methods and results. *Inquiry*. 2021;58:00469580211059731.
doi: 10.1177/00469580211059731
3. Esposito A, Ferraresi A, Vallino L, Garavaglia B, Dhanasekaran DN, Isidoro C. Three-dimensional *in vitro* cell cultures as a feasible and promising alternative to two-dimensional and animal models in cancer research. *Int J Biol Sci*. 2024;20(13):5293-5311.

doi: 10.7150/ijbs.96469

4. Urzì O, Gasparro R, Costanzo E, *et al*. Three-dimensional cell cultures: the bridge between *in vitro* and *in vivo* models. *IJMS*. 2023;24(15):12046. doi: 10.3390/ijms241512046
5. Kreutzer FP, Meinecke A, Schmidt K, Fiedler J, Thum T. Alternative strategies in cardiac preclinical research and new clinical trial formats. *Cardiovasc Res*. 2022;118(3):746-762. doi: 10.1093/cvr/cvab075
6. Han X, Cai C, Deng W, *et al*. Landscape of human organoids: ideal model in clinics and research. *Innovation (Camb)*. 2024;5(3):100620. doi: 10.1016/j.xinn.2024.100620
7. Cacciamali A, Villa R, Dotti S. 3D cell cultures: evolution of an ancient tool for new applications. *Front Physiol*. 2022;13:836480. doi: 10.3389/fphys.2022.836480
8. Tebon PJ, Wang B, Markowitz AL, *et al*. Drug screening at single-organoid resolution via bioprinting and interferometry. *Nat Commun*. 2023;14(1):3168. doi: 10.1038/s41467-023-38832-8
9. Soheilmoghaddam F, Rumble M, Cooper-White J. High-throughput routes to biomaterials discovery. *Chem Rev*. 2021;121(18):10792-10864. doi: 10.1021/acs.chemrev.0c01026
10. Engel M, Belfiore L, Aghaei B, Sutija M. Enabling high throughput drug discovery in 3D cell cultures through a novel bioprinting workflow. *SLAS Technol*. 2022;27(1):32-38. doi: 10.1016/j.slast.2021.10.002
11. Johnson PA, Menegatti S, Chambers AC, *et al*. A rapid high throughput bioprinted colorectal cancer spheroid platform for in vitro drug- and radiation-response. *Biofabrication*. 2023;15(1):014103. doi: 10.1088/1758-5090/ac999f
12. Da Silva VA, Sharma R, Shteinberg E, *et al*. Machine learning approaches to 3D models for drug screening. *Biomedi Mater Dev*. 2024;2(2):695-720. doi: 10.1007/s44174-023-00142-4
13. Kim MH, Singh YP, Celik N, *et al*. High-throughput bioprinting of spheroids for scalable tissue fabrication. *Nat Commun*. 2024;15(1):10083. doi: 10.1038/s41467-024-54504-7
14. Mazzocchi A, Soker S, Skardal A. 3D bioprinting for high-throughput screening: drug screening, disease modeling, and precision medicine applications. *Appl Phys Rev*. 2019;6(1):011302. doi: 10.1063/1.5056188
15. Huskin G, Chen J, Davis T, Jun HW. Tissue-engineered 3D in vitro disease models for high-throughput drug screening. *Tissue Eng Regen Med*. 2023;20(4):523-538. doi: 10.1007/s13770-023-00522-3
16. Wang X, Luo Y, Ma Y, Wang P, Yao R. Converging bioprinting and organoids to better recapitulate the tumor microenvironment. *Trends Biotechnol*. 2024;42(5): 648-663. doi: 10.1016/j.tibtech.2023.11.006
17. Tofani LB, Avelino TM, De Azevedo RJ, *et al*. Biofabricated 3D intestinal models as an alternative to animal-based approaches for drug toxicity assays. *Tissue Eng Regen Med*. 2025;22(2):181-194. doi: 10.1007/s13770-024-00694-6
18. Kesti M, Fisch P, Pensalfini M, Mazza E, Zenobi-Wong M. Guidelines for standardization of bioprinting: a systematic study of process parameters and their effect on bioprinted structures. *BioNanoMaterials*. 2016;17(3-4):193-204. doi: 10.1515/bnm-2016-0004
19. Putrama IM, Martinek P. Heterogeneous data integration: challenges and opportunities. *Data Brief*. 2024;56:110853. doi: 10.1016/j.dib.2024.110853
20. Rickert CA, Lieleg O. Machine learning approaches for biomolecular, biophysical, and biomaterials research. *Biophys Rev*. 2022;3(2):021306. doi: 10.1063/5.0082179
21. Yu J, Yao D, Wang L, Xu M. Machine learning in predicting and optimizing polymer printability for 3D bioprinting. *Polymers (Basel)*. 2025;17(13):1873. doi: 10.3390/polym17131873
22. Rafieyan S, Ansari E, Vasheghani-Farahani E. A practical machine learning approach for predicting the quality of 3D (bio)printed scaffolds. *Biofabrication*. 2024;16(4):045014. doi: 10.1088/1758-5090/ad6374
23. Sun J, Yao K, An J, Jing L, Huang K, Huang D. Machine learning and 3D bioprinting. *IJB*. 2024;9(4):717. doi: 10.18063/ijb.717
24. Ahmed E, Mulay P, Ramirez C, Tirado-Mansilla G, Cheong E, Gormley AJ. Mapping biomaterial complexity by machine learning. *Tissue Eng Part A*. 2024;30(19-20):662-680. doi: 10.1089/ten.tea.2024.0067
25. Freeman S, Calabro S, Williams R, Jin S, Ye K. Bioink formulation and machine learning-empowered bioprinting optimization. *Front Bioeng Biotechnol*. 2022;10:913579. doi: 10.3389/fbioe.2022.913579
26. Shin J, Kang R, Hyun K, *et al*. Machine learning-enhanced optimization for high-throughput precision in cellular droplet bioprinting. *Adv Sci*. 2025;12(20):2412831. doi: 10.1002/advs.202412831
27. Ruberu K, Senadeera M, Rana S, *et al*. Coupling machine learning with 3D bioprinting to fast track optimisation of extrusion printing. *Appl Mater Today*. 2021;22:100914. doi: 10.1016/j.apmt.2020.100914
28. Vitacolonna M, Bruch R, Schneider R, *et al*. A spheroid whole mount drug testing pipeline with machine-learning based image analysis identifies cell-type specific differences

in drug efficacy on a single-cell level. *BMC Cancer*. 2024;24(1):1542.
doi: 10.1186/s12885-024-13329-9

29. Fritschen A, Lindner N, Scholpp S, *et al*. High-scale 3D-bioprinting platform for the automated production of vascularized organs-on-a-chip. *Adv Healthc Mater*. 2024;13(17):2304028.
doi: 10.1002/adhm.202304028

30. Gu Z, Fu J, Lin H, He Y. Development of 3D bioprinting: from printing methods to biomedical applications. *Asian J Pharma Sci*. 2020;15(5):529-557.
doi: 10.1016/j.ajps.2019.11.003

31. Santoni S, Gugliandolo SG, Sponchioni M, Moscatelli D, Colosimo BM. 3D bioprinting: current status and trends—a guide to the literature and industrial practice. *Bio-des Manuf*. 2022;5(1):14-42.
doi: 10.1007/s42242-021-00165-0

32. Ramiah P, Du Toit LC, Choonara YE, Kondiah PPD, Pillay V. Hydrogel-based bioinks for 3D bioprinting in tissue regeneration. *Front Mater*. 2020;7:76.
doi: 10.3389/fmats.2020.00076

33. Chen XB, Fazel Anvari-Yazdi A, Duan X, *et al*. Biomaterials / bioinks and extrusion bioprinting. *Bioact Mater*. 2023;28:511-536.
doi: 10.1016/j.bioactmat.2023.06.006

34. Ng WL, Lee JM, Yeong WY, Win Naing M. Microvalve-based bioprinting – process, bio-inks and applications. *Biomater Sci*. 2017;5(4):632-647.
doi: 10.1039/C6BM00861E

35. Zhang J, Wehrle E, Rubert M, Müller R. 3D Bioprinting of Human Tissues: Biofabrication, Bioinks, and Bioreactors. *IJMS*. 2021;22(8):3971.
doi: 10.3390/ijms22083971

36. Datta P, Barui A, Wu Y, Ozbolat V, Moncal KK, Ozbolat IT. Essential steps in bioprinting: from pre- to post-bioprinting. *Biotechnol Adv*. 2018;36(5):1481-1504.
doi: 10.1016/j.biotechadv.2018.06.003

37. Choi JW, Kang SJ, Choi JI, Kwack K, Kim M. Role of Nuclear-receptor-related 1 in the synergistic neuroprotective effect of umbilical cord blood and erythropoietin combination therapy in hypoxic ischemic encephalopathy. *IJMS*. 2022;23(5):2900.
doi: 10.3390/ijms23052900

38. Murphy SV, De Coppi P, Atala A. Opportunities and challenges of translational 3D bioprinting. *Nat Biomed Eng*. 2020;4(4):370-380.
doi: 10.1038/s41551-019-0471-7

39. Tarassoli SP, Jessop ZM, Jovic T, Hawkins K, Whitaker IS. Candidate bioinks for extrusion 3D bioprinting—a systematic review of the literature. *Front Bioeng Biotechnol*. 2021;9:616753.
doi: 10.3389/fbioe.2021.616753

40. Yu J, Park SA, Kim WD, *et al*. Current advances in 3D bioprinting technology and its applications for tissue engineering. *Polymers*. 2020;12(12):2958.
doi: 10.3390/polym12122958

41. Panwar A, Tan LP. Current status of bioinks for micro-extrusion-based 3D bioprinting. *Molecules*. 2016;21(6):685.
doi: 10.3390/molecules21060685

42. Kong Z, Wang X. Bioprinting technologies and bioinks for vascular model establishment. *IJMS*. 2023;24(1):891.
doi: 10.3390/ijms24010891

43. Yu C, Schimelman J, Wang P, *et al*. Photopolymerizable biomaterials and light-based 3D printing strategies for biomedical applications. *Chem Rev*. 2020;120(19):10695-10743.
doi: 10.1021/acs.chemrev.9b00810

44. Li W, Wang M, Ma H, Chapa-Villarreal FA, Lobo AO, Zhang YS. Stereolithography apparatus and digital light processing-based 3D bioprinting for tissue fabrication. *iScience*. 2023;26(2):106039.
doi: 10.1016/j.isci.2023.106039

45. Wang Z, Abdulla R, Parker B, Samanipour R, Ghosh S, Kim K. A simple and high-resolution stereolithography-based 3D bioprinting system using visible light crosslinkable bioinks. *Biofabrication*. 2015;7(4):045009.
doi: 10.1088/1758-5090/7/4/045009

46. Strauß S, Schroth B, Hubbuch J. Evaluation of the reproducibility and robustness of extrusion-based bioprinting processes applying a flow sensor. *Front Bioeng Biotechnol*. 2022;10:831350.
doi: 10.3389/fbioe.2022.831350

47. Pössl A, Hartzke D, Schlupp P, Runkel FE. Optimized cell mixing facilitates the reproducible bioprinting of constructs with high cell viability. *Appl Sci*. 2021;12(1):326.
doi: 10.3390/app12010326

48. Grijalva Garces D, Strauß S, Gretzinger S, *et al*. On the reproducibility of extrusion-based bioprinting: round robin study on standardization in the field. *Biofabrication*. 2023;16(1):015002.
doi: 10.1088/1758-5090/acfe3b

49. Strauß S, Grijalva Garces D, Hubbuch J. Analytics in extrusion-based bioprinting: standardized methods improving quantification and comparability of the performance of bioinks. *Polymers*. 2023;15(8):1829.
doi: 10.3390/polym15081829

50. Schwab A, Levato R, D'Este M, Piluso S, Eglin D, Malda J. Printability and shape fidelity of bioinks in 3D bioprinting. *Chem Rev*. 2020;120(19):11028-11055.
doi: 10.1021/acs.chemrev.0c00084

51. Upton A, Mylona A, Zimbitas G. Utilising design of experiment to design an optimised bioink for 3D bioprinting. *J Mater Sci*. 2025;60(25):10467-10477.
doi: 10.1007/s10853-025-11076-1

52. Chen H, Liu Y, Balabani S, Hirayama R, Huang J. Machine learning in predicting printable biomaterial formulations for direct ink writing. *Research*. 2023;6:0197. doi: 10.34133/research.0197

53. Yang Y, Jia Y, Yang Q, Xu F. Engineering bio-inks for 3D bioprinting cell mechanical microenvironment. *IJB*. 2022;9(1):632. doi: 10.18063/ijb.v9i1.632

54. An J, Chua CK, Mironov V. Application of machine learning in 3D bioprinting: focus on development of big data and digital twin. *IJB*. 2024;7(1):342. doi: 10.18063/ijb.v7i1.342

55. Maharjan S, Ma C, Singh B, *et al*. Advanced 3D imaging and organoid bioprinting for biomedical research and therapeutic applications. *Adv Drug Deliv Rev*. 2024;208:115237. doi: 10.1016/j.addr.2024.115237

56. Shin J, Lee Y, Li Z, Hu J, Park SS, Kim K. Optimized 3D bioprinting technology based on machine learning: a review of recent trends and advances. *Micromachines*. 2022;13(3):363. doi: 10.3390/mi13030363

57. Wu D, Xu C. Predictive modeling of droplet formation processes in inkjet-based bioprinting. *J Manuf Sci Eng*. 2018;140(10):101007. doi: 10.1115/1.4040619

58. Sarah R, Rohauer R, Schimmelpfennig K, Limon SM, Lewis CL, Habib A. Data-driven optimization of bioink formulations for extrusion-based bioprinting: a predictive modeling approach. *J Manuf Sci Eng*. 2025;147(10):101001. doi: 10.1115/1.4069041

59. Nadernezhad A, Groll J. Machine learning to explain printability induced by rheology additives. ChemRxiv. 2021. doi: 10.26434/chemrxiv-2021-41mn8

60. Tang M, Jiang S, Huang X, *et al*. Integration of 3D bioprinting and multi-algorithm machine learning identified glioma susceptibilities and microenvironment characteristics. *Cell Discov*. 2024;10(1):39. doi: 10.1038/s41421-024-00650-7

61. Choi YM, Na D, Yoon G, *et al*. Prediction of patient drug response via 3D bioprinted gastric cancer model utilized patient-derived tissue laden tissue-specific bioink. *Adv Sci (Weinh)*. 2025;12(10):e2411769. doi: 10.1002/advs.202411769

62. Sarah R, Schimmelpfennig K, Rohauer R, Lewis CL, Limon SM, Habib A. Characterization and machine learning-driven property prediction of a novel hybrid hydrogel bioink considering extrusion-based 3D bioprinting. *Gels*. 2025;11(1):45. doi: 10.3390/gels11010045

63. Habib A, Sarah R, Tuladhar S, Khoda B, Limon SM. Modulating rheological characteristics of bio-ink with component weight and shear rate for enhanced bioprinted scaffold fidelity. *Bioprinting*. 2024;38:e00332. doi: 10.1016/j.bprint.2024.e00332

64. Janani G, Priya S, Dey S, Mandal BB. Mimicking native liver lobule microarchitecture in vitro with parenchymal and non-parenchymal cells using 3D bioprinting for drug toxicity and drug screening applications. *ACS Appl Mater Interfaces*. 2022;14(8):10167-10186. doi: 10.1021/acsami.2c00312

65. Szűcs D, Fekete Z, Guba M, *et al*. Toward better drug development: three-dimensional bioprinting in toxicological research. *IJB*. 2023;9(2):663. doi: 10.18063/ijb.v9i2.663

66. Royo F, Garcia-Vallicrosa C, Azparren-Angulo M, Bordanaba-Florit G, Lopez-Sarrio S, Falcon-Perez JM. Three-dimensional hepatocyte spheroids: model for assessing chemotherapy in hepatocellular carcinoma. *Biomedicines*. 2024;12(6):1200. doi: 10.3390/biomedicines12061200

67. Maloney E, Clark C, Sivakumar H, *et al*. Immersion bioprinting of tumor organoids in multi-well plates for increasing chemotherapy screening throughput. *Micromachines*. 2020;11(2):208. doi: 10.3390/mi11020208

68. Parodi I, Di Lisa D, Pastorino L, Scaglione S, Fato MM. 3D bioprinting as a powerful technique for recreating the tumor microenvironment. *Gels*. 2023;9(6):482. doi: 10.3390/gels9060482

69. Ma Y, Deng B, He R, Huang P. Advancements of 3D bioprinting in regenerative medicine: exploring cell sources for organ fabrication. *Heliyon*. 2024;10(3):e24593. doi: 10.1016/j.heliyon.2024.e24593

70. Langer EM, Allen-Petersen BL, King SM, *et al*. Modeling tumor phenotypes in vitro with three-dimensional bioprinting. *Cell Rep*. 2019;26(3):608-623.e6. doi: 10.1016/j.celrep.2018.12.090

71. Estermann M, Bisig C, Septiadi D, Petri-Fink A, Rothen-Rutishauser B. Bioprinting for human respiratory and gastrointestinal in vitro models. *Methods Mol Biol*. 2020;2140:199-215. doi: 10.1007/978-1-0716-0520-2_13

72. Schmidt K, Berg J, Roehrs V, Kurreck J, Al-Zeer MA. 3D-bioprinted HepaRG cultures as a model for testing long term aflatoxin B1 toxicity in vitro. *Toxicol Rep*. 2020;7:1578-1587. doi: 10.1016/j.toxrep.2020.11.003

73. Ide I, Nagao E, Kajiyama S, Mizoguchi N. A novel evaluation method for determining drug-induced hepatotoxicity using 3D bio-printed human liver tissue. *Toxicol Mech Methods*. 2020;30(3):189-196. doi: 10.1080/15376516.2019.1686795

74. Ort C, Chen Y, Ghagre A, Ehrlicher A, Moraes C. Bioprintable, stiffness-tunable collagen-alginate microgels for increased throughput 3D cell culture studies. *ACS Biomater Sci Eng*. 2021;7(6):2814-2822. doi: 10.1021/acsbiomaterials.1c00129

75. Lawlor KT, Vanslambrouck JM, Higgins JW, *et al.* Cellular extrusion bioprinting improves kidney organoid reproducibility and conformation. *Nat Mater*. 2021;20(2):260-271. doi: 10.1038/s41563-020-00853-9

76. Bouwmeester MC, Bernal PN, Oosterhoff LA, *et al.* Bioprinting of human liver-derived epithelial organoids for toxicity studies. *Macromol Biosci*. 2021;21(12):e2100327. doi: 10.1002/mabi.202100327

77. Kang HK, Sarsenova M, Kim DH, *et al*. Establishing a 3D *in vitro* hepatic model mimicking physiologically relevant to *in vivo* state. *Cells*. 2021;10(5):1268. doi: 10.3390/cells10051268

78. Datta P, Wu Y, Yu Y, Moncal KK, Ozbolat IT. A scaffold free 3D bioprinted cartilage model for in vitro toxicology. *Methods Mol Biol*. 2021;2147:175-183. doi: 10.1007/978-1-0716-0611-7_15

79. Hong S, Song JM. A 3D cell printing-fabricated HepG2 liver spheroid model for high-content in situ quantification of drug-induced liver toxicity. *Biomater Sci*. 2021;9(17):5939-5950. doi: 10.1039/d1bm00749a

80. Geevarghese R, Somasekharan LT, Bhatt A, Kasoju N, Nair RP. Development and evaluation of a multicomponent bioink consisting of alginate, gelatin, diethylaminoethyl cellulose and collagen peptide for 3D bioprinting of tissue construct for drug screening application. *Int J Biol Macromol*. 2022;207:278-288. doi: 10.1016/j.ijbiomac.2022.02.191

81. Tröndle K, Miotto G, Rizzo L, *et al*. Deep learning-assisted nephrotoxicity testing with bioprinted renal spheroids. *Int J Bioprint*. 2022;8(2):528. doi: 10.18063/ijb.v8i2.528

82. Wang P, Sun L, Li C, *et al*. Study on drug screening multicellular model for colorectal cancer constructed by three-dimensional bioprinting technology. *Int J Bioprint*. 2023;9(3):694. doi: 10.18063/ijb.694

83. Huang B, Wei X, Chen K, Wang L, Xu M. Bioprinting of hydrogel beads to engineer pancreatic tumor-stroma microtissues for drug screening. *Int J Bioprint*. 2023; 9(3):676. doi: 10.18063/ijb.676

84. Fan Z, Wei X, Chen K, Wang L, Xu M. 3D bioprinting of an endothelialized liver lobule-like construct as a tumor-scale drug screening platform. *Micromachines (Basel)*. 2023;14(4):878. doi: 10.3390/mi14040878

85. Yu M, Ni M, Xu F, *et al*. NSUN6-mediated 5-methylcytosine modification of NDRG1 mRNA promotes radioresistance in cervical cancer. *Mol Cancer*. 2024; 23(1):139. doi: 10.1186/s12943-024-02055-2

86. Gu WJ, Liu XX, Shen YW, *et al*. TRIM4 enhances small-molecule-induced neddylated-degradation of CORO1A for triple negative breast cancer therapy. *Theranostics*. 2024;14(18):7023-7041. doi: 10.7150/thno.97662

87. Ali ASM, Berg J, Roehrs V, *et al*. Xeno-free 3D bioprinted liver model for hepatotoxicity assessment. *Int J Mol Sci*. 2024;25(3):1811. doi: 10.3390/ijms25031811

88. do Amaral SR, Amantino CF, Atanasov A, *et al*. Photodynamic therapy as a novel therapeutic modality applying quinizarin-loaded nanocapsules and 3D bioprinting skin permeation for inflammation treatment. *Pharmaceuticals (Basel)*. 2024;17(9):1169. doi: 10.3390/ph17091169

89. Suwannakot P, Zhu L, Tolentino MAK, *et al*. Electrostatically cross-linked bioinks for jetting-based bioprinting of 3D cell cultures. *ACS Appl Bio Mater*. 2024;7(1):269-283. doi: 10.1021/acsabm.3c00849

90. Shrestha S, Lekkala VKR, Acharya P, Kang SY, Vanga MG, Lee MY. Reproducible generation of human liver organoids (HLOs) on a pillar plate platform via microarray 3D bioprinting. *Lab Chip*. 2024;24(10):2747-2761. doi: 10.1039/d4lc00149d

91. Lu TY, Ji Y, Lyu C, *et al*. Bioprinted high cell density liver model with improved hepatic metabolic functions. *Biomaterials*. 2025;320:123256. doi: 10.1016/j.biomaterials.2025.123256

92. Feng T, Wei L, Zhou C, *et al*. Light-based 3D bioprinting of testicular organoid as an in vitro model for reproductive toxicity assessment. *ACS Biomater Sci Eng*. 2025;11(7):4357-4367. doi: 10.1021/acsbiomaterials.5c00414

93. Hu Y, Nicolas GM, Cai Y, Dai X, Ma S. Epidermal and dermal cell-composed organospheres to assess microplastic-induced skin toxicity. *Biomaterials*. 2026;324:123513. doi: 10.1016/j.biomaterials.2025.123513

94. Chandarana C, Sane D, Mishra S, Chaubey A, Gohil U, Prajapati B. Recent advances in bioink research for biomedical applications. *Biomed Mater Dev*. 2025. doi: 10.1007/s44174-025-00478-z

95. Alonzo M, Dominguez E, Alvarez-Primo F, *et al*. A comparative study in the printability of a bioink and 3D models across two bioprinting platforms. *Mater Lett*. 2020;264:127382. doi: 10.1016/j.matlet.2020.127382

96. Mandrycky C, Wang Z, Kim K, Kim DH. 3D bioprinting for engineering complex tissues. *Biotechnol Adv*. 2016;34(4):422-434.
doi: 10.1016/j.biotechadv.2015.12.011

97. Murphy SV, Atala A. 3D bioprinting of tissues and organs. *Nat Biotechnol*. 2014;32(8):773-785.
doi: 10.1038/nbt.2958

98. Yu C, Jiang J. A perspective on using machine learning in 3D bioprinting. *IJB*. 2020;6(1):253.
doi: 10.18063/ijb.v6i1.253

99. Elbadawi M, McCoubrey LE, Gavins FKH, *et al*. Disrupting 3D printing of medicines with machine learning. *Trends Pharmacol Sci*. 2021;42(9):745-757.
doi: 10.1016/j.tips.2021.06.002

100. Visan AI, Negut I. Integrating artificial intelligence for drug discovery in the context of revolutionizing drug delivery. *Life*. 2024;14(2):233.
doi: 10.3390/life14020233

101. Elbadawi M, Muñiz Castro B, Gavins FKH, *et al*. M3DISEEN: a novel machine learning approach for predicting the 3D printability of medicines. *Int J Pharma*. 2020;590: 119837.
doi: 10.1016/j.ijpharm.2020.119837

102. Ong JJ, Castro BM, Gaisford S, *et al*. Accelerating 3D printing of pharmaceutical products using machine learning. *Int J Pharma: X*. 2022;4:100120.
doi: 10.1016/j.ijpx.2022.100120

103. Rahmani AM, Yousefpoor E, Yousefpoor MS, *et al*. Machine learning (ML) in medicine: review, applications, and challenges. *Mathematics*. 2021;9(22):2970.
doi: 10.3390/math9222970

104. Jovel J, Greiner R. An introduction to machine learning approaches for biomedical research. *Front Med*. 2021;8:771607.
doi: 10.3389/fmed.2021.771607

105. Cano G, Garcia-Rodriguez J, Garcia-Garcia A, *et al*. Automatic selection of molecular descriptors using random forest: application to drug discovery. *Expert Syst Appl*. 2017;72:151-159.
doi: 10.1016/j.eswa.2016.12.008

106. Rodríguez-Pérez R, Bajorath J. Evolution of support vector machine and regression modeling in chemoinformatics and drug discovery. *J Comput Aided Mol Des*. 2022;36(5):355-362.
doi: 10.1007/s10822-022-00442-9

107. Gupta R, Srivastava D, Sahu M, Tiwari S, Ambasta RK, Kumar P. Artificial intelligence to deep learning: machine intelligence approach for drug discovery. *Mol Divers*. 2021;25(3):1315-1360.
doi: 10.1007/s11030-021-10217-3

108. Tsuneki M. Deep learning models in medical image analysis. *J Oral Biosci*. 2022;64(3):312-320.
doi: 10.1016/j.job.2022.03.003

109. Chen W, Liu X, Zhang S, Chen S. Artificial intelligence for drug discovery: resources, methods, and applications. *Mol Ther Nucleic Acids*. 2023;31:691-702.
doi: 10.1016/j.omtn.2023.02.019

110. Ravindra Padalkar G, Dinkar Patil S, Mallikarjun Hegadi M, Kailash Jaybhaye N. Drug discovery using generative adversarial network with reinforcement learning. In: *2021 International Conference on Computer Communication and Informatics (ICCCI)*. IEEE; 2021:1-3.
doi: 10.1109/ICCCI50826.2021.9402449

111. Wang J, He R, Wang X, Li H, Lu Y. MCF-DTI: multi-scale convolutional local–global feature fusion for drug–target interaction prediction. *Molecules*. 2025;30(2):274.
doi: 10.3390/molecules30020274

112. Zhang L, Zhang H, Ai H, *et al*. Applications of machine learning methods in drug toxicity prediction. *CTMC*. 2018;18(12):987-997.
doi: 10.2174/1568026618666180727152557

113. Vo AH, Van Vleet TR, Gupta RR, Liguori MJ, Rao MS. An overview of machine learning and big data for drug toxicity evaluation. *Chem Res Toxicol*. 2020;33(1):20-37.
doi: 10.1021/acs.chemrestox.9b00227

114. Parvatikar PP, Patil S, Khaparkhuntikar K, *et al*. Artificial intelligence: machine learning approach for screening large database and drug discovery. *Antiviral Res*. 2023;220:105740.
doi: 10.1016/j.antiviral.2023.105740

115. Judson R, Elloumi F, Setzer RW, Li Z, Shah I. A comparison of machine learning algorithms for chemical toxicity classification using a simulated multi-scale data model. *BMC Bioinformatics*. 2008;9(1):241.
doi: 10.1186/1471-2105-9-241

116. Pu L, Naderi M, Liu T, Wu HC, Mukhopadhyay S, Brylinski M. eToxPred: a machine learning-based approach to estimate the toxicity of drug candidates. *BMC Pharmacol Toxicol*. 2019;20(1):2.
doi: 10.1186/s40360-018-0282-6

117. Yang H, Sun L, Li W, Liu G, Tang Y. In silico prediction of chemical toxicity for drug design using machine learning methods and structural alerts. *Front Chem*. 2018;6:30.
doi: 10.3389/fchem.2018.00030

118. Fu R, Chen Z, Tian H, *et al*. A review on the applications of machine learning in biomaterials, biomechanics, and biomanufacturing for tissue engineering. *Smart Mater Med*. 2025;6(2):171-204.
doi: 10.1016/j.smaim.2025.06.003

119. Tuna C, Ouzir N, Dubois D, *et al*. Automated defect classification in aerospace x-ray images using CNNs. *eJNDT*. 2025;30(8).
doi: 10.58286/31418

120. Cumbajin E, Rodrigues N, Costa P, *et al*. A systematic review on deep learning with CNNs applied to surface defect detection. *J Imaging*. 2023;9(10):193.

doi: 10.3390/jimaging9100193

121. Zhang Z, Zhou X, Fang Y, Xiong Z, & Zhang T. AI-driven 3D bioprinting for regenerative medicine: from bench to bedside. *Bioact Mater*. 2025;45:201-230. doi: 10.1016/j.bioactmat.2024.11.021

122. Wang J, Heshmati Aghda N, Jiang J, Mridula Habib A, Ouyang D, Maniruzzaman M. 3D bioprinted microparticles: Optimizing loading efficiency using advanced DoE technique and machine learning modeling. *Int J Pharma*. 2022;628:122302. doi: 10.1016/j.ijpharm.2022.122302

123. Ng WL, Chan A, Ong YS, Chua CK. Deep learning for fabrication and maturation of 3D bioprinted tissues and organs. *Virtual Phys Prototyping*. 2020;15(3):340-358. doi: 10.1080/17452759.2020.1771741

124. Bao D, Wang L, Zhou X, Yang S, He K, Xu M. Automated detection and growth tracking of 3D bio-printed organoid clusters using optical coherence tomography with deep convolutional neural networks. *Front Bioeng Biotechnol*. 2023;11:1133090. doi: 10.3389/fbioe.2023.1133090

125. Bone JM, Childs CM, Menon A, *et al*. Hierarchical machine learning for high-fidelity 3D printed biopolymers. *ACS Biomater Sci Eng*. 2020;6(12):7021-7031. doi: 10.1021/acsbiomaterials.0c00755

126. Lee J, Oh SJ, An SH, Kim WD, Kim SH. Machine learning-based design strategy for 3D printable bioink: elastic modulus and yield stress determine printability. *Biofabrication*. 2020;12(3):035018. doi: 10.1088/1758-5090/ab8707

127. Chen H, Zhang B, Huang J. Recent advances and applications of artificial intelligence in 3D bioprinting. *Biophys Rev*. 2024;5(3):031301. doi: 10.1063/5.0190208

128. Xu Y, Sarah R, Habib A, Liu Y, Khoda B. Constraint based Bayesian optimization of bioink precursor: a machine learning framework. *Biofabrication*. 2024;16(4):045031. doi: 10.1088/1758-5090/ad716e

129. Shin J, Kang M, Hyun K, *et al*. Machine learning driven optimization for high precision cellular droplet bioprinting. BioRxiv. 2024:2024;611131. doi: 10.1101/2024.09.04.611131

130. Rezvani A, Bigverdi M, Rohban MH. Image-based cell profiling enhancement via data cleaning methods. *PLoS One*. 2022;17(5):e0267280. doi: 10.1371/journal.pone.0267280

131. Dehbozorgi P, Ryabchykov O, Bocklitz T. A systematic investigation of image pre-processing on image classification. *IEEE Access*. 2024;12:64913-64926. doi: 10.1109/ACCESS.2024.3395063

132. Asachi M, Alonso Camargo-Valero M. Multi-sensors data fusion for monitoring of powdered and granule products: Current status and future perspectives. *Adv Powder Technol*. 2023;34(7):104055. doi: 10.1016/j.apt.2023.104055

133. Kush JC. Integrating sensor technologies with conversational AI: enhancing context-sensitive interaction through real-time data fusion. *Sensors*. 2025;25(1):249. doi: 10.3390/s25010249

134. Yetgin A. Revolutionizing multi-omics analysis with artificial intelligence and data processing. *Quant Biol*. 2025;13(3):e70002. doi: 10.1002/qub2.70002

135. Zhang J, Che Y, Liu R, Wang Z, Liu W. Deep learning-driven multi-omics analysis: enhancing cancer diagnostics and therapeutics. *Brief Bioinform*. 2025;26(4):bbaf440. doi: 10.1093/bib/bbaf440

136. You S, Fan Y, Chen Y, *et al*. Advancements and prospects of deep learning in biomaterials evolution. *CR-PHYS-SC*. 2024;5(9):102116. doi: 10.1016/j.xcrp.2024.102116

137. Tripathi S, Mandal SS, Bauri S, Maiti P. 3D bioprinting and its innovative approach for biomedical applications. *MedComm (2020)*. 2023;4(1):e194. doi: 10.1002/mco2.194

138. Ning H, Zhou T, Joo SW. Machine learning boosts three-dimensional bioprinting. *IJB*. 2023;9(4):739. doi: 10.18063/ijb.739

139. Bonatti AF, Vozzi G, De Maria C. Enhancing quality control in bioprinting through machine learning. *Biofabrication*. 2024;16(2):022001. doi: 10.1088/1758-5090/ad2189

140. Al-Kharusi G, Dunne NJ, Little S, Levingstone TJ. The role of machine learning and design of experiments in the advancement of biomaterial and tissue engineering research. *Bioengineering*. 2022;9(10):561. doi: 10.3390/bioengineering9100561

141. Setiya A, Jani V, Sonavane U, Joshi R. MolToxPred: small molecule toxicity prediction using machine learning approach. *RSC Adv*. 2024;14(6):4201-4220. doi: 10.1039/D3RA07322J

142. Kamble SD, Singh SC, Ashwani Kumar, Dwivedi G, eds. *Tissue Engineering and Regenerative Medicine: Advances and Applications*. 1st edition. CRC Press, Taylor & Francis Group; 2025. doi: 10.1201/9781003536352

143. Bonatti AF, Vozzi G, Chua CK, Maria CD. A deep learning quality control loop of the extrusion-based bioprinting process. *Int J Bioprint*. 2022;8(4):620. doi: 10.18063/ijb.v8i4.620

144. Arduengo J, Hascoet N, Chinesta F, Hascoet JY. Open-loop control system for high precision extrusion-based bioprinting through machine learning modeling. *J Mach Eng*. 2024;24(1):103-117.

doi: 10.36897/jme/186044

145. Sani AR, Zolfagharian A, Kouzani AZ. Artificial intelligence-augmented additive manufacturing: insights on closed-loop 3D printing. *Adv Intell Syst*. 2024;6(10):2400102.
doi: 10.1002/aisy.202400102

146. Arduengo J, Hascoët N, Chinesta F, Hascoet JY. Closed-loop control of extrusion-based bioprinting through real-time computer vision. *J Mach Eng*. 2025;25(2):28-42.
doi: 10.36897/jme/205422

147. Rahmani Dabbagh S, Ozcan O, Tasoglu S. Machine learning-enabled optimization of extrusion-based 3D printing. *Methods*. 2022;206:27-40.
doi: 10.1016/j.ymeth.2022.08.002

148. Inayathullah S, Buddala R. Review of machine learning applications in additive manufacturing. *Results Eng*. 2025;25:103676.
doi: 10.1016/j.rineng.2024.103676

149. Tian S, Stevens R, McInnes BT, Lewinski NA. Machine assisted experimentation of extrusion-based bioprinting systems. *Micromachines (Basel)*. 2021;12(7):780.
doi: 10.3390/mi12070780

150. Hashemi A, Ezati M, Zumberg I, *et al*. Characterization and optimization of a biomaterial ink aided by machine learning-assisted parameter suggestion. *Mater Today Commun*. 2024;40:109777.
doi: 10.1016/j.mtcomm.2024.109777

151. Zhang C, Elvitigala KCML, Mubarok W, Okano Y, Sakai S. Machine learning-based prediction and optimisation framework for as-extruded cell viability in extrusion-based 3D bioprinting. *Virtual Phys Prototyping*. 2024;19(1):e2400330.
doi: 10.1080/17452759.2024.2400330

152. Ronzetti M, Simeonov A. A comprehensive update on the application of high-throughput fluorescence imaging for novel drug discovery. *Expert Opin Drug Discov*. 2025;20(6):785-797.
doi: 10.1080/17460441.2025.2499123

153. Vinken M, Grimm D, Baatout S, *et al*. Taking the 3Rs to a higher level: replacement and reduction of animal testing in life sciences in space research. *Biotechnol Adv*. 2025;81:108574.
doi: 10.1016/j.biotechadv.2025.108574

154. Ayad A. Bioinspired NeuroPods: AI-Enhanced 4D Composite Bioprinting Revolutionizing Brain-on-Chip and Neural Regeneration; 2025.
doi: 10.20944/preprints202507.1943.v1

155. Biehn SE, Goncalves LM, Lehmann J, *et al*. BioPrint meets the AI age: development of artificial intelligence-based ADMET models for the drug-discovery platform SAFIRE. *Future Med Chem*. 2024;16(7):587-599.
doi: 10.4155/fmc-2024-0007

156. Safir F, Vu N, Tadesse LF, *et al*. Combining acoustic bioprinting with AI-assisted raman spectroscopy for high-throughput identification of bacteria in blood. *Nano Lett*. 2023;23(6):2065-2073.
doi: 10.1021/acs.nanolett.2c03015

157. Satpathy A, Datta P, Wu Y, Ayan B, Bayram E, Ozbolat IT. Developments with 3D bioprinting for novel drug discovery. *Expert Opin Drug Discov*. 2018;13(12):1115-1129.
doi: 10.1080/17460441.2018.1542427