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Review

Trends in 3D Manufacturing of Microdevices for Biomedical Applications

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Abstract

Over the past decades, microfabrication technologies have been essential tools in the creation and fabrication of biomedical microfluidic devices useful for diagnostics, biosensing, drug delivery, and organ-on-a-chip applications. Soft lithography is one of the most widely used conventional microfabrication techniques and can achieve a high resolution (~100 nm) and excellent fidelity of the replica but requires a high level of expertise, expensive equipment, and access to cleanrooms, which is not widely available and makes it difficult to scale up and adopt. Moreover, the material limitations and the complicated fabrication steps of conventional lithographic methods limit the fast prototyping of advanced microfluidic platforms. These limitations have been overcome in recent years with the integration of 3D printing and soft lithography, and, now, the rapid, cost-effective, and customizable fabrication of high-quality master molds of PDMS-based microfluidic devices is possible. Modern 3D printing technologies provide great material versatility, design flexibility, high manufacturing efficiency, and a much shorter and lower cost of fabrication. This review critically discusses the recent advancements of the 3D printing-assisted soft lithography method in biomedical microfluidic device fabrication, focusing on fabrication techniques, materials for 3D printing, hybrid fabrication strategies, and representative biomedical applications. Moreover, the current developments of high-resolution additive manufacturing, multi-material fabrication, and eco-friendly manufacturing are discussed, and insights into the future development of next-generation bio-medical microfluidic systems are provided.

Keywords: 3D printing; microfluidic; microfluidic device; soft lithography; chip fabrication; biosensors; drug delivery; biomedical microfluidics

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1. Introduction

The fabrication of microdevices for biomedical applications ranging from complex Lab-on-a-Chip (LOC) platforms to microneedle arrays and drug-eluting stents has undergone a radical metamorphosis over the last decade [1]. Historically, the field was tethered to top-down manufacturing techniques derived from the semiconductor industry, such as photolithography and reactive ion etching (RIE). While precise, these methods were

plagued by a high capital expenditure, the necessity of rigid ISO-certified cleanrooms, and a fundamental inability to create true three-dimensional, non-planar geometries [2]. Among the primary benefits of microfluidic technology is cost-effectiveness along with the integration of laboratory techniques on a chip, leading to a lower consumption of the reagents and, thus, reducing the required sample volume [3,4]. As we move through 2026, the paradigm has shifted toward cost-effective additive manufacturing (AM). During the last ten years, the trend in microfluidics has been towards planar fabrication processes capable of creating small-scale and fine-scale structures. These smaller machines are created to perform certain functions—to detect some types of chemicals, to perform a separation, or to analyze the biological samples—at just a fraction of the time and consumable materials required by the traditional laboratory apparatus. This has not only been made possible by the cheaper hardware but also by a mix of superior materials, quicker computers, and enhanced resolution of fabrication [5]. The initial methods such as 2PP were previously too slow to be practical, but, with developments in scan rates and beam control, they have become really practical in both research and manufacturing. Today, the integration of high-speed femtosecond lasers and parallelized voxel scanning has increased the throughput by several orders of magnitude, making it a viable candidate for the serial production of complex scaffolds [6]. Simultaneously, Projection Micro-Stereolithography (PμSL) has emerged as the "economic middle ground." By utilizing a Digital Micromirror Device (DMD) to project entire layers of UV light at once, PμSL systems now routinely achieve resolutions below 5 μm. This allows for the fabrication of organ-on-a-chip devices with integrated micro-valves and sensors at a fraction of the cost of traditional cleanroom-based soft lithography [7]. Several technological advancements have brought forward the various fabrication methods for the development of microfluidic devices. A multitude of materials are used for the manufacturing of microfluidic devices, which show different properties [4]. Different behaviors are displayed when being processed [8]. Therefore, the fabrication methods are tailored to the specific material and its properties. Additionally, cost effectiveness is a critical factor to enhance the feasibility and scalability of fabricating the devices [9]. To understand the relative merits and limitations between different microfluidic fabrication methods, a comparative analysis of the various fabrication techniques for microfluidic devices is needed. Photolithography and soft lithography are high-resolution patterning techniques with established protocols but utilize cleanroom facilities and costly equipment and are time-consuming, rendering them less useful for quick development [10–12]. Thermoplastic-based processes such as hot embossing and injection molding are appropriate for large-scale production but come with high initial tooling expenses and increased setup times [12,13].

The overall progress in 3D printing technology and the application towards biotechnology is presented in (Figure 1). In 2026, the focus has shifted toward functionalized and stimuli-responsive biomaterials. Like bio-inks and hydrogels, Polylactic Acid (PLA) and Poly(ethylene glycol) diacrylate (PEGDA) resins are complex cell-laden bio-inks that exhibit thixotropic behavior, allowing for hte extrusion-based bioprinting of vascularized tissue constructs. Bioresorbable polymers polycaprolactone (PCL) and silk fibroin derivatives allow for microimplants that maintain structural integrity for a predetermined period before being safely metabolized by the body, eliminating the need for secondary removal surgeries [14].

The integration of 3D printing in the fabrication of microfluidic devices is widely embraced by inventors catering to their variety of materials and sizes. 3D printing, or direct ink writing, is an additive manufacturing method that progressively adds materials in a layer-by-layer fashion on a non-contact substrate through a nozzle to create micro-scaled customized structures directly from a computer-aided design (CAD) model [1]. Although it has become popular in recent years, the roots of AM can be traced back to the 1980s when

Chuck Hull invented one of the earliest AM technologies, stereolithography (SLA). Since then, several printing techniques have been developed, such as Selective Laser Sintering (SLS), Fused Deposition Modeling (FDM), and Digital Light Processing (DLP), each with unique advantages in terms of resolution, material utilization, and manufacturing speed. Technological development has greatly broadened the applications of AM in biomedical microfluidics [15,16]. 3D printing advanced from prototyping to full-scale manufacturing by the 2000s, particularly in the automotive, healthcare, and aerospace industries. Several 3D printing methods have also been created for biomedical use, typically classified according to the structural material employed, such as hydrogels, biopolymers, and composite scaffolds, and the principle of deposition underneath, as indicated in Table 1. The latest advancements in 3D printing have completely transformed both the technical design and modern manufacturing processes. It makes the ideal fit for sustainable fabrication, as the processing of 3D printing involves the addition of material instead of etching or removal, making it a more sustainable and inexpensive alternative [16]. Its primary assets include the easy modifications of a product at a designed level without limiting its spatial arrangement and quick manufacturing. The effect of such innovative techniques can be seen in various sectors, from medical to industry [17].

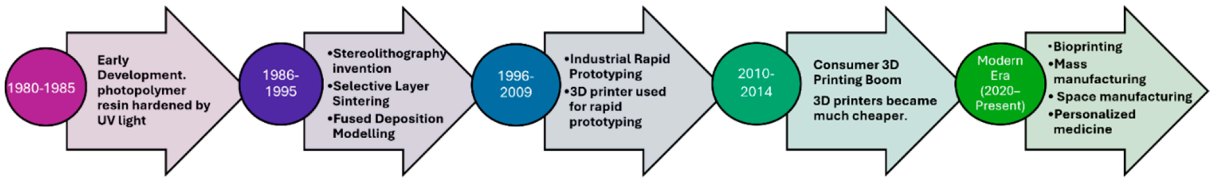


Figure 1. Illustration of the evolution of 3D printing from early photopolymer-based systems to advanced techniques and manufacturing applications.

Table 1. Comparative Analysis of 3D Printing Techniques.

Technique	Resolution µm	Materials	Post-Processing Needs	References
Aerosol Jet Printing (AJP)	10–50 µm	Conductive nanoparticle inks, polymers, biomaterials	Thermal sintering/curing (for conductive inks), solvent evaporation	[18]
Two-Photon Polymerization (2PP)	0.1–0.2 µm (100–200 nm)	Photosensitive resins, PEGDA, IP-L, IP-Dip, hybrid photopolymers	Solvent development, UV post-curing (if required)	[19]
FDM (Fused Deposition Modelling)	100–300 µm	PLA, ABS, PETG, Nylon	Support removal, sanding, painting	[20]
SLA (Stereolithography)	25–100 µm	Photopolymer resins (Tough 2000, Rigid 10K, Elastic 50A)	Resin cleaning, UV curing, sanding	[21,22]
SLS (Selective Laser Sintering)	60–120 µm	Nylon, TPU, polymer composites	Powder removal, dyeing, and polishing	[23,24]
DLP (Digital Light Processing)	25–50 µm	Photopolymer resins, eco-friendly composites	Resin cleaning, UV curing	[25,26]
EBM (Electron Beam Melting)	~100 µm	Titanium alloys, cobalt-chrome	Support removal, heat treatment	[27,28]
Binder Jetting	50–100 µm	Metal powders, ceramics, sand	Metal powders, ceramics, sand	[29–31]

Initially, 3D printing was developed to make macroscopic parts, but it is now heading towards the creation of active, functional nanodevices. As a mechanistically distinct bottom-up process over traditional top-down nanolithography, 3D nanoprinting enables the fabrication of nanostructures with elaborate spatial shapes and a wider range of materials, creating new frontiers in miniaturized device engineering [32]. Among emerging 3D printing technologies, hybrid 3D printing technologies have gained a significant distinction because of their ability to combine multiple fabrication principles into a unified process [33]. One such method known as Faraday printing incorporates aerosol-based additive deposition and subtractive etching, allowing wafer-scale high-resolution patterning. Utilizing electric fields to guide nanoparticle aerosols as hard masks, it produces feature sizes as low as ~14 nm. The process provides a scalable and low-cost path compared to traditional lithography and, therefore, has potential for use in next-generation micro/nanofabrication applications [34]. Concurrently, 2PP provides a sub-100 nm spatial resolution via nonlinear optical absorption to directly write complex 3D architectures, including photonic crystals, micromechanical systems, and cell scaffolds [35–37]. Accompanying these developments, microfluidic device use has grown exponentially across numerous fields, where they have transformed laboratory and analytical methods.

The most transformative trend of the current era is the integration of artificial intelligence (AI) into the "digital thread" of manufacturing. In the mid-2010s, print failure was a "black box" problem. In 2026, in situ monitoring powered by machine-learning (ML) algorithms detects microscopic defects in real time, adjusting exposure parameters on the fly to ensure "born-qualified" parts. The way microfluidic devices are designed is one of the more engaging advances in recent years, which is being impacted by artificial intelligence. Conventionally, to design a microfluidic chip, dozens of simulations would be run, the geometry adjusted manually, and the process repeated until a geometry worked well enough. Such a method is tedious and requires a lot of intuition on the part of the researcher. Machine-learning models now can be trained to make predictions of how a channel will perform even before anything is ever made. For example, ref. [38] is where a fast sequence pair algorithm was implemented by one group of researchers to automate the choice of chip layouts [39], whereas a group of researchers used Bayesian optimization to discover good structural geometries without using exhaustive simulations. The practical advantage is that now researchers are able to test thousands of design options within a limited time and concentrate on the ones that actually promise. This is important because the industry is shifting to the use of wearable health trackers and small patient diagnostic instruments. This is because AI tools can be used to customize the geometry of devices to extremely precise requirements, such as a certain biosensor optimizing the flow rate or two fluids to be completely mixed in a low-length channel [40]. In other fields, outside of health uses, microfluidic systems are being considered in heat management in electronics, where, at the micro scale, fluid flow can easily create heat that is much more efficiently removed than in other methods [41].

In this review, we critically review the recent developments on the 3D-printing-based soft lithography for the fabrication of biomedical microfluidic devices, focusing on high-resolution 3D printing, master mold fabrication, printable materials, and hybrid manufacturing strategies. We also explore the impact of these technological advances on the widespread use of microfluidic platforms throughout the biomedical, chemical, and industrial fields. Lastly, we discuss the recent progress in scaling up and making microfluidic devices robust and economically viable, which will guide future directions for next-generation PDMS-based microfluidic systems.

2. Design and Fabrication of Biomedical Microfluidic Devices

2.1. Microfluidic Chip Design

Standardized technical drawings and modeling rules establish essential guidelines that manufacturers must follow during the development of microfluidic devices. Microfluidic device development has leveraged the latest microfabrication techniques to create devices with a <100 μm resolution, but the occurrence and impact of print artifacts affect fluidic performance. Stair-stepping is an example of an artifact produced during layer-by-layer deposition from both stereolithography and FDM-developed devices that produce surface roughness that disrupts the laminar flow and thus increases pressure drops [42]. Other artifacts include a channel collapse as seen in softer materials, including hydrogels, and channels that were not developed with any support that limits the aspect ratio achievable and the integrity of the structure [43]. The post-curing or fluid (i.e., liquid) contact swelling of the resin used to create a microchannel deforms the geometry and directly alters the flow resistance and mixing properties. These artifacts introduce a gap from design to fabrication where the intended geometries differ from what is made [44]. Modern design processes use Computer-Aided Design (CAD), Fusion, USA, tools that enable the creation of digital prototypes along with detailed engineering drawings. Several CAD software solutions provide microfluidic mold design features that include special characteristics to address the design requirements [45]. CAD/CAE-integrated rapid prototyping enables less constrained design freedom, faster iterations, and manufacturing process simplifications in comparison to the standard lithographic or molding methods. The digital workflows of CAD/CAE enable automatic mold designs, including the ability to reduce the amount of human error, all while speeding up the development process [3]. AutoCAD possesses sufficient 2D drafting and parametric modeling functions, which work well for schematic drawings and dimensional planning [46]. SolidWorks offers advanced parametric modeling capabilities together with built-in simulation features, which enable the complete fluid dynamics analysis and direct production conversion [47]. The cloud platform of Autodesk Fusion offers CAM and generative design capabilities, which work best for iterative mold optimization and prototyping [48]. TinkerCAD, Autodesk, Inc. USA, provides an easy-to-use platform for basic design visualization and introductory design work, mainly for educational use [49]. The browser-based CAD system Onshape delivers real-time collaboration with versioning and high-precision geometry editing features, which make it suitable for designing microfluidic channels and molds [50]. Advancements in design automation have yielded a more accurate and reliable means of fabricating microfluidic chips. The CAD tools are now tolerant of printer variability, resin shrinkage, and misalignment between layers, leading to the reliable integration of multiple layers. The production process now functions with less risk of unexpected costlier issues. The research published in Scientific Reports (2025) [51] details how voxel-aware slicing and adaptive exposure methods enhance the resolution quality using low-cost approaches. The system prevents unprintable designs from running using real-time feedback mechanisms that stop the curing process proposed in the ACM paper. The AI-controlled closed-loop learning system described in Nature Communications Engineering (2024) [52] functions as an open-ended refinement that works with fabrication-design differences to fabricate microfluidic chips that achieve a reproducible accuracy and reliability at an industrial scale. The design for the mold of the microfluidic device is built on Onshape, PTC Inc. USA, taking advantage of its parametric model features to establish channel geometries and chamber designations.

2.2. Materials for Microfluidic Chip Fabrication

2.2.1. Plastic

Plastics are polymers and are, by definition, synthetic polymers that can be shaped into solid objects. All plastics are polymers; however, not all polymers are plastics. "Plastics" usually refers to processable and solid polymers, as shaped by heat and pressure [53]. Thermoplastics such as ABS, PLA, and Nylon are ideal candidates for additive manufacturing (Figure 2) because they possess tunable mechanical properties, are relatively easy to process, and are typically available as either filament or powder. For example, PLA is biodegradable and made from renewable feedstocks, and has good printability and surface finish properties but is not as durable as ABS. Both ABS and PLA provide an opportunity for different colored prints. ABS has superior toughness, ductility, and thermal resistance. Nylon has fantastic strength and flexibility and is regularly used to produce functional parts and is often blended with aluminum powder in applications using sintering [54].

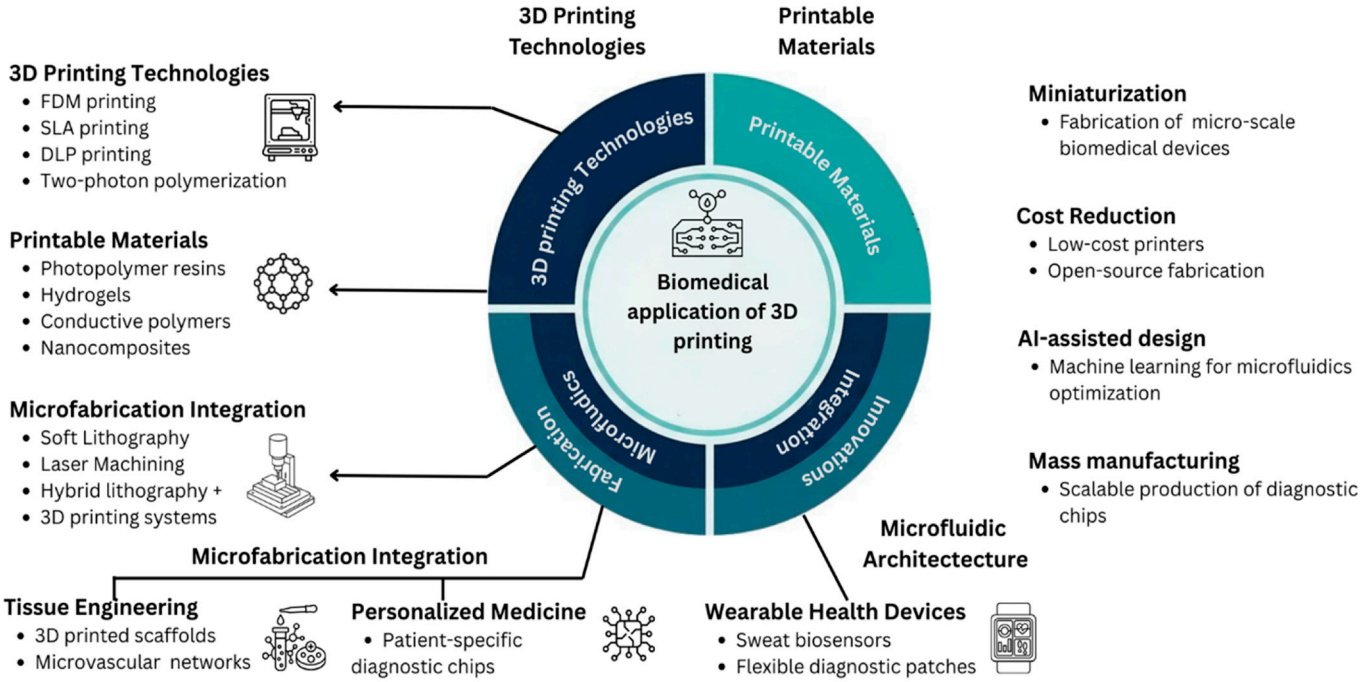


Figure 2. An integrated overview of biomedical 3D printing, showcasing how advanced technologies, materials, and microfabrication enable innovative, cost-effective healthcare solutions.

2.2.2. Polymer

Polymers, made up of long chains of identical monomer units, are distinct from plastics in that they may be present in more than one state, such as liquid, gel, or solid, and are not necessarily moldable [55]. Since the 1990s, polymers have dominated the replacement of traditional materials such as glass and silicon in microfluidic device construction because of their cost benefits, biocompatibility, and processability [56]. Their mass-producibility without toxic etching chemicals like hydrofluoric acid (HF) makes them especially appealing for biomedical and clinical diagnostic applications. Polymers provide controllable physical and chemical properties, such as stiffness, surface tension, and optical transparency, and are amenable to fast prototyping methods like soft lithography and 3D printing. Their availability has democratized microfluidic manufacturing beyond traditional MEMS laboratories. Selecting the material to use in a microfluidic device is not a simple task; it depends on what the device is meant to do, what fluids it will carry, and how it is going to be made. Polymethyl methacrylate (PMMA), polystyrene, polyacrylamide, PFPEs (perfluoropolyethers), and agarose gel are the most widely used polymers. Both have advantages.

When the item to be used requires resistance to harsh chemicals or heat, such as when operating in areas of high temperatures or high density of such chemicals, materials such as PEEK (polyether ether ketone) and COC (cyclic olefin copolymer) are usually a better option due to their resilience in (Figure 2) [57].

2.2.3. Elastomer

Out of all materials, however, elastomers, and PDMS (polydimethylsiloxane), in particular, have become a de facto material in the microfluidics laboratory. PDMS is gas-permeable, transparent, and relatively easy to manipulate with soft lithography methods. It may be poured into a mold, dried, and removed in one piece, giving fine channel structures and features as small as the submicron. This convenience has rendered it a favorite in biological studies, where rapid prototyping is essential, and images require optical clarity [58]. The only limitation is that it absorbs small hydrophobic molecules, which can interfere with drug assays and fluorescence microscopy. Surface treatment methods, like oxygen plasma oxidation, are used to generate silanol groups in PDMS, enabling the irreversible adhesion to substrates of glass, silicon, or other compatible polymers. The irreversible bond formed by the silanol groups on PDMS is essential when fabricating microfluidic chips constructed of laminated multilayers to produce a leak-proof microfluidic chip [59]. According to Borók et al. (2021) [58], plasma modification not only increases the surface hydrophilicity but also induces chemical and morphological changes on PDMS surfaces, enhancing their bonding capability and stability in microfluidic assemblies [60]. Recently, alternative elastomers have also been considered, such as styrene–ethylene–butylene–styrene (SEBS) and perfluoropolyether (PFPE)-based materials. These new types of elastomers have a better chemical resistance, lower drug absorption, and the ability to be fabricated using scalable manufacturing processes, such as injection molding and extrusion, than PDMS [61,62].

Emerging Elastomeric Alternatives for Soft Lithography: From Material-Centric to Application-Driven Design

Although PDMS has remained the dominant elastomer for soft lithography for more than two decades, recent advances in biomedical microfluidics have shifted the material selection from a PDMS-centric approach toward an application-specific engineering strategy [63]. This transition has been driven by the increasing complexity of organ-on-a-chip systems, wearable biosensors, implantable microfluidics, droplet-based single-cell analysis, and pharmaceutical screening platforms, all of which impose distinct physicochemical, mechanical, and manufacturing requirements that cannot be simultaneously satisfied by a single elastomer [64]. Consequently, contemporary microfluidic research no longer aims to replace PDMS universally but instead focuses on selecting elastomeric materials according to the intended biological environment, solvent compatibility, molecular transport characteristics, and manufacturing scalability. Recent critical reviews published in *Lab on a Chip* identify this transition as one of the most important developments in next-generation biomedical microfluidics, emphasizing that future fabrication strategies will rely on hybrid material systems integrated with high-resolution additive manufacturing rather than a single substrate platform [65].

The highly crosslinked network of siloxanes (Si–O–Si) gives PDMS an outstanding combination of optical transparency (in the visible range, typically >92%), low autofluorescence, oxygen permeability (typically 600–800 Barrer), and curing shrinkage, which is typically below 2% depending on the curing ratio [66]. Such physicochemical properties allow the accurate replication of micro- and submicron-scale features fabricated by photolithography, stereolithography (SLA), and now increasingly by two-photon polymerization (2PP) master molds. Moreover, oxygen plasma treatment transforms the surface of

methyl groups to Si–OH groups, which enables the formation of covalent Si–O–Si bonds with glass, silicon, and other PDMS layers without compromising the optical transparency for the purposes of fluorescence microscopy, confocal imaging, and the observation of live cells [67]. These characteristics make PDMS the material of choice for organ-on-a-chip devices, microphysiological systems, microvascular models, electrochemical biosensors, and multiplexed platforms for lab-on-a-chip devices, in which these critical design requirements for gas exchange, optical interrogation, and rapid prototyping are crucial. Recent reviews have all ended with the same conclusion: that none of the commercially available printable elastomers to date can replicate the optical, biological, and fabrication benefits of PDMS.

As microfluidic devices move from prototyping in the laboratory to clinical use and commercialization, there are a number of intrinsic disadvantages to PDMS that have become more prominent. The hydrophobic siloxane matrix depletes compounds such as steroids, anticancer drugs, fluorescent tracers, lipophilic metabolites, and signaling molecules through its hydrophobic properties, leading to changes in the diffusion kinetics and to poor reproducibility in long-term biological experiments [68]. This type of adsorption is particularly problematic in the liver-on-chip, blood–brain barrier-on-chip, kidney-on-chip, and tumor-on-chip systems, as it can lead to inaccurate pharmacokinetic and pharmacodynamic measurements. In addition, PDMS is also known to be very soluble in aromatic and chlorinated organic solvents and to have poor resistance to long-term mechanical loading, with uncrosslinked oligomers migrating into biological media, and to regain its hydrophobic character when activated by plasma. All these conditions severely restrict long-term analytical stability and create major obstacles for the regulatory clearance and industrial realization of PDMS-based microfluidic devices. Accordingly, the material-dependent molecular adsorption and the solvent incompatibility of PDMS are considered important challenges for PDMS to be used in pharmaceutical development and precision medicine, according to recent reviews of organ-on-a-chip [69].

To address these limitations, styrene–ethylene–butylene–styrene (SEBS) has emerged as one of the most promising thermoplastic elastomers for next-generation soft lithography. Unlike chemically cross-linked PDMS, SEBS possesses a microphase-separated architecture consisting of rigid polystyrene domains dispersed within a flexible ethylene–butylene matrix, providing excellent mechanical resilience while substantially reducing the nonspecific adsorption of hydrophobic compounds [70]. Consequently, SEBS preserves the effective concentration of therapeutic agents during prolonged perfusion experiments, making it particularly advantageous for drug-screening microfluidics, metabolomics, wearable diagnostic platforms, and organ-on-a-chip systems requiring a quantitative pharmaceutical evaluation. From a manufacturing perspective, SEBS is compatible with high-throughput industrial processes such as hot embossing, roll-to-roll replication, injection molding, and, increasingly, with hybrid 3D-printing-assisted mold replication, thereby overcoming one of the principal commercialization limitations of PDMS [71]. Recent wearable and implantable microfluidic studies have highlighted thermoplastic elastomers, including SEBS and TPU, as leading candidates for disposable biomedical devices because they combine mechanical flexibility with industrial manufacturability and improved chemical robustness [72].

The other rapidly emerging material class is fluorinated elastomers based on perfluoropolyethers (PFPEs) that have been drawing a great deal of attention for their use in chemically challenging microfluidic applications [73]. The combination of a fluorinated molecular backbone, combined with negligible swelling with aggressive organic solvents, extremely low nonspecific biomolecular adsorption, and outstanding resistance to fluorinated oils commonly used in droplet microfluidics, make PFPE elastomers uniquely suited to the demands of this new microfluidics application. The properties allow the stable

droplet production of monodisperse droplets, high-throughput single-cell encapsulation, directed evolution, and continuous-flow chemical synthesis in conditions of significant PDMS deformation or failure from solvents [74]. Therefore, PFPE has gained more relevance for pharmaceutical microreactors, single-cell omics, droplet-based diagnostics, and chemically intensive analytical microfluidics. Today, however, the increased cost of raw materials, the requirements of the surface activation procedures, and the relatively small market availability of PFPE limit its use to specialized, high-performance applications and not to routine laboratory prototyping.

One of the most notable research developments for the past three years that is continuing into 2024–2026 is the integration of high-performance AM production with the application-specific engineering of elastomer materials. In contrast to establishing a universal master mold for PDMS casting, the current trends increasingly take advantage of high-resolution SLA, digital light processing (DLP), and two-photon polymerization (2PP) to generate reusable molds for a variety of elastomer systems such as PDMS, SEBS, TPU, Ecoflex, and PFPE [4]. At the same time, significant efforts are being invested in the development of SLA-printable elastomeric resins having similar elastic moduli to that of PDMS, multimaterial "print–pause–print" fabrication techniques, and hybrid mold designs that can combine a rigid structure with an elastomeric membrane into the same fabrication process. The developments allow the fabrication of integrated microvalves, micropumps, and deformable microactuators, and minimize the post-assembly complexity and manufacturing reproducibility. These advancements signal a move towards a hybrid manufacturing process in the future, one that combines multiple materials and multiple resolutions that will rely on the elastomer's functionality instead of its previous tradition.

2.3. Approaches in Microfluidic Chip Fabrication

Conversely, emergent prototyping processes such as 3D printing and xerography provide low-expense, cleanroom-free, and design-tolerant options, allowing for the quick iteration of device architectures. These techniques are especially beneficial in educational environments and initial device development, where quickness and flexibility are paramount. PLA and PMMA have the highest tensile strength of the materials and are great for applications that require structural strength, whereas PDMS has the most flexibility and is viable in low-temperature applications. Polyamide and ABS have a balanced performance and are available with smooth or matte finishes. They are great options for general-purpose prototyping. The combination of different melting points and different surface finishes with the materials provides the user with an even wider option of materials, allowing them to fit the functional and aesthetic requirements of the user. The presented Table 2 provides a comparative analysis of the various fabrication techniques for microfluidic devices.

Table 2. Overview of microfluidic device fabrication techniques and materials.

	Method	Materials	Channel Size	Resolution (µm)	Complexity	Post-Processing Requirement	Scalability	Throughput	References
Precision	3D Printing	PLA, resin	150–500 µm	High (10–100 µm)	Moderate complexity	Post-curing, surface smoothing	High	Very fast	[75]
	Soft Lithography	PDMS	10–50 µm	Moderate (1–10 µm)	Moderate complexity	Mold fabrication, curing, and bonding	Low to medium	Moderate	[11,76]
	Photolithography	Silicon, glass	1–10 µm	High (<1 µm)	High complexity	Requires cleanroom, masks, and etching	High	Slow	[10,77]
Industrial scale	Injection Molding	Thermoplastics	30–100 µm	High (0.5–5 µm)	High initial setup	Low postprocessing; mold polishing	Low	Fast	[13,78]
	Hot Embossing	Thermoplastics	20–100 µm	Moderate (1–10 µm)	Moderate complexity	Requires heating, pressure, and demolding	Medium to high	Slow	[38]
	Laser cutting	Glass, PMMA	150–300 µm	Moderate	Low complexity	Edge polishing may be needed	Low	Very fast	[79]
	Micro-milling	PMMA, metals	50–200 µm	Low to moderate	High complexity	Burr removal, surface finishing	Low to medium	Slow	[80,81]
Low-cost	Xurography	PVC, resins	200–500 µm	Moderate	Low complexity	Minimal post-processing	Low	Very fast	[82]
	E-Beam lithography	Silicon, polymers	<1 µm	Moderate	Very high complexity	Vacuum systems, resist development	Very low	Very slow	[4]

Table 2. *Cont.*

	Material	Tensile Strength (MPa)	Melting Point (°C)	Surface Finish	Biomedical Applications	Availability	References
Plastic	Polyamide (Nylon)	~40 MPa	257 °C to 262 °C	Smooth, machinable	Moderate: Low protein adsorption	High	[83]
	ABS	43 MPa	200 °C to 250 °C	Matte to glossy	Low: Potential cytotoxicity from monomers	High	[84]
	PLA	46–60 MPa	150 °C to 180 °C	Glossy, translucent options	Moderate: Low cytotoxicity	Very high	[85,86]
Polymer	PMMA	48–76 MPa	~160 °C	High clarity, glossy	Moderate	High	[87]
	Polystyrene	~28–32 MPa	210 °C to 240 °C	Rigid, glossy	High: Good protein adsorption	High	[88]
	Polyacrylamide	Brittle (low tensile)	300 °C	Gel-like, smooth (hydrated)	High: Low cytotoxicity	Moderate	[89,90]
Elastomer	PDMS	~2 MPa (flexible)	−35 °C to −49 °C	Clear, castable	High: Low protein adsorption	Moderate	[91,92]
	Natural Rubber (NR)	~21–25 MPa	80 °C to 145 °C (Softens)	Matte, flexible	Low: potential allergenicity	Moderate	[93]
	NBR (Nitrile Rubber)	~11–14 MPa	−25 °C to 20 °C (Softens)	Smooth, oil-resistant	Low	Moderate	[94]

The major microfabrication techniques are quantitatively compared from the perspective of fabrication resolution, minimal attainable channel dimension, channel surface roughness, material compatibility, manufacturing cost, throughput, and scalability in Table 2. For micro- and nanofabrication with a high dimensional accuracy and low surface roughness, there are two methods, photolithography and electron-beam lithography, which are expensive and require cleanroom facilities and have limited scalability for rapid prototyping. Additive manufacturing methods, on the other hand, offer a faster fabrication time, reduced costs, and material versatility, but the dimensions and surface finish of channels are still limited by the additive manufacturing technology used. Overall, soft lithography remains a good balance between fabrication, fidelity, manufacturing cost, and design, and design flexibility, especially when used in conjunction with high-resolution 3D-printed master molds. In recent years, the new manufacturing methods have been increasingly used to combine several fabrication methods to achieve a compromise between precision and scalability, cost, and manufacturing efficiency for next-generation biomedical microfluidic devices.

Soft Lithography

Soft lithography has become a unique technology due to its ability to print on flexible, large-area substrates with a resolution of ~35 μm, accomplished by printing, embossing, and molding techniques. It may produce or replicate submicrometric shapes using elastomeric stamps, especially elastomers such as polydimethylsiloxane (PDMS) for their flexibility [95,96]. The emergence of soft lithography enabled the field of microfluidics to grow dramatically. Nonetheless, the large majority of PDMS microfluidic devices are still fabricated with a great deal of manual labor, require clumsy external control systems, and involve difficult-to-use experimental setups, making commercialization problematic [97]. Most of the soft-lithography-based research has employed polydimethylsiloxane (PDMS) as the elastomer due to its affordability, high degree of conformability, transparency, and biocompatibility [98]. Soft lithography is employed to make microstructures from elastomers by spin-coating, casting, or injection molding a liquid prepolymer of a suitable elastomer against a prefabricated master having a patterned relief structure. A single master can produce a large number of elastomeric parts, each of which can be utilized repeatedly in patterning for a wide range of applications across different domains [99]. This method is low-cost and straightforward and does not require strict environmental controls; therefore, it is very accessible for laboratory-scale uses [38]. Speaking of low cost, cost assessments suggest PDMS chips generated via soft lithography can be made for about USD ~3 per device [100], and PDMS materials have a cost of ~USD 40 kg^{-1} [101]. For small batch quantities, outsourcing fabrication may cost at least on the order of tens of USD per device (for example, roughly USD 60 for 100 devices). The economical production of biocompatible and flexible microchannels has led to the emergence of soft lithography as a flexible biomedical platform to produce microfluidic chips and microelectromechanical systems (MEMSs) for research, diagnosis, and treatment [102]. Apart from its application in microfluidics and chip fabrication, it has unfolded as a novel advancement in cell imprinting to study the cell topography at a nano/micro scale for enhanced cell-based studies. The fundamental idea behind fabricating materials for cell-based research is the ability of the materials to redesign or mimic the physiochemical environment of the cellular niches [103]. These efforts have been made to understand the cellular interactions, proliferation, adhesion, morphology, and biological aspects associated with the cell's growth and development [2]. As an example, Shahriyari et al. (2020) [104] showed that cell-imprinted substrates made from polydimethylsiloxane (PDMS) and gelatin methacryloyl (GelMA) hydrogels from soft lithography could change breast cancer cells' viability and drug susceptibility to doxoru-

bicin, illustrating the future potential of this method for cancer biology and drug testing applications [104].

2.4. Glass Capillary Fusing

Glass has continued to find use in microfluidics, especially in conditions where droplets are produced or emulsions are being manipulated. Its usefulness is due to its chemical inertness, optical quality, and good understanding of surface chemistry, which are useful in applications where polymer-based devices may absorb reagents or degrade [105]. The capillary geometries of glass capillary electrophoresis are enabled on microfluidic platforms through thermal bonding. Capillary geometries that would be challenging to realize with soft polymers can be realized using glass capillaries embedded within microfluidic platforms. The glass capillaries yield the desired volumetric/flow rates, junctions, and droplet generators [106]. PDMS chips are flexible and inexpensive but are susceptible to solvent-induced swelling and non-selective adsorption. Glass-based microfluidics avoid these limitations through the elimination of the need for specialized infrastructure and their neutrality towards other substrates and chemicals [107,108]. Recent advancements have expanded the capabilities of glass capillary fusing in microfluidics for droplet generation by the controlled breakup of a dispersed phase in a continuous phase. It is carried out by joining and fusing round and square glass capillaries into coaxial configurations through thermal or chemical processes, facilitating 3D hydrodynamic focusing for monodisperse droplet generation with a low shear deformation [108]. Droplet microfluidics, either on glass or polymer chips, has turned out to be one of the most useful in the discipline. The concept is straightforward: create the droplets of a certain fluid in another immiscible fluid, and each droplet would be a miniature closed reaction chamber. These droplets are small, which means they can heat and cool within a relatively short time, mix reagents within a short time, and be sorted or analyzed at very high speed. These accomplishments have rendered droplet systems favorites in drug screening, single-cell sequencing, and chemical synthesis—everywhere a high throughput and small volumes count [106,109].

2.5. Stereolithography

Stereolithography (SLA), an additive manufacturing technique using light to cure photopolymers layer-on-layer, provides the high-resolution and rapid prototyping of microfluidic devices with intricate geometries and a seamless unibody construction [110]. The high resolution, design freedom, and seamless fabrication of enclosed microchannels, without complex assembly, have made SLA a mainstay in the fabrication of microfluid devices [111]. Recent advancements in multi-resin SLA have expanded the applications of SLA beyond conventional limits, as demonstrated by Ahmed et al. (2022), who fabricated microfluidic chips that included embedded Quake valves through masked SLA [112]. Through indigenously printed rigid and elastomeric valve and pump components, Ahmed et al. (2022) [112] were able to provide embedded actuation. Monia Kabandana et al. (2022) [113] published a thorough review of SLA among several 3D-printing modalities that outlined the advantages of SLA over other 3D-printing modalities for point-of-care diagnostics and drug delivery applications, such as the higher resolution and versatility of SLA methods [113]. The recent research in SLA ink formulation has greatly extended the device functionality and material performance. Bhattacharjee et al. created elastomeric PDMS-like materials from PDMS-methacrylate macromers, allowing for flexible microfluidic elements with enhanced chemical and optical performance [111]. Aside from actuation and imaging, SLA-printed microfluidic platforms have also shown high-sensitivity biosensing functionality. Sharafeldin et al. designed 3D-printed immunoarrays through SLA for ultra-sensitive cancer biomarker detection, utilizing chitosan-hydrogel-

based detection chambers and a chemiluminescence readout [114]. Lee et al. demonstrated SLA-based microfluidic devices from transparent, non-swelling WaterShed resin for rapid pathogen detection—namely, *E. coli* assays, which utilized helical microchannels [115]. The fabrication strategies discussed in the preceding sections provide the technological foundation for modern biomedical microfluidic devices. In particular, the combination of 3D printing with soft lithography enables the rapid fabrication of PDMS-based microfluidic platforms with an improved design flexibility, reduced manufacturing cost, and enhanced reproducibility. The following sections highlight the representative biomedical applications in which these fabrication strategies have enabled advances in diagnostics, organ-on-a-chip systems, drug delivery, and tissue engineering.

Despite its promise, SLA methods also have several drawbacks, including the limited resin type, required post-processing, and channel fidelity. Some of these drawbacks are being mitigated with emerging methods such as embedded channel printing and hybrid resin systems, which provide the potential for biosensing platforms with multiple capabilities. With these new avenues of SLA methods in conjunction with microfluidics, the marriage of these two manufacturing methods will be a game changer, providing scalable, tunable, and cost-effective biomedical diagnostic alternatives [116].

2.5.1. Emerging High-Resolution Additive Manufacturing Strategies for Soft Lithography

Stereolithography (SLA), digital light processing (DLP), and fused deposition modeling (FDM) have been important technologies for rapid microfluidic mold fabrication; however, the resolution of these methods is typically limited to the microscale, which hinders biomimetic capillary network fabrication, nanoporous membrane fabrication, and the fabrication of complex hierarchical microarchitectures [3]. For this reason, the recent work has focused on multi-resolution additive manufacturing that combines the high precision of fabrication techniques with the scalability and cost-effectiveness of PDMS replica molding to extend the geometric capabilities of traditional soft lithography. Of these, two-photon polymerization (2PP) stands out as the state-of-the-art technology for the manufacture of nanoscale molds. 2PP is based on nonlinear femtosecond laser-induced polymerization, and it is possible to fabricate suspended microchannels, biomimetic vascular networks, high-aspect-ratio microfilters, and the architecture of an organ-on-chip with feature sizes approaching 100–200 nm, which is impossible with conventional layer-by-layer printing [117]. Despite its comparatively low throughput and limited build volume, the recent studies have shown that 2PP has gained tremendous significance in precision biomedical manufacturing systems such as neural interfaces, hollow microneedles, blood–brain barrier models, and single-cell microfluidic platforms.

To address these constraints, the recent research has concentrated on hybrid multi-resolution manufacturing, of which SLA, DLP, 2PP, direct laser writing, and material jetting are examples in which all these techniques can be used in one manufacturing process [117]. These hierarchical approaches allow for a speedy fabrication of macroscale fluidic designs while selectively using nanoscale printing for the incorporation of functionally important components, such as microvalves, gradient generators, nanoporous membranes, and embedded sensing interfaces [118]. This strategy has significantly enhanced the fabrication efficiency while maintaining absolute structural precision and allowed the creation of multi-material organ-on-chip platforms, integrated electrochemical biosensors, wearable microfluidic platforms, and patient-specific biomedical platforms. Together, these developments show a clear shift from single-resolution fabrication to hybrid, multi-material, and multi-scale manufacturing, and suggest 3D printing-assisted soft lithography will provide a versatile platform for next-generation biomedical microfluidics fabrication.

2.5.2. Universal Adaptability of Hybrid 3D Printing–Soft Lithography for Multi-Material and Multi-Scale Microfluidics

The transition from rapid prototyping to a platform for a more diverse range of multi-material, multi-scale microfluidic devices has paved the way for hybrid manufacturing combining additive manufacturing and soft lithography. This technology, which combines the benefits of high-resolution 3D printing with elastomer replica molding, is expected to provide increased design flexibility beyond the limits of conventional photolithography and allow for the creation of hierarchical structures ranging from nanometer to centimeter scales. The Table 3 summarize the various approaches for building multiscale devices using 3D printing and soft lithography. Recent studies have shown that master molds fabricated by SLA, DLP, and two-photon polymerization (2PP) can be replicated not only in PDMS but also in a variety of other elastomers as per the application requirements of mechanical, chemical, and biological properties. The versatility has fueled the growth of organ-on-a-chip development, wearable biosensors, flexible bioelectronics, droplet microfluidics, and implantable biomedical devices [117].

Table 3. Universal adaptability of hybrid 3D printing–soft lithography for multi-material and multi-scale biomedical microfluidic fabrication.

Hybrid Manufacturing Strategy	Scale Achieved	Compatible Replica Materials	Representative Biomedical Applications	Major Engineering Advantage	Reference
SLA + PDMS soft lithography	Microscale (10–500 μm)	PDMS	Organ-on-a-chip, biosensors, microreactors	High replication fidelity and rapid prototyping	[119]
Dlp + sebs replication	Microscale	SEBS, PDMS	Drug screening, wearable diagnostics	Reduced drug absorption and improved scalability	[120]
2pp + PDMS replica molding	Nano–micro (100 nm–100 μm)	PDMS, PFPE	Artificial capillary networks, neural chips, BBB-on-chip	Nanoscale precision and true 3D freeform fabrication	[121]
Hybrid SLA + 2pp	Multi-scale	PDMS, SEBS, PFPE	Vascularized organ-on-chip, kidney-on-chip	Simultaneous macro- and nanoscale fabrication	[121]
Multimaterial vat photopolymerization + soft lithography	Multi-scale	PDMS, Ecoflex, TPU	Flexible biosensors, wearable microfluidics, implantable devices	Integration of rigid and flexible materials within a single platform	[122]

Recent developments also show that, with the combination of SLA or DLP to fabricate molds on the microscale in a fast time and localized 2PP or direct laser writing (DLW) to add a nanoscale functional element like a nanoporous membrane, biomimetic capillary networks, microfilters, and embedded sensing interfaces, a hierarchical multi-resolution fabrication is possible [74]. In a hybrid workflow, such as this, the fabrication time is greatly shortened, and, in situations requiring nanoscale precision, the performance is maintained. In addition, new multimaterial vat photopolymerization, sequential resin exchange, and embedded printing technologies allow for the incorporation of rigid frameworks, flexible membranes, conductive microelectrodes, and stimuli-responsive hydrogels into a single microfluidic device. These advances are paving the way for the next genera-

tion of organ-on-chip systems, integrated electrochemical biosensors, programmable drug delivery platforms, and personalized microfluidic diagnostics and have made hybrid 3D printing–soft lithography one of the most promising manufacturing approaches available for the scalable fabrication of biomedical microdevices [66].

2.6. Biomedical Applications of 3D-Printed Microfluidic Devices

Microchip technologies have revolutionized the use of microfluidics for biomedical applications at the lab scale by enabling dynamic and physiologically relevant cell culture and organ modeling. Lab-on-a-chip devices preserve hepatocyte cultures under flow, allowing for a better nutrient–waste exchange and the recreation of liver-specific functions. Oxygen and hormone gradients can model zonal liver phenotypes. Advances in microfabrication permit the fabrication of microscale liver constructs [123].

Parallel breakthroughs have also been made in modeling neural tissue. For instance, Sharma et al. created an all-human nerve-on-a-chip platform where human neurons and Schwann cells were co-cultured in photolithography-defined microchannels. Such a system was able to show extended neurite outgrowth, partial myelination, and measurable nerve conduction velocities, thus establishing a physiologically relevant model for electrophysiological, ultrastructural, and functional analysis (Figure 3) [124]. Paper-based microfluidic platforms and wearable health monitoring devices have increased in the past 20 years in large part because of the need to monitor health continuously and non-invasively, beyond the hospital, and in real time. The best illustration of the extent to which this field has developed would be glucose monitoring, which, today, can measure the glucose not only in blood but also in sweat, saliva, and interstitial fluid, and the accuracy is sufficient to be useful in clinical practice in most applications. The glucose sensor is by far the best-investigated biosensing device, which is a sign not only of its clinical significance but also of the state of definitions of the underlying electrochemistry. [125,126]. The interesting follow-up to this concept is to use glucose to operate the devices themselves. Microfluidic biofuel cells produce electricity through the oxidation of glucose in blood or serum by using oxidizing agents attached to a catalyst-coated surface on the anode and have been displayed in a non-rigid, rigid, skin-like format [127]. Likewise, [128] created a low-cost 3D-printed glucose biosensor, and the attraction is clear: a wearable that will be powered by the body fluid it is also scanning. Although the power output of these kinds of cells remains relatively small, this may be a viable method to use low-power sensors where only the transmission of data is required on a periodical basis. Beyond hepatic systems, microfluidics has also improved our ability to model neural tissues. Adriani et al. established a 3D neurovascular microfluidic model using a perfusable platform together with neurons, astrocytes, and cerebral endothelial cells to mimic key blood−brain barrier (BBB) functions [129].

Nervous-system-on-a-chip platforms, including the biomimetic platform developed by McAlpine, utilize FDM-produced polycaprolactone microchannels and tri-chamber geometries to co-culture neurons, glia, and epithelial cells within fluidically isolated compartments. This enables any research into brain development, intercellular signaling, and the mechanisms of neurodegenerative disease to be done with enhanced reproducibility and flexibility [111]. Kidney-on-a-chip platforms are utilized to overcome the limitations that 2D cultures present in predicting xenobiotic clearance and allow the simulation of filtration, secretion, and reabsorption pathways in a flow-directed environment that is more representative of native 3D conditions [130,131]. Here, Sakolish et al. created a tissue-on-a-chip of proximal tubule tissue in combination with physiologically based pharmacokinetic (PBPK) modeling that accurately predicted the clearance and reabsorption of xenobiotics [127,130].

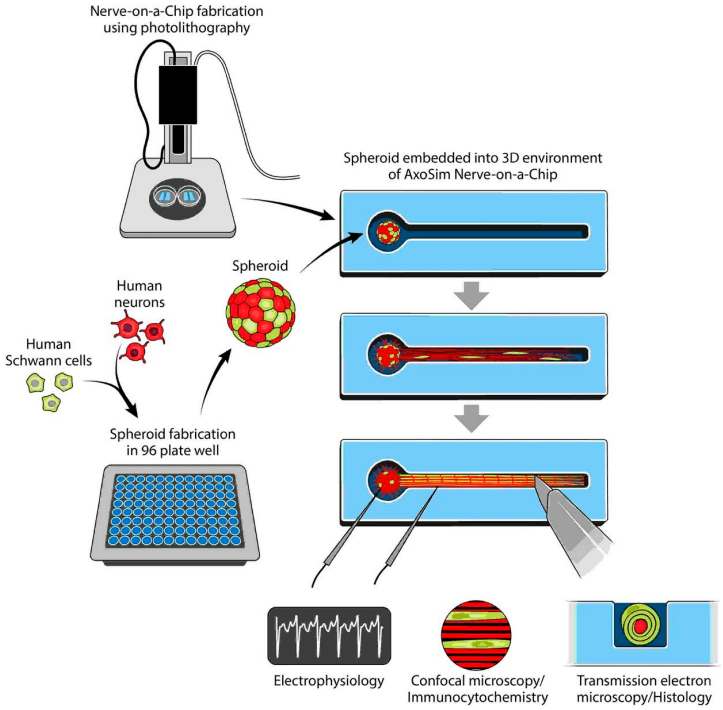


Figure 3. Schematic of Human Nerve-on-a-Chip (HNoaC) fabrication and characterization. Human Schwann cells and neurons form spheroids in a 96-well plate; spheroids are embedded in a photolithography-fabricated 3D AxoSim Nerve-on-a-Chip microenvironment to enable axonal outgrowth. The system is evaluated by electrophysiology, confocal microscopy/immunocytochemistry, and transmission electron microscopy/histology (reproduced from Ref. [124]. Open access, 2019Nature).

Together, these studies highlight the utility of organ-on-a-chip platforms to mimic the intricate organ-level physiology and reflect their increasing potential for predictive pharmacology, toxicological screening, and drug discovery. Additionally, microphysiological systems recapitulate the proximal tubule polarity, provide suitable biomarkers, and exhibit biochemical and transport processes that mimic in vivo processes. These tissue chips improve the pharmacokinetics prediction and give additional information about the toxicity, organ interaction, and drug action [132]. Together, these illustrate the versatility of microfluidic platforms to solve the difficulty of replicating complex organ-level physiology for research and therapeutic development [133].

2.6.1. Glucose Monitoring

Over the past 20 years, wearable sensors and microfluidic paper-based devices (uPADs) have developed into powerful platforms for applications in a variety of fields, including clinical diagnostics. As has been extensively documented in the literature, wearable technology, often referred to as wearable gadgets, is a category of technical devices that may be worn by a patient or consumer and usually contain tracking information about fitness and health. Characterizing non-invasive diagnostic technologies can benefit both those who use them as diagnostic tools to swiftly access patient clinical data and those who utilize them for continuous monitoring [128,134]. Pu et al. (2016), for instance, characterized the utilization of a microfluidic system with a graphene-modified electrochemical sensor for continuous glucose monitoring and illustrated how microfluidic systems collaborating with nanomaterials could revolutionize the field of wearable and real-time health-monitoring technologies [135,136]. Microfluidic channels can be fabricated using SLA, DLP, and FDM, as can system enclosures and flexible diagnostic platforms, while various types of PDMS, PLA, PEGDA, and flexible photopolymer resins are used based on the specific sensing

platform. 3D printing technology allows for the quick fabrication of patient-specific devices incorporating microfluidic architectures and cuts fabrication costs and assembly complexity. The marriage of additive manufacturing and electrochemical sensing has vastly enhanced the ability to miniaturize devices, design flexibility, and point-of-care applicability.

2.6.2. COVID-19 Diagnosis and Drug Discovery

The coronavirus disease 2019 (COVID-19) epidemic has intensified the research on diagnostics and antivirals, posing challenges such as the containment of the COVID-19 epidemic through population-wide diagnostic testing. SARS-CoV-2 nucleic acid is found in the nasopharyngeal secretions of infected patients, reinforcing the research on diagnostic tools, including nasopharyngeal (NP) swabs, as established by Oland G et al. [137]. Microfluidic technologies provide strong platforms for both the detection and drug discovery of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), moving the drug discovery infrastructure to more decentralized, rapid, and replaceable platforms [137]. 3D printing has enabled compact microfluidic systems that can execute sample preparation and isothermal/pCR-based amplification within one cartridge for simplified and portable point-of-care devices or workflows that were once confined to the benchtop. Along with the inclusion of 3D-printed microchannels, embedded heaters, and optical readouts, our systems can achieve rapid, low-cost, and disposable SARS-CoV-2 detection [138]. New prospects for the production of compact, reusable, reasonably priced, and mass-produced electrically interfaced sensors are opened up by the use of MEMS technology [139]. The detection of specific antibodies could identify if an individual has either contracted COVID-19 or has immunity against it. And, while rapid detection can be accomplished with nucleic acid or antibody-based methods, devices based on mass-manufactured MEMS devices could be used, like the CMOS MEMS-based nanomechanical sensor designed by Yen and Chiu, which has proven to be reliable and cheap for small molecule detection [140]. Microfluidic devices allow for the separation, reaction, detection, and cell culture to occur inside sealed microscale systems, reducing the contamination from external aerosol sources. In addition, the reduced thermal cycling time due to their rapid heat transfer and small reaction volumes increases the efficient nucleic acid amplification [141].

Together, these advances highlight the changing function of 3D printing in responding to the pandemic not just as a potential short-term remedy for supply chain failure but as a frontier technology in the biomedical field. As the field develops and evolves, one potential to streamline the development of COVID-19 diagnostics and therapeutics could be through the combination of 3D printing with AI-based drug design and microfluidic technology [142]. For COVID-19 diagnostics and drug-screening platforms, additive manufacturing has primarily been employed to fabricate microfluidic cartridges, reaction chambers, micromixers, and sample-processing devices using SLA, DLP, and material extrusion techniques. Printable materials including biocompatible photopolymer resins, PLA, and PDMS-based replica molds enable the rapid fabrication of disposable diagnostic chips with a reduced manufacturing time and cost. These manufacturing approaches facilitate a rapid outbreak response through decentralized production and rapid design iteration.

2.6.3. Microfluidic Fuel Cells for Energy Generation

The increasing global demand for energy and related environmental concerns from conventional non-renewable energy sources have heightened the focus on sustainable power generation technologies. For microsystems, particularly lab-on-a-chip biochemical sensors and portable electronics, a portable, reliable, fully integrated energy source is critical. Microfluidic fuel cells (MFCs) provide unique advantages over conventional fuel cells in that they have a large area-to-volume ratio, and they can be portable, cheap, and

fully integrated into miniaturized platforms [143]. Conventional renewable sources, like photovoltaics and wind, have limited energy generation due to intermittency and relatively low conversion efficiencies versus fuel cells that can efficiently convert chemical energy into electrical energy at efficiencies as much as 60% [144].

Miniaturized fuel cells build on the benefits of conventional designs, letting one achieve higher power densities and better mass transport, as well as possibly faster start-up times in portable and wearable systems or systems able to produce energy on demand. These systems are under active investigation for powering integrated biosensors, lab-on-a-chip diagnostic platforms, and mobile communication or transport devices [145]. A typical fuel cell comprises an anode and a cathode, each functionalized with a catalyst to accelerate electrochemical reactions [146]. The fuel undergoes oxidation at the anode, releasing electrons and generating positive ions. Electrons travel through an external circuit to the cathode, while ions migrate through an electrolyte membrane. The circuit is completed, and therefore, power is generated. Microfluidics can serve to enhance the kinetics of the reactions and the overall performance of the cell because of its high surface-to-volume ratios, tunable diffusion zones, and a completely independent source of control for the fuel and oxidant streams [143]. Enzymatic fuel cells (EFCs) are a subtype of biofuel cells that use enzymes as biocatalysts to oxidize biofuels like glucose. However, free enzymes in solutions can be less stable and expensive. As a solution, Noh et al. emerged with an EFC by covalently attaching glucose oxidase to carboxylated polyterthiophene nanoparticle layers. The design facilitated the oxidation of glucose to gluconic acid and hydrogen peroxide, which were then reduced at the cathode. The whole system achieved a power density of 0.78 mW cm^{-2}, an open-circuit voltage of 0.48 V, and a lifetime of 16 days [147]. Additionally, Dector et al. reported a flexible, air-breathing microfluidic fuel cell capable of operating glucose from human blood and serum. Microfluidic fuel cells (MFCs) may provide enhanced sustainability in biomedical applications and wearable devices, as they passively utilize ambient fuels and oxygen to generate energy [148].

2.6.4. 3D-Printed Micro-Chip in Drug

3D-printed microfluidic chips are evolving the way drugs can be delivered, making it possible to make highly customized devices designed for each individual patient. These tiny chips let doctors and researchers control exactly how and when a drug is released, which helps make treatment more effective and reduces unwanted side effects. Despite these exciting possibilities, there are still some practical obstacles to overcome before these chips can become routine in hospitals and clinics. For example, recent studies have looked at how 3D printing is being used to make microfluidic chips, especially focusing on the types of materials used and new ways of printing. Scientists highlight that better materials are needed to make these devices work well in the body. The researchers in [149] have shown that 3D-printed chips can carefully control drug release, but there are still issues, like the need for extra steps to further improve the chip-fabricated surface and the limits of the current materials. Another study looked at using these chips to make nanomedicines continuously but found that scaling up the process and making sure each chip is exactly the same are still big challenges [150].

Three-dimensional (3D) printing, which is also known as additive manufacturing (AM), is one of the several advancements in pharmaceutical technology that, when integrated with drug delivery, has paved the way towards moving from standardized, one-size-fits-all drug delivery systems to patient-tailored drug delivery systems. With AM, it has become possible to prepare personalized drug products with controlled overdose and varied shapes, sizes, and release characteristics using altered drug products with high plasticity to decide on the dose, shape, and size to fulfill the individual patient re-

quirements (Figure 4). This is particularly valuable for patients requiring variable doses, such as pediatric, geriatric, and obese populations. Furthermore, AM can provide the on-demand production of drug products with an easy, formulated AM process without any requirement of the prior optimization of the drug product formulation and also with a minimum wastage of drugs and drug excipients, unlike conventional processes, which require extensive work-up and a large number of drugs and excipients. This AM process utilizing 3D-printing technology has the advantage of rapid fabrication through technologies like FDM and SLA (stereolithography) that allow for easy customization with the least wastage of drugs and drug products. Another important advantage of AM is that a drug product with multiple drug payloads with complex release characteristics could be fabricated in a single unit, which is a great challenge in conventional formulation methods. The FDA has recently approved the 3D-printed tablet of levetiracetam, also known as Spritam®, an antiepileptic drug. Thus, 3D printing for drug delivery systems holds a lot of promise in developing attractive solutions for the biomedical field. Moreover, AM, along with other advancements in pharmaceutical technologies, will further play a crucial role in the efficient drug delivery of patient-tailored medicines, paving the way for the realization of personalized medicine. Recent advances in polymeric microneedles further complement 3D-printed drug delivery platforms by enabling minimally invasive and controlled transdermal administration. Biocompatible polymers such as hyaluronic acid, polyvinylpyrrolidone (PVP), poly(lactic acid) (PLA), polycaprolactone (PCL), and polyethylene glycol (PEG)-based hydrogels have been extensively investigated for fabricating dissolving and hydrogel-forming microneedles with tunable drug-release kinetics, improved patient compliance, and reduced systemic side effects. The integration of additive manufacturing with polymeric microneedle technology provides a promising strategy for personalized drug delivery and next-generation controlled-release therapeutics [151]. In drug-delivery applications, additive manufacturing enables the fabrication of microfluidic drug reservoirs, microneedles, controlled-release devices, and personalized dosage systems using SLA, DLP, FDM, and extrusion bioprinting. Materials including PEGDA, PCL, PLA, hydrogels, and biodegradable polymers permit the fabrication of patient-specific therapeutic platforms with controlled geometry and release characteristics. The principal manufacturing advantages include customization, the reduced material consumption, and the rapid production of complex drug-delivery architectures.

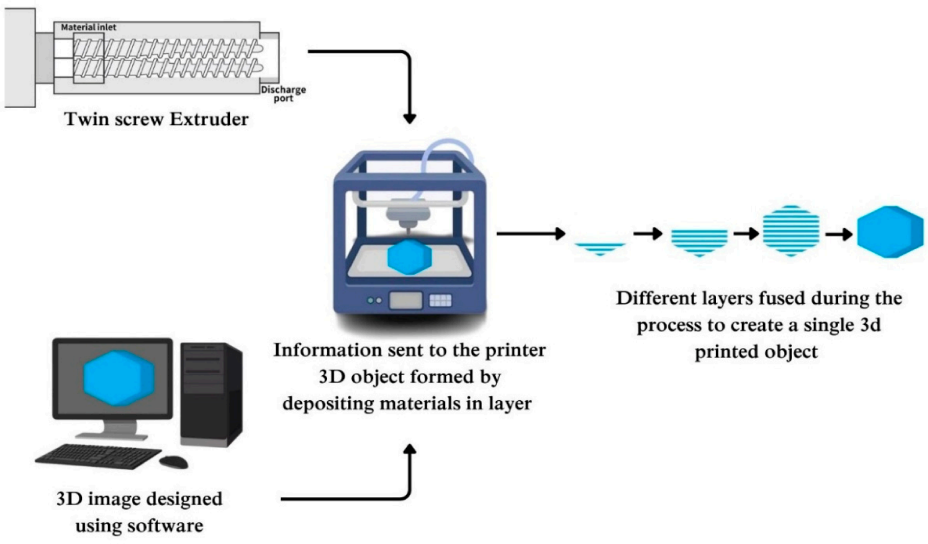


Figure 4. Illustrative representation of methods of fabrication using 3D printing of tablets, demonstrating design in CAD, extrusion, layering, and multi-layered tablets.

2.6.5. 3D Bioprinting of Tissues and Organs

Bioprinting, which means seeding living cells and biomaterials in a patterned manner, is now a legitimate research area. We discuss the advantages and disadvantages of the three main bioprinting technologies: inkjet, microextrusion, and laser-assisted bioprinting [152]. 3D bioprinting is being used in regenerative medicine to provide a solution to the global organ and tissue shortage [153]. Unlike non-biological printing, 3D bioprinting presents a set of unique challenges, including choosing materials, choosing the right cells, and understanding the growth and differentiation of the printed cells [154]. These are engineering and scientific challenges that need to be addressed by integrating technologies from fields such as engineering, biomaterial science, cell biology, physics, and medicine [155]. To date, 3D bioprinting has successfully created and transplanted various types of tissues such as multilayered skin, bone, vascular grafts, tracheal splints, heart tissue, and cartilaginous structures [156]. In addition, 3D bioprinting is also being used for other applications such as high-throughput 3D bioprinted tissue models for research, drug discovery, and toxicology [157].

Although polymeric biomaterials such as PCL, silk fibroin, GelMA, and collagen are widely used in 3D bioprinting because of their excellent biocompatibility and printability, their limited mechanical strength restricts their application in load-bearing bone repair. Consequently, recent research has increasingly focused on biodegradable magnesium (Mg)-based scaffolds, which provide temporary mechanical support while promoting osteogenesis through the controlled release of Mg^{2+} ions. Their gradual degradation also minimizes stress shielding and eliminates the need for secondary implant-removal surgery, making them promising candidates for orthopedic applications. The recent *Materials Science and Engineering R* (2026) review highlights architected magnesium scaffolds as an emerging direction in bone tissue engineering.

Beyond polymeric scaffolds, LPBF-fabricated magnesium TPMS scaffolds represent an emerging strategy for load-bearing tissue engineering. Recent SH-TPMS architectures enable the precise control of pore geometry, elastic modulus, and mass transport while providing hierarchical porous networks that promote bone regeneration. These studies highlight the growing importance of topology optimization combined with additive manufacturing for personalized orthopedic implants [158].

In parallel, scaffold topology optimization has become as equally important as material selection. TPMS and spinodal architectures provide highly interconnected porous networks that improve the mechanical performance, nutrient transport, and cell infiltration while enabling better control over scaffold degradation. Combined with additive manufacturing technologies such as laser powder bed fusion (LPBF), these architected magnesium scaffolds represent a promising alternative to conventional polymeric scaffolds for patient-specific load-bearing bone implants. In tissue engineering, additive manufacturing directly prints cell-laden scaffolds, vascular networks, and tissue constructs using extrusion bioprinting, DLP bioprinting, and two-photon polymerization. Bioinks based on GelMA, collagen, alginate, PEGDA, and PCL enable the fabrication of mechanically stable and biologically functional constructs. These manufacturing technologies provide the precise spatial control of cells and biomaterials while facilitating patient-specific scaffold fabrication and improved reproducibility.

Biomaterial Selection for Load-Bearing Bone Tissue Engineering

While polymeric biomaterials such as polycaprolactone (PCL), silk fibroin, GelMA, and collagen remain widely used in 3D bioprinting because of their excellent biocompatibility and printability, their relatively low mechanical strength limits their application in load-bearing bone repair. Consequently, recent research has increasingly focused on

biodegradable magnesium (Mg)-based scaffolds, which provide temporary mechanical support while releasing Mg^{2+} ions that promote osteogenesis, angiogenesis, and bone remodeling. Their gradual degradation also reduces stress shielding and eliminates the need for secondary implant-removal surgery, making them promising candidates for next-generation orthopedic implants. The recent *Materials Science and Engineering R* (2026) review identifies architected magnesium scaffolds as a rapidly emerging direction in bone tissue engineering.

Beyond the material composition, the current research emphasizes topology optimization to improve the scaffold performance. TPMS architectures, including Gyroid and Diamond geometries, provide highly interconnected porous networks that enhance mechanical stability, permeability, nutrient transport, and cell infiltration while enabling the independent tuning of the elastic modulus and degradation behavior. More recently, spinodal architectures have emerged as an alternative topology, offering improved stress distribution, damage tolerance, and mass transport compared with conventional lattice scaffolds. Combined with additive manufacturing techniques such as laser powder bed fusion (LPBF), these architected magnesium scaffolds enable the fabrication of patient-specific implants with an optimized mechanical and biological performance, representing a significant advancement over conventional polymer-based scaffolds for load-bearing bone regeneration.

Tissue Bioprinting Strategies

There are various types of technologies used for the deposition and patterning of biological materials: inkjet [159,160] and laser-assisted printing [161] (Figure 5).

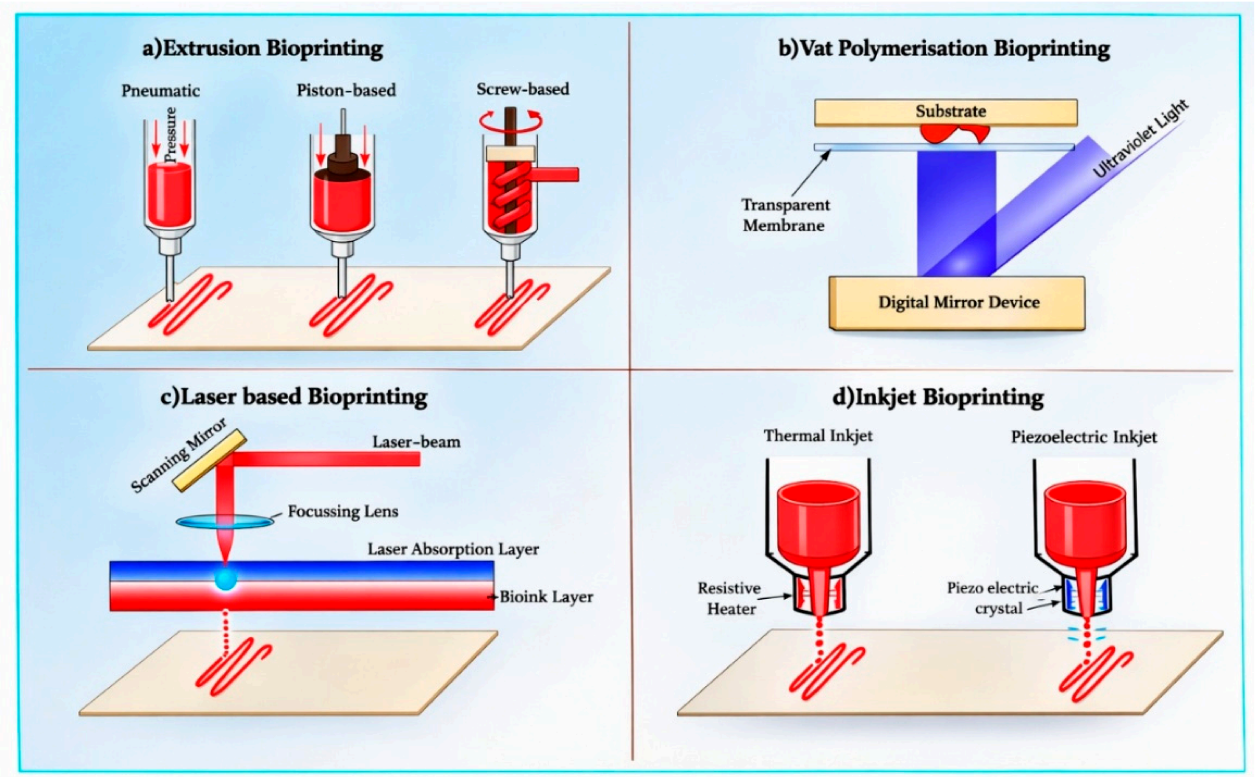


Figure 5. This schematic summarizes four major bioprinting techniques: extrusion-based (pneumatic, piston, and screw-driven); vat polymerization using UV light curing; laser-based material transfer; and inkjet bioprinting (thermal and piezoelectric). Each method represents a distinct approach for controlled deposition of bioinks in tissue engineering applications (Reproduced with from ref. [162], Open access, 2024 MDPI).

Inkjet bioprinting. Inkjet printers are also known as drop-on-demand printers, as shown in Figure 5. They are like standard office printers, except that they use thermal or piezoelectric energy to force tiny droplets of cell-containing bioink onto a substrate. They are quick and relatively specific, although found to be ineffective with high-viscosity material and are occasionally destructive to the cells when ejected [163]. Microextrusion extrusion printers that squeeze material through a small opening in continuous filaments are more common since they can be used on a larger variety of material types and are less costly [159] (the third dimension in addition to the x and y axes). Currently, inkjet-based bioprinters are specifically engineered to process and build biological materials, with an enhanced resolution, precision, and speed. These printers utilize either thermal or acoustic force [163,164] to deposit a droplet of liquid onto a substrate, which may support or constitute part of the final construct.

Vat Polymerization Bioprinting. Vat polymerization bioprinting, as represented in Figure 5, is a light-assisted additive manufacturing technique that relies on the spatially controlled photopolymerization of a liquid photosensitive bioresin. In general, the process begins with a digitally designed three-dimensional model that is converted into sliced layers, which are then sequentially fabricated through selective light exposure. In the configuration shown, a digital mirror device acts as the light modulation system, projecting patterned ultraviolet light through a transparent membrane onto the resin. Vat polymerization processes such as stereolithography and digital light processing are used to cure the resins on a layer-by-layer basis using controlled light exposure. These techniques yield extremely smooth surface finishes and fine features and can be used to microfabricate microfluidic channel surfaces where the surface quality is a determinant of the flow behavior. Laser-assisted bioprinting (LAB) is a different technology—the focused laser pulse transfers material on a donor ribbon to a receiving substrate with no nozzle at all, therefore removing clogging altogether. LAB can print at extremely high cell densities (up to 108 cells/mL) using the single-cell resolution, and the cell viability following printing is typically good. It has one major disadvantage, namely, throughput, whereby it is slow compared to inkjet or microextrusion. In bioprinting applications, this approach is particularly valuable for constructing intricate scaffolds, microarchitectures, and cell-laden structures, although challenges such as the limited material compatibility and potential phototoxicity must be carefully managed.

Microextrusion bioprinting. One of the most common and economical nonbiological 3D printers generally incorporates the use of microextrusion (Figure 5). They enable the painless and non-hypodermic delivery of drugs by only penetrating the very surface (the stratum corneum) of the skin without the activation of nerve endings. Recent experiments have also taken advantage of high-resolution 3D-printed master molds to create microneedle arrays with highly controlled tip geometries (cone, pyramid, and others), which can be optimized to penetrate the skin and release drugs at the desired kinetics. Post-processing operations such as controlled drying can be used to achieve an even finer tip sharpness without modifying the overall structure [165]. A particularly exciting application is the combination of microneedle delivery with photodynamic therapy (PDT) to treat cancer. The photosensitizer drug used in this method is incorporated into the microneedle matrix and can be released at the tumor site, and the light activation of the photosensitizer generates reactive oxygen species (ROS) that selectively kill cancer cells [166]. Local delivery with light-triggered activation minimizes the systemic side effects and enhances the precision of treatment—a nice illustration of how microfabrication can facilitate more targeted therapy.

Laser-assisted bioprinting. Laser-assisted bioprinting (LAB) uses the laser-induced forward transfer (LIFT) principle [53]. The technology was first developed for metal transfer. Later, it was adapted for biological material, including peptides, DNA, and cells

(Figure 6) [167]. LAB is less common than the inkjet or microextrusion bioprinting methods. However, it is still emerging as a promising technique in tissue and organ engineering, as shown in Figure 5. A typical LAB setup includes a laser beam focused by an optical system made of lenses and mirrors. This focuses the beam to a specific point on a bio-ribbon that supports the bio-sample on a donor transparent substrate typically made of glass, having a thin absorbing film at the top, usually made of metals like gold or titanium, and a bio-sample layer at the bottom, comprising the cells and/or hydrogel materials in a bio-ink solution. The laser beam creates a power peak that is absorbed by the absorber layer, creating a vaporization bubble that pushes the bio-inks towards the collector substrate.

The LAB resolution depends on the laser fluence, surface tension, wettability, and their combination; the air gap between the depositing bio-ribbon and the substrate; and the bio-layer thickness and viscosity. The main advantage of the nozzle-free LAB is the absence of clogging with cells and biomaterials, which is a common problem with other bioprinting techniques. LAB has successfully printed mammalian cells across a range of viscosities, from 1 to 300 mPa/s, with minimal impact on their viability and functionality. LAB can dispense cells at a concentration up to 10^8 cells/mL, achieving a micro-scale resolution of nearly one cell per drop. This operates at a laser pulse repetition of 5 kHz and speeds up to 1600 mm/s [161].

Therefore, they used LAB (Laser-Assisted Bioprinting) to create a cellularized skin construct in order to find out if they were able to 3D-print the right cell densities for tissue engineering in a layerable tissue construct, and the results show that they are, but the potential applications for this technology for creating large tissue engineering constructs are limited, so more research needs to be done [168]. In vivo 3D LAB, the bioprinting of nano-hydroxyapatite has also been demonstrated using a mouse calvaria 3D defect model [169]. A 3 mm-diameter, 600 µm-deep calvarial hole was filled with bio-ink as a first pilot proof-of-concept demonstration of this technique. Another medical application of laser 3D printing has also recently come to light as the first-ever 3D-printed tracheal splint was recently inserted into the airways of an 8-year-old patient suffering from localized tracheobronchomalacia and requiring the ongoing surgical repair of compromised airways [170]. It was a custom-made bio-resorbable version and has recently been shown to function without any need for further surgical intervention. Further, in vivo bioprinting may be required using biocompatible materials that can be integrated into host tissues in the body. Again, more research would be needed to improve the functionality of the printed tissues. Most enhancements would also likely be required for applicable and practical use by including the patient's cells, which can later form a new functional part of the damaged or diseased tissue.

In the context of the design and application of microstructured platforms in biomedicine, microneedling is achieving a high momentum using 3D-printed microneedle arrays and microfluidic devices. It can be seen in Figure 6 that the most recent developments are related to precision design and control over structural characteristics, as well as the integration of functional materials and biomedical applications.

Figure 6A: Microneedle arrays prepared by the replica molding of a mold prepared by high-resolution 3D printing. The procedure is as follows: the additive manufacturing of a master (master mold) allows one to obtain with a high precision the microfeatures required. By micromolding and loading drugs in the polymer matrix or by adsorbing them on the surface, the polymeric microneedles are ready to use. It is necessary to carefully manage the sequence of the residues washed and the dehydration-induced shrinkage. The shrinkage is controlled by the evaporation rate of the solvents and by the polymer network densification. It allows a decrease in the dimensions of the structures, maintaining their mechanical strength. This allows control of the tip sharpness and the aspect ratio of

the microneedles, which are very important parameters with which to modulate the skin penetration efficiency and drug delivery efficacy. Cone- and pyramid-shaped microneedles were obtained, and the tip width and height presented a high reproducibility and precision, which can modulate the insertion force, mechanical strength, and interstitial fluid of the skin, thus increasing the transdermal drug delivery efficacy [171].

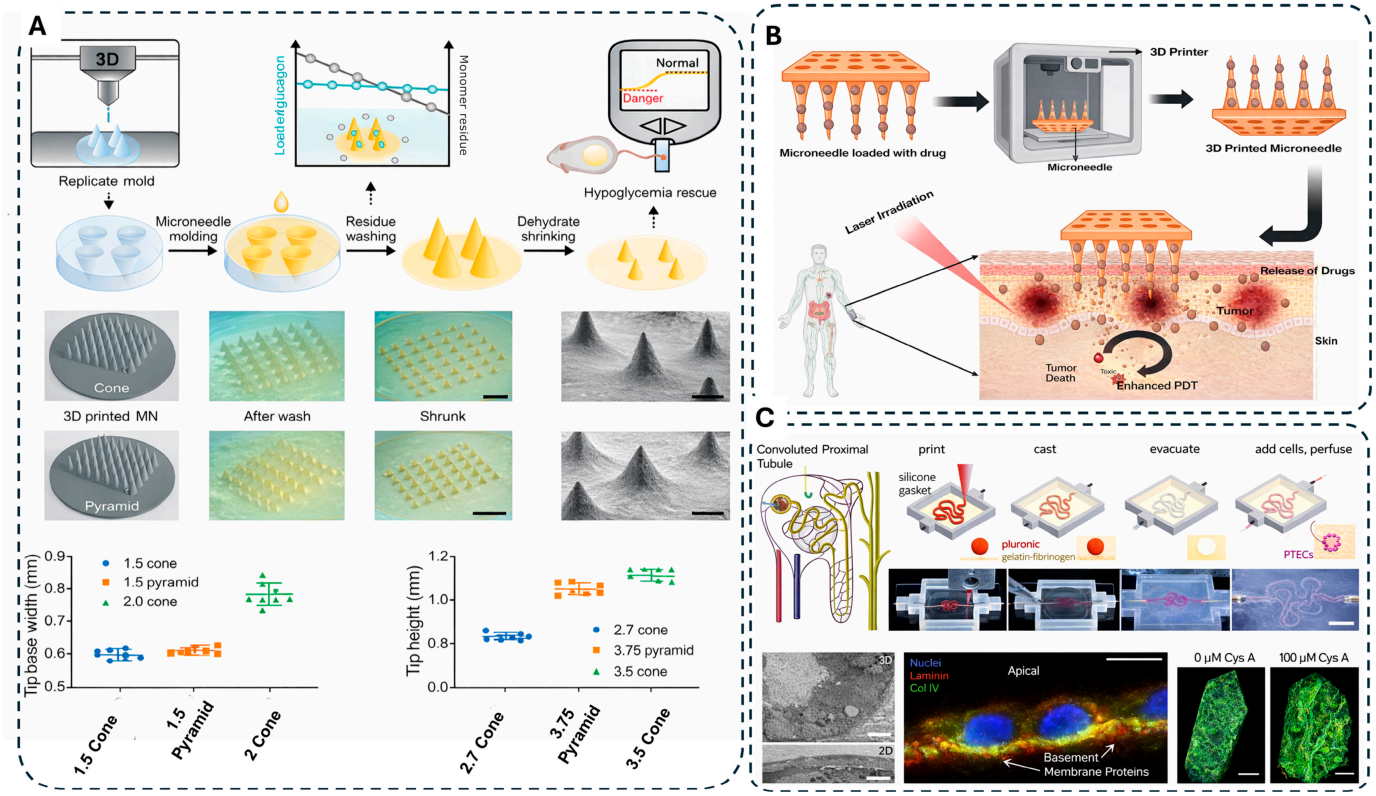


Figure 6. Representative examples of 3D-printed biomedical microdevices: (**A**) high-resolution 3D-printed microneedle arrays fabricated using replica molding (reproduced from Ref. [171], Open access, 2022 Wiley); (**B**) drug-loaded microneedles for localized cancer therapy (reproduced from ref. [172], Open access, 2025 Frontiers); and (**C**) biomimetic kidney-on-a-chip platform for renal tissue engineering (reproduced from ref. [173], Open access, 2025, MDPI).

Figure 6B: One potential fabrication method to build upon is shown in Figure 6B, which demonstrates a fully 3D-printing-based method to fabricate drug-loaded microneedles for localized cancer therapy. Current fabrication methods involve coating the microneedles with drugs and/or injecting drugs into the microneedles. Incorporating drugs into the printable material allows for a controlled drug release within the structure of the microneedle. When applied to the skin, the microneedles penetrate the stratum corneum and form delivery pathways that do not rely on systemic circulation, thereby decreasing the side effects. The system is also paired with photodynamic therapy (PDT), where the illumination of the photosensitizer-loaded microneedles results in the production of ROS that causes the apoptosis and necrosis of cancer cells. Microneedle-mediated drug delivery paired with laser-activated PDT provides more targeted therapy and increased penetration into solid tumors.

The micro-scale geometry was optimized for the least invasiveness while preserving sufficient mechanical strength for easy skin insertion. This study presents an additive manufacturing approach that not only bridges drug delivery and therapeutic activation but also holds great promise for precision oncology [172].

Recent advances in microneedle-mediated transdermal drug delivery have further expanded the biomedical applications of additive manufacturing by enabling minimally invasive, localized, and controlled therapeutic delivery. Three-dimensional printing facilitates the fabrication of customized microneedle arrays with a precisely controlled geometry, mechanical strength, and drug-loading capacity, thereby improving the skin penetration efficiency and sustained drug release. Such platforms have demonstrated considerable potential for treating psoriasis, acne, superficial tumors, scars, alopecia, and other dermatological disorders while improving patient compliance and reducing systemic adverse effects [174].

Complementing these microfabrication approaches, Figure 6C presents the development of a biomimetic microfluidic platform designed to replicate the physiological microenvironment of the renal proximal tubule. At a shorter length scale, recently, microfabrication techniques have been used to provide a method for the examination of the response of tubular cells to a variety of stimuli, as shown in (Figure 6C). In this study, the authors develop a very sophisticated "biomimetic" model of the renal proximal tubule, which they name their "Kidney on a Chip," or KOAC. The workflow to create this device involves several soft lithography steps and different casting techniques that result in a microchannel structure that replicates the general arrangement of renal tubules, indicating a design with larger lumens and smaller side branches. The devices, which resemble short 6–8 cm lengths of 3 mm-wide tubing, are coated with a specific extracellular matrix (ECM) to ensure a tight adhesion of the cells and seeded with growing epithelial cell strains, which, after two weeks under static conditions, are polarized and are used after an additional week under continuous perfusion that imposes defined shear stress to the cells (shear stress regulates cell position, shape, and tubular function by coordinating the expression of different transporters). Fluorescence microscopy imaging revealed nuclei and cytoskeletons as well as basement membrane proteins and thus indicated that on-chip, three-dimensional tissue-analogue structures were formed. The "Kidney on a Chip" (KOAC) device, as they name it, is claimed to provide a valuable system that can potentially assess the functions of the entire kidney on a small chip, and the authors claim that these devices would be useful to do dynamic in vitro drug testing under flow conditions that better represent an in vivo condition allowing more accurate measurements of pharmacokinetics and drug-induced nephrotoxicity than existing in vitro models. Indeed, microfluidics and cellular engineering appear to be two interesting approaches in which to investigate disease models or potential novel drugs in a more personalized way.

Taken together, these images demonstrate the impact of microfabrication and microfluidics on biomedical engineering. Panels A and B focus on microneedle arrays for minimally invasive drug delivery with precise control over the geometry and functionality of drug delivery. Panel C focuses on microfluidic biochips for creating highly physiological and functional tissue models. The integration of these technologies within biomedical engineering is indicative of a larger movement toward multi-functional, engineered, scalable, and application-specific devices that maximize the use of both topographic precision and biological function [173].

3. Future Prospects

The convergence of 3D-printing-assisted soft lithography and microfluidics has fundamentally transformed the fabrication of PDMS-based biomedical microdevices, enabling rapid, scalable, and cost-effective mold manufacturing for next-generation biomedical applications. This review focuses on how additive manufacturing and, more specifically, the techniques mentioned above (stereolithography, SLA; FDM; and 2PP) have advanced from prototyping to the fabrication of small-scale, high-resolution, and multi-material

devices, which permit the construction of complex microfluidic devices with custom-designed functionalities [1,3]. Recent advances in additive manufacturing are also expanding beyond polymer-based microfluidic fabrication toward architected smart materials and four-dimensional (4D) printing. Programmable metallic systems, including additively manufactured NiTi alloys with encoded microstructures, demonstrate how advanced manufacturing can precisely tailor geometry-dependent functional behavior, highlighting the growing role of intelligent materials and computational design in next-generation biomedical manufacturing. Although current applications remain largely outside conventional microfluidics, these developments illustrate the broader evolution of additive manufacturing toward multifunctional and adaptive device fabrication [175]. By integrating 3D printing with soft lithography and computer-aided design (CAD) mold making, researchers can produce their microchips without the burdens of a clean room and elude most regulations associated with the cleanroom process while also using a broader range of materials, including thermoplastics, polymers, and elastomers such as PLA, PMMA, PDMS, and SEBS [4,58] These advances have allowed researchers to construct organ-on-a-chip platforms, diagnostic devices for COVID-19, drug delivery devices, and microfluidic devices for fuel cell applications, showing the utility of printed microdevices as models for different physiological conditions, in point-of-care tests, and as portable biosensor power sources [124,138,147,149].

However, challenges remain with respect to consistent surface properties, biocompatibility, and clinical lateralization, particularly with respect to the regulatory approval before such devices can be used in healthcare settings. The future advancements of 3DP microfluidics include hybrid 3D-printing-style approaches such as the Faraday printing and 2PP techniques, which could potentially allow for additives to be printed in a single step, allowing for the finer features and resolution while the patterning with multi-materials is progressing, and it is leading to an overall integration, rather than mixing, of materials [36,176]. An equally promising direction is the application of topology-optimized biodegradable scaffolds for bone tissue engineering. Recent advances in TPMS and the spinodal architecture have demonstrated that the scaffold topology can independently regulate the mechanical stiffness, permeability, nutrient transport, and degradation behavior without altering the base material composition. When combined with biodegradable magnesium alloys and high-resolution metal additive manufacturing, these architected scaffolds exhibit improved osseointegration, enhanced vascularization, and reduced stress shielding compared with conventional lattice-based designs. Furthermore, computational topology optimization integrated with artificial intelligence is expected to accelerate the development of patient-specific orthopedic implants by simultaneously optimizing the structural integrity and biological performance. These developments highlight the expanding role of additive manufacturing beyond microfluidics, extending its impact toward next-generation regenerative medicine and personalized bone implant design. A new revolution in the field of personalized medicine could potentially be achieved by using 3D printing in conjunction with AI design and microfluidic automation to generate on-demand personalized drug delivery devices and diagnostics for every individual patient [142]. Future advancements in regulatory frameworks and materials science will place 3D-printed microfluidics at the core of a new generation of biomedical engineering, sustainable manufacturing, and point-of-care diagnostics.

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