Review article

3D printed microfluidics and microelectronics

Ryan D. Sochol, Eric Sweet, Casey C. Glick, Sung-Yueh Wu, Chen Yang, Michael Restaing, Liwei Lin

Abstract

Submillimeter-scale domains offer wide-ranging benefits for chemical and biological fields, which have motivated researchers to develop a diversity of strategies for manufacturing integrated microfluidic systems. Historically, microfluidic device construction has predominantly relied on micromachining technologies that are rooted in the semiconductor and microelectromechanical systems (MEMS) industries. These methodologies have enabled microfluidic platforms to be fabricated with fully integrated microelectronics—a critical requirement for applications such as electrophoresis and dielectrophoresis (DEP), surface acoustic wave (SAW) actuation, digital microfluidics (e.g., via electrowetting-on-dielectric (EWOD) phenomena), and on-chip electrochemical detection. Despite the distinguishing capabilities afforded by conventional microfabrication protocols, a number of inherent limitations have given rise to increasing interest in alternative approaches for microdevice construction in the form of additive manufacturing or “three-dimensional (3D) printing”. Here we review recent progress in the development of both 3D printed microfluidics and 3D printed microelectronics. We evaluate the distinctive benefits and constraints associated with emerging 3D printing technologies with respect to the fabrication of both microfluidic and microelectronic systems. Lastly, we examine the potential use of 3D printing-based approaches for manufacturing microfluidic devices with integrated microelectronics.

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1. Introduction

The controlled manipulation of fluids at submillimeter length scales affords a multitude of advantages for applications in chemistry and biology [1–3], including rapid thermal and biochemical diffusion times [4], low reagent volumes [5], laminar flow profiles [6], precision handling of microparticles (e.g., microbeads and living cells) [7,8], and controlled regulation of microenvironmental characteristics [9,10]. To benefit from these characteristics, researchers have utilized and/or adapted conventional micromachining methods to fabricate fluidic systems at smaller scales [11–13]. Initially, these protocols involved manufacturing microfluidic devices comprised of standard semiconductor materials, including silicon [14] and glass [15,16]; however, disadvantages associated with the use of such materials for microfluidic applications engineered the predominant method for fabricating microfluidic devices in the lab: soft lithography [17–19]. Building upon the elastomeric replication methods developed at Bell Labs [20], Duffy et al. introduced a technique for micromolding and bonding the silicone elastomer, poly(dimethylsiloxane) (PDMS), to form enclosed channels for transporting fluids [21]. An example of a soft lithography protocol for micromolding a single layer of PDMS is shown in Fig. 1 – left, which consists of five fundamental steps: (i) photoresist (e.g., SU-8) is spin-coated onto a Si wafer; (ii) microchannel designs are photolithographically defined (e.g., using a photomask and UV light); (iii) the exposed photoresist is chemically developed, which selectively removes undesired photoresist; (iv) liquid PDMS is poured onto the Si wafer with patterned photoresist, which serves as a negative master; and (v) after the PDMS is thermally cured, the molded PDMS is removed from the Si wafer, allowing individual devices to be cut and then punched with holes at designated inlet/outlet port locations [22–24]. Following this micromolding process, the PDMS devices can be bonded to a substrate (e.g., a glass slide or another PDMS layer) using methods including UV ozone or Oxygen plasma treatment to form enclosed microchannels.

Soft lithography can also be extended to construct microfluidic devices comprised of multiple discrete layers that are bonded together—a process termed “multilayer soft lithography” [25,26]. The use of multiple layers allows for each tier to serve a distinct functionality. For example, certain layers can operate as relatively rigid components, while other layers can operate as flexible or deformable components to yield fluidic routing capabilities that mimic those of electronic circuits [27–29]. In addition to differences in physical or mechanical functions, each layer can also be designed with distinct biochemical properties, such as multilayer microfluidic systems comprised of an intervening permeable layer that supports biochemical transport for biological studies [30–33]. Researchers have also developed methods to create non-planar molds for PDMS micromolding, such as by executing multiple photolithography steps [34] or using grayscale lithography techniques [35–38]. These approaches are fundamental to applications including microfluidic raling via microchannels with multiple heights [39–42] and hydrodynamic arraying of cells in multilevel trapping structures [43–45].

Fig. 1. Conceptual illustrations of a fabrication process for constructing a single-layer microfluidic system with integrated electronics. (Left) Soft lithography protocol for micromolding poly(dimethylsiloxane) (PDMS). (Right) Photolithography-based protocol for patterning metal electrodes, pads, and interconnects onto a glass substrate. (Bottom) The micromolded PDMS is bonded to the metal-patterned glass substrate (e.g., via UV Ozone or O₂ plasma treatment) to form enclosed microfluidic channels with integrated electronics.
Although researchers have demonstrated the use of solely fluidic microdevices for diverse biochemical applications [46], the incorporation of microelectronics with microfluidics can greatly extend the capabilities of self-contained lab-on-a-chip technologies. A variety of techniques can be employed to integrate electronic components with microfluidic systems. One approach involves the manual insertion of conducting wire [47] or other electrode materials [48] into microfluidic channels or ports. Alternatively, the protocols for soft lithography can be adjusted to achieve PDMS bonding to a substrate with a planar electronics layer, such as a glass slide [49] or PCB board [50]. An example protocol for fabricating a microfluidic device with embedded electrodes is illustrated in Fig. 1. The process for fabricating the metal-patterned glass substrate includes five key steps: (i) photoresist is spin-coated onto a glass substrate; (ii) electrode designs are photolithographically defined; (iii) a thin layer of a secondary metal to support electrode adhesion is deposited (e.g., via physical vapor deposition (PVD) or electroplating); (iv) a layer of a primary metal electrode is deposited; and then (v) the substrate in chemically developed, resulting in liftoff (i.e., removal) of the undesired photoresist-metal features (Fig. 1 – right). Thereafter, micromolded PDMS can be bonded to the metal-glass substrate, resulting in enclosed microchannels that interface with metal electrodes, pads, and interconnects (Fig. 1 – bottom). To support this bonding process and the ultimate sealing of the microchannels, researchers have also augmented conventional techniques with surface treatments, such as adhesive layers [51], plasma surface modification [52], dielectric barrier discharge [53], and modified Parylene layers [54].

An alternative approach for electronics integration is to augment the microchannels directly (rather than the planar substrate) by fabricating electroactive PDMS composites. Such composites can be achieved by mixing liquid-phase PDMS with a conductive nanoparticle filler, such as carbon black [55], silver [55], zinc [56], or carbon nanotubes [57], prior to thermal curing. This technique allows for the assembly of vertical sidewall electrodes directly in contact with the microfluidic channel [58] and can also be used to place other active polymer composites adjacent to microfluidic channels [59].

The ability to incorporate microelectronics into microfluidic systems has enabled a wide range of on-chip capabilities. In a number of cases, direct fluid contact with the electrodes is not required, such as for electrode-generated heat sources [60–62] or cell manipulation via magnetic fields [63–65]. Similarly, electrically generated effects can be performed with isolated electrodes for applications including fluorescence-activated cell sorting [66], electrophoretic fluid [67] and valve manipulation [68–70], and droplet electrocoalescence [71, 72]. For electrowetting-on-dielectric (EWOD) – a process by which individual microfluidic droplets can be manipulated by dielectrically altering their surface energy [73] – only partial electrode isolation is required as fluid droplets remain in direct contact with a common grounding electrode while isolated from control electrodes by a layer of dielectric material [74,75]. In contrast, electrodes are directly integrated into microfluidic systems when a direct conducting path into the fluid is needed, such as for electrophoresis [76], dielectrophoresis [77,78], fluid manipulation via electrokinetic effects [79,80], and hydrogel [81–83] and cell manipulation [84,85].

Although the aforementioned methods of microdevice construction afford numerous benefits in terms of microscale precision and microelectronics integration, limitations inherent to such protocols remain a pervasive impediment to progress in chemical and biological fields [86]. A critical barrier for those outside of engineering fields is that gaining access to the necessary equipment for device construction (e.g., in microfabrication facilities) is often difficult, and may require considerable technical training and high usage fees [87]. Furthermore, the clean room-based procedures for Si wafer processing are typically executed manually, which can be exceedingly cost, time, and labor-intensive [88]. These issues are exacerbated when fabricating multilayer or multilevel device designs that require distinct tiers to be manually aligned and/or assembled – procedures that can diminish the precision and reproducibility associated with microdevice manufacturing [89,90]. Thus, replicating microfluidic and microelectronic advancements on-site can be challenging. Another critical issue is the intrinsic restriction of monolithicity, which renders relatively common features of macroscale fluidic components (e.g., circular channels with varying diameter, non-planar physical architectures, etc.) difficult or impossible to achieve in microscale domains. This monolithicity also constrains the assembly and packaging of microfluidic systems to relatively planar geometries [91]. More significantly, planar systems restrict the geometry of applied electromagnetic fields [92] as planar electrodes cannot generate parallel electric fields [93] (e.g., a requirement for optimal capacitive cell cytometry and droplet detection [94]). Consequently, alternative micromanufacturing methods capable of bypassing the aforementioned limitations could offer significant promise for diverse academic and industrial fields. This potential has motivated research into the use of additive manufacturing for microfluidic devices, which has already begun to expand the general understanding of the inherent advantages – and key areas for further development – of 3D printed microfluidic devices [95,96].

2. Additive manufacturing approaches

Additive manufacturing – widely referred to as “three-dimensional (3D) printing” – encompasses a number of strategies for constructing 3D structures through point-by-point and/or layer-by-layer processes. In general, computer-aided design (CAD) tools are used to generate a digital 3D model (e.g., in STL file format), which is then imported into computer-aided manufacturing (CAM) software corresponding to a specific 3D printer or 3D printing process. Lastly, the resulting 3D printing code (e.g., G-code) is electronically imported into the 3D printer to enable autonomous device construction. Although researchers have developed a wide range of 3D manufacturing methodologies for applications throughout broad academic and industrial fields (e.g., selective laser sintering, laminated object manufacturing, and binder jetting), the micro/nanoscale 3D printing techniques with advantageous characteristics for lab-on-a-chip systems stem from three fundamental approaches: (i) extrusion-based 3D printing, such as fused deposition modelling and direct ink writing, (ii) stereolithography, and (iii) multijet (or polyjet) modelling.

2.1. Extrusion-based 3D printing

At present, extrusion or nozzle-based 3D printing technologies have garnered the most interest across academic, industrial, and commercial spaces. In 1988, S. Scott Crump introduced the first extrusion-based 3D printing approach. Stemming from his experiences making a toy frog (for his daughter) using a hot glue gun loaded with a mixture of polyethylene and candle wax, S. Scott Crump described and patented an extrusion-based method termed “fused deposition modelling (FDM)”, by which a 3D object is formed using dispensing heads (e.g., nozzles) to directly deposit heated thermoplastic materials onto a substrate via a point-to-point, layer-by-layer process (Fig. 2a). FDM – alternatively referred to as “fused filament fabrication (FFF)” as FDM is Trademarked by Stratasys, Ltd. – supports the 3D printing of a variety of thermoplastic or thermosetting materials, such as acrylonitrile butadiene styrene (ABS), polylactic acid (PLA), and polyethylene terephthalate (PET). In the late 1990s, Cesaro and Calvert adapted this concept to extrude and deposit pseudoplastic materials [98], including ceramics and composites, via a technique termed “robocasting”. Further extensions of these methodologies in which materials or “inks” are extruded through a nozzle and deposited point-to-point, layer-by-layer to generate 3D structures without requiring thermal processing steps (i.e., heating or cooling) are characterized as “direct ink writing (DIW)” [99–101].

2.2. Stereolithography

In 1981, Hideo Kodama presented and demonstrated several strategies for building 3D objects by exposing a liquid-phase photo-hardening
polymer to light in layer-by-layer protocols [102]. Although he filed an initial patent application, Kodoma did not file a full patent specification. In 1984, Charles W. Hull filed a patent for a similar system, which he termed a "stereolithography apparatus (SLA)" [103]. SLA 3D printing involves using a bath of liquid-phase photoreactive material and focused light to photocure (i.e., solidify) the material in specified locations in a point-by-point, layer-by-layer fashion to ultimately fabricate a 3D object comprising cured material (Fig. 2b) [103]. It should be noted that the initialism "SLA" has since come to be used to describe the process, rather than the apparatus; however, the initialism "SL" is often used instead. In developing SLA, Hull also created the widely-used STL file format for 3D models, and pioneered the digital slicing and hatching (i.e., infill) approaches that underlie many 3D printing technologies. "Direct Laser Writing (DLW)" – an extension of SLA in which two-photon absorption phenomena are harnessed to initiate spatially-controlled photopolymerization at a single point in space – has enabled 3D manufacturing with resolutions down to the 100 nm range [104]. Subsequent adaptations of SLA have included: (i) the use of projection-based photoexposure (e.g., via digital micromirror device (DMD) or digital light processing (DLP) technologies) to cure an entire layer at once (in contrast to the point-by-point process inherent to the use of a focused laser); (ii) continuous-exposure versions of projection-based concepts, such as continuous liquid interface production (CLIP) [105]; and recently, (iii) holographic approaches for curing entire volumes in a single step [106].

2.3. Multijet modelling

In the early 1990s, Yamane et al. invented a technique for building 3D structures by inkjet printing a photosetting or thermosetting
material layer-by-layer [107], which combined with the simultaneous printing of a sacrificial support material [108] and parallel dispensing strategies [109], became the basis for “Multijet Modelling (MJM)” approaches. Referred to as either “Multijet” or “Polyjet” 3D printing, MJM entails the use of high numbers of microscale inkjets in parallel to simultaneously deposit microdroplets of photopolymer/photoplastic materials and sacrificial support materials in a line-by-line, layer-by-layer process (with continual UV photocuring) to produce 3D objects (Fig. 2c). After completion of the 3D printing process, the support material – typically a water-soluble gel-like material or a meltable wax – can be removed through post-processing procedures [110,111].

3. Microfluidic systems via 3D printing

3.1. 3D printed transfer molding

One of the earliest examples of utilizing 3D printing technologies for microfluidic applications involved shaping of elastomeric polymers using a 3D printed mold [112]. McDonald et al. applied an earlier MJM approach, referred to as “solid-object printing”, to 3D print various molds for PDMS micromolding (Fig. 3a), enabling microfluidic systems with serpentine channels and multilayered via’s [112]. Subsequently, researchers have extended this work to create molds using SLA [113] and MJM [114]. In addition to patterning features using external molds, researchers have also 3D printed molds of internal features, which can be removed after PDMS curing [115–118]. For example, Hwang et al. created multiple MJM 3D printed molds that can be assembled to surround liquid-phase PDMS during the curing process, and then removed thereafter (relying on the flexibility of PDMS) to create complex PDMS channel architectures (Fig. 3b) [117]. Costa et al. used a similar 3D printed template molding technique to create a “Thrombosis-on-a-Chip” device by: (i) using SLA-printed 3D microchannel templates (120–400 μm in diameter) designed to mimic the shape of healthy and diseased (narrowed) vascular structures; (ii) using the templates for PDMS casting; and then (iii) removing the 3D printed templates to leave behind empty microchannels within the solidified PDMS (Fig. 3c) [118]. Additionally, Glick et al. introduced a double-sided molding procedure, which supports single-step fabrication of structures including thin membranes as well as double-sided alignment structures to decrease the time and labor associated with assembling multilayer microfluidic systems with many distinct layers (Fig. 3d) [119]. Compared to the concept of 3D printing an entire microfluidic system, the use of 3D printing for fabricating molds provides several advantages: (i) each mold can be used for the fabrication of multiple microfluidic devices, saving on 3D printing times and costs, and (ii) the process is compatible with conventional microfluidic fabrication materials, most notably PDMS [120–123]. The latter benefit allows for researchers to employ similar micromolding procedures, yet achieve geometric characteristics that would be exceedingly difficult to achieve using conventional methods. Nonetheless, the molds are still limited in geometric versatility by the requirement that they must be able to support demolding processes. Thus, although 3D printed transfer molding procedures can overcome issues associated with clean room-based wafer processing, many of the limitations associated with protocols subsequent to wafer mold fabrication remain.

3.2. Microfluidic systems via extrusion-based 3D printing

Among the types of extrusion-based 3D printing, FDM currently represents the most widely used approach for commercial desktop 3D printing. Although a number of efforts have employed FDM to build fluidic systems [124–128], the inherent trade-off between feature resolution and fabrication time has limited its efficacy for microfluidics manufacturing [95]. Instead, the use of extrusion-based 3D printing for microfluidics applications has predominantly involved employing DIW methods to deposit sacrificial materials or “fugitive inks” [101], which can then be casted and subsequently removed. In particular, the Jennifer Lewis group has pioneered a number of fugitive ink-based DIW strategies for resolving 3D microfluidic systems. In one of the earliest of these approaches, Therriault et al. presented a four-step protocol for constructing 3D microfluidic networks: (i) DIW is employed to 3D print a network comprised of a fugitive ink; (ii) the 3D printed network is then casted with a surrounding liquid resin; (iii) the resin is solidified via a curing process; and (iv) the fugitive ink is heated to support liquefaction, enabling vacuum-based extraction to leave behind a 3D network of hollow, interconnected microfluidic channels (Fig. 4a) [99].
Wu et al. adapted this approach by applying an omnidirectional printing technique [129] to print free-floating fugitive ink within a reservoir of a photocurable hydrogel (Fig. 4b) [130]. After the printing process, the researchers photocured the surrounding hydrogel and then evacuated the liquid-phase fugitive ink via vacuum. The resulting system included vascular-inspired 3D microchannels within the hydrogel matrix (Fig. 4b) [130]. Using a similar approach, Miller et al. 3D printed a 3D sacrificial network; however, in this case, the 3D sacrificial network was encapsulated with living cells and ECM before being dissolved in media [131]. Gelber et al. also 3D printed sacrificial structures using a carbohydrate glass fugitive ink, which was used to demonstrate a 3D combinatorial fluid mixer (Fig. 4c) [132]. Kolesky et al. further extended this approach in a combinational method than involved using DIW to bioprint two distinct cell-laden gels adjacent to a fugitive ink, which was ultimately removed and then lined with endothelial cells to emulate microvasculature [133]. It is important to note, however, that such sacrificial approaches are not limited only to extrusion-based processes as demonstrated by Li et al. employing wax jetting for sacrificial material deposition for subsequent casting (Fig. 4d) [134].

A significant advantage of conventional polymer filament-based FDM for microfluidics is the ability to print using multiple filament material extrusion heads [135], which Li et al. utilized to fabricate microchannels with embedded membranes made from a porous material in a single step for the detection of nitrate content in soil [136].

Notably, MacDonald et al. compared the accuracy and precision of FDM-printed microfluidics with respect to alternative 3D printing approaches and observed that ~600 μm peak-to-peak surface abnormalities in FDM-based microchannels – created using a ~300 μm-wide extrusion nozzle – provided additional surface area for laminar flow interfacial contact that expedited diffusive mixing [137]. Thus, FDM can be employed to fabricate FDM-printed laminar flow microfluidic mixers; however, the use of FDM-printed microfluidic devices should be restricted to applications in which unintended multi-fluid mixing would not negatively affect the performance of the device [137].

3.3. Microfluidic systems via stereolithography

In recent years, SLA has emerged as the predominant method by which researchers 3D print entire microfluidic systems [138–142]. Au et al. evaluated mail-order SLA-based microfluidic devices designed with rectangular microchannels that varied in size, revealing channel resolutions on the order of 300–400 μm and also presenting methods to improve optical clarity (Fig. 5a) [90]. Concurrently, Shallan et al. presented the concept of using DMD projection-based SLA to fabricate 3D microfluidic gradient and microdroplet generators (Fig. 5b) [138]. Bhargava et al. developed a number of discrete and reconfigurable elements, such as junctions as well as microfluidic resistors in the form of 750 × 750 μm² microchannels with varying lengths (and therefore,
resistances) [139]. These elements were utilized for microfluidic applications including laminar mixing and droplet generation (Fig. 5c) [139]. Macdonald et al. revealed that SLA-printed microchannels more reliably and accurately replicated as-designed dimensions (~26 ± 20 μm wider) with lower surface roughness than those fabricated using FDM (~109 ± 36 μm narrower) or Polyjet (~40 ± 36 μm narrower) [137]. The results revealed that SLA offers an effective technology for fabricating microfluidic devices for applications in which limited laminar flow mixing is required, such as for diffusive particle separation [137]. To support cell culture within a 3D printed microfluidic device, Urrios et al. demonstrated the use of several types of DLP-based SLA to fabricate microfluidic systems using a photocurable low-MW poly(ethylene glycol) diacylate (MW 250) (PEG-DA-250) [140]. In contrast to the aforementioned systems with static components, Au et al. also presented 3D printed microfluidic valves with deformable membranes, which were employed to create a peristaltic pump comprised of three valves and a multi-fluid perfusion chamber comprised of four valves (Fig. 5d) [141]. Other groups have since demonstrated additional SLA-based valving capabilities for 3D printed microfluidic systems [142,143].

In terms of the maximum achievable feature resolution, SLA is the only 3D printing approach that has been demonstrated, as of the writing of this review, capable of fabricating microchannels with sub-100 μm features, on a scale more comparable to that possible using conventional microfluidics manufacturing techniques [144]. Using a commercially available SLA resin, Monaghan et al. demonstrated square partial-microchannels as small as 50 μm×50 μm are achievable when fabricated onto a flat surface, which can then be sealed to form an enclosed microchannel [145]. Below this 50 μm limit, the pixelated resolution of the UV light source resulted in unintended curing of resin inside the channels. Because the precise chemical formulation of the SLA resin has a significant effect on the practical resolution of SLA-printed features, Gong et al. developed customized PEGDA-based SLA resins with optimized formations of the UV absorbors molecules as well as lower viscosities than commercial resins [146], which enabled them to fabricate microchannel networks with 60 μm-tall voids and 20 μm-thick membranes [143]. Recently, the Nordin group further optimized a custom SLA-resin to achieve 18 μm × 20 μm microchannels [147], which to the authors' knowledge, marks the smallest 3D printed microchannels reported in the literature at this time. Additionally, Kotz et al. created an SLA-compatible silica nanocomposite that enabled conversion to transparent fused silica glass (via heat treatment) following the 3D printing process, and demonstrated resolutions on the order of tens of microns [148]. Thus, customization of SLA-compatible photomaterials appears to be a critical area of research to further improve the feature resolution and material versatility of SLA-printed microfluidic systems.

Researchers have also leveraged the submicron-scale precision of DLW to 3D print structures within conventionally fabricated microfluidic channels [149–151]. To date, DLW approaches have achieved the highest feature resolutions for 3D printing [152–154]; however, similar to extrusion-based 3D printing, this feature resolution can also be a limitation. Specifically, for DLW, the trade-off between voxel size (i.e., the 3D point of two-photon polymerization) and 3D printing time has typically limited the total build volume of 3D printed structures to within the 100 μm⁴ to 1 mm³ range [155]. Thus, initial efforts towards using DLW for 3D printed microfluidics involved direct-writing structures within pre-fabricated, single-layer PDMS microfluidic channels [149,150]. By first loading the photocurable material into microfluidic channels, researchers were able to use DLW to photocure complex geometric...
structures in situ to facilitate improved diffusion-based mixing dynamics [149] and construct multidirectional fluidic vias [150]. Lamont et al. recently extended this approach to 3D print microfluidic diode components within PDMS microchannels [151].

One condition of note for SLA-based methods, however, is that the 3D printed structures must be self-supporting. For geometries that do not satisfy this condition, fully integrated support structures (e.g., pillar-like ribs) must be added to the design to facilitate successful prints [105]. Although such structures can be manually removed from macroscale objects following the 3D printing process, doing so for submillimeter-scale systems can be extremely challenging or unfeasible [110].

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**Fig. 6.** MJM-based 3D printed microfluidic systems. (a) A DNA-inspired microfluidic system architecture comprised of eight embedded microfluidic channels [110]. (b) Schematic illustration and results for 3D printed modular microfluidic components assembled by means of non-3D printed rubber O-rings and metal pins [157]. (c) Fundamental 3D printed microfluidic circuit components (left), including a microfluidic capacitor, diode, and two transistor designs, and a single-input-based multi-flow controller (right) comprised of four distinct microfluidic transistors [110]. (d) Multi-material 3D printed “Quake Valves” comprised of photoplastic and a flexible photomaterial for the membrane [162]. (e) Multi-material 3D printed microfluidic capacitor (left) and transistors (right) comprised of a photoplastic material as well as a flexible photomaterial for deformable diaphragms and sealing O-rings [163].
3.4. Microfluidic systems via multijet modelling

The ability to simultaneously 3D print device materials as well as sacrificial support materials has enabled MJM-based microfluidic systems to be constructed with the most complex physical geometries of any additive manufacturing approach. For example, a 3D microfluidic system with a DNA double helix-like architecture comprised of eight microfluidic channels is shown in Fig. 6a [110]. Initially, efforts to utilize MJM to 3D print microfluidic devices involved the production of relatively simple, straight channel geometries, yet demonstrated the potential for integrating non-3D printed parts, such as membrane inserts [156]. Lee et al. extended this concept by presenting a modular, breadboard-inspired technique in which discrete microfluidic components (e.g., channels, mixers, junctions, etc.) could be connected through the use of non-3D printed rubber O-rings and metal pins to realize functional devices [Fig. 6b] [157]. Taking advantage of the 3D structural versatility of MJM, Sweet et al. demonstrated a 3D multi-fluid concentration gradient generator for clinical drug screening applications [158]. To investigate the potential of using MJM to enhance device autonomy, Sochol et al. 3D printed a fundamental class of microfluidic circuit components – namely microfluidic capacitors, diodes, and transistors (capable of pressure-gain) (Fig. 6c – left) [110]. Larger, fully integrated microfluidic circuits were also 3D printed (comprised of multiple components), including a full-wave rectifier and single-input-regulated multi-flow controller (Fig. 6c – right) [110]. Sweet et al. later extended the use of these components by integrating several 3D printed fluidic circuit elements in order to realize finger-powered fluidic pumping and mixing systems [159].

An important benefit of MJM is that devices can be printed not only with a single part material and a support material [160], but also with additional part materials (or functional gradings of materials) to realize multi-material 3D printed microfluidic systems [161,162]. To demonstrate this concept, Keating et al. 3D printed a “Quake Valve” [26] with a rigid photoplastic for the overall system, but with a flexible rubber-like material for the valving membrane (Fig. 6d) [162]. Recently, Hubbard et al. demonstrated multi-material microfluidic capacitors, diodes, and transistors, which comprised two distinct materials: (i) a non-compliant photoplastic material for functionally ‘rigid’ features, and (ii) a flexible photomaterial for deformable diaphragms and sealing O-rings (Fig. 6e) [163].

Despite the aforementioned advancements, it is important to note that although MJM technologies provide considerable advantages in terms of multi-material integration, build volumes, print speeds, and geometric versatility, MJM material selection remains limited to a relatively small number of proprietary materials [164,165]. Among the materials that are available, the vast majority are limited in terms of biocompatibility, which may impede the adoption of MJM approaches for biological and biomedical microfluidic applications [111]. In response, various techniques have been demonstrated that improve MJM material biocompatibility, primarily by preventing leaching of cytotoxic monomers into contacting fluid. For example, conformal PDMS and polystyrene-based coatings offer one route to enhance endothelial cell adherence to inner microchannel surfaces for improved efficiency of cell lysis [166]. Similarly, researchers have observed that polyurethane-based scaffold drop-casting coatings can improve both substrate cytocompatibility and hydrophilicity for enhanced attachment and proliferation of human umbilical vein endothelial cells (HUVECs) on 3D printed surfaces [167].

The use of sacrificial support materials presents challenges for microfluidics as all internal voids (e.g., microchannels) are filled with these materials directly after the 3D printing process, which can demand significant post-processing procedures as well as component design changes. For example, to remove sacrificial wax support materials from device microchannels, Sochol et al. executed a multistep protocol including: (i) immersing the devices in mineral oil heated to 80 °C; (ii) manually inputting hot mineral oil through the microchannels via a syringe; and (iii) inputting pressurized air through the microchannels [110]. In addition, the microfluidic components had to be designed with additional input/output ports to facilitate this process, such as fluidic diodes that required four ports rather than the standard two (Fig. 6c – bottom left) [110]. The use of water-soluble support materials can alleviate the need for such design changes; however, it is important to note that the removal process for such materials is diffusion dominated. In contrast to wax-based support materials, which can be liquefied upon heating, water-soluble gel-based support materials can only be removed by either physically dislodging it [162] or allowing the material to dissolve over time (often over multiple days) [137,163,168]. The diffusion-limited challenges associated with the dissolution of gel-based support material from within microchannels with complex shapes and enclosed structures [169] often guide the design of devices to support physical removal by using primarily straight and/or millimeter-scale microchannels that can accommodate the insertion of a removal tool [156,162]. Although the addition of multiple access ports and external stimuli (e.g., sonication) can accelerate the dissolution process [163], the removal time is directly related to the length of internal microchannels and inversely related to the microchannel diameter. As a result, many microdevice geometries, such as the DNA-inspired microfluidic system shown in Fig. 6a, would be difficult or unfeasible to achieve due to the challenges associated with the water-soluble support material removal process.

4. Microelectronics via 3D printing

4.1. 3D printing of conductive materials

In contrast to the area of 3D printed microfluidics in which advancements have mainly stemmed from demonstrating devices with newly manufacturable forms (e.g., microchannel geometries and sizes), the field of 3D printed microelectronics has instead focused predominantly on function – i.e., achieving printable conductive materials with desired electrical characteristics [170]. At present, researchers have primarily employed extrusion-based 3D printing approaches for electronics applications; however, there have been adaptations of such processes to enable new capabilities. In particular, Ahn et al. demonstrated an omnidirectional printing strategy to achieve flexible and spanning microelectrodes with out-of-plane vias (Fig. 7a) [129]. Adams et al. extended this technique to 3D print electrically conductive antennas onto convex and concave substrates (Fig. 7b) [171]. Notably, Zhou et al. further extended these strategies to 3D print a silver-nanoparticle ink to create both in-plane and out-of-plane passive radio frequency (RF) structures, including various designs of inductors, transformers, and oscillators (Fig. 7c) [172]. The researchers were able to integrate fully printed structures with discrete transistors to create RF circuits capable of being directly incorporated with complementary metal–oxide–semiconductor (CMOS) chips [172]. To improve the potential for out-of-plane 3D printing, Skylar-Scott et al. demonstrated a laser-enhanced DIW approach in which a laser is used to selectively anneal conductive inks during the deposition process to create conductive metallic interconnects and freestanding spiral architectures (Fig. 7d) [173]. Liu et al. presented an additional adaptation of DIW, termed “low-temperature DIW (LTDW),” which enabled 3D printing of highly porous 3D LiFePO4 electrodes [174]. Although the aforementioned works provide a number of deposition strategies, fundamentally, it is the conductivity (and reproducibility) of printed materials that underlie to efficacy of 3D printed microelectronics.

One of the key challenges of 3D printing electrically conductive inks is that the porosity of fabricated parts may cause electrical shorts due to the spreading of the inks on surface layers [175] or between stacked layers [176]. To reduce such issues, one approach is to use micromachining techniques to build fine channel features that serve to guide the deposition of conductive materials, while electronic components can be manually placed in desired locations (Fig. 8a) [177]. Alternatively, through process
optimization, conductive inks can be directly printed without the need for guiding grooves [178–182]. For example, researchers have reported resistivities for silver inks in the range of $1 \times 10^{-7} \Omega \text{m}$ to $1 \times 10^{-5} \Omega \text{m}$ [177, 183]. To improve the properties of deposited silver inks, researchers have demonstrated that local annealing of printed silver conductive traces yielded a resistivity of $4.3 \times 10^{-8} \Omega \text{m}$ – close to the bulk silver resistivity of $1.9 \times 10^{-8} \Omega \text{m}$ [184]. Further advancements will be enabled by research into alternative, application-specific inks with additional desirable properties, such as elasticity and viscoelasticity, biocompatibility, high temperature stability and controllable porosity [185–188].

As the capabilities of DIW increase, the much-needed validation of the technology and its potential uses in the real world are critically important. Gubanova et al. integrated DIW with CMOS manufacturing to construct ion-sensitive field-effect transistors (ISFETs) for micro volume analysis [189]. Other groups have bypassed CMOS manufacturing and 3D printed mesoscale versions of embedded circuitry components, such as capacitors, inductors, and high pass filters as well as copper-based microwave metamaterials [190,191]. Additional strategies have enabled more complex integration of conductive materials into 3D printing processes for electronics. For example, Muth et al. presented...
an embedded 3D printing approach that involved extruding conductive ink inside of a reservoir of liquid photopolymer to form resistive sensing elements for flexible strain sensors [192]. Researchers have also demonstrated that the extrusion process itself can be adapted, such that multiple materials are 3D printed simultaneously from a single nozzle [193]. In particular, Frutiger et al. fabricated capacitive soft strain sensors through an extrusion-based multicore-shell printing strategy (Fig. 8b) [193]. Microchannels filled with liquid metals at room temperature, such as mercury, gallium, and their alloys, also offer a potential route to improve the speed and geometric complexity of liquid metal-integrated microfluidic structures [194].

Although extrusion techniques represent the most popular 3D printing strategy for manufacturing conductive structures, researchers have explored alternative approaches as well. Interest in light driven 3D technologies such as SLA/DLP and DLW for the creation of conductive structures has increased in recent years due to the superior geometric controls, material customization, and scalability [195–201]. For example, Odent et al. presented elastic and conductive ionic composite hydrogels that are compatible with SLA processes and demonstrated both elastic deformation and conductivities up to 2.9 S m$^{-1}$ (Fig. 8c) [199]. Recently, researchers have adapted DLP-based 3D printing techniques to achieve multiple material prints— with conductive and non-conductive regions— including conductive structures composed of multi-walled carbon nanotubes (MWCNTs) [195]. On a much smaller scale, DLW has been used to 3D print gold microstructures through two photon metal-salt reduction of a polymer gold composite material [196]. Researchers have also investigated the utilization of a selective laser sintering technique for carbon nanotube (CNT) wrapped thermoplastic polyurethane (TPU) powders, revealing conductivity of up to 10 $\Omega$ m at 1 wt% CNTs [202].

To provide an alternative to DIW of conductive materials, Wu et al. presented an approach that entails 3D printing a structure with empty

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**Fig. 8.** Microelectronic systems via 3D printing. (a) 3D printing of electronic modules by combining FDM, micromachining, and DIW technologies [177]. (b) Capacitive strain sensors fabricated by a multicore-shell extrusion-based 3D printing process [193]. (c) Elastic deformation and restoration of an SLA-printed structure comprised of an elastic, transparent, conductive ionic composite hydrogel [199]. (d) Electronic components and systems fabricated by the combination of MJM and liquid metal paste filling approaches [203]. (e, f) Electronic systems fabricated by integrating SLA, DIW, and “pick-and-place” strategies, including: (e) a timer circuit [210], and (f) a six-sided gaming die comprising a microprocessor, an accelerometer, and light-emitting diodes [211].
channels, which are subsequently filled with a conductive liquid metal paste (Fig. 8d) [203]. This strategy enabled fabrication of electronic components including resistors, inductors, and capacitors, as well as integrated circuits, such as an inductor and capacitor resonant tank capable of passive wireless sensing functions. Similar to prior works, however, the resistivity of the filled liquid metal paste was measured as $3.6 \times 10^{-6} \Omega \text{m}$ due to the poor packing density of silver particles inside the channels and inefficient curing processes [203]. Agarwala et al. adapted this approach to achieve microchannel strain sensors showing improved conductivity and long term stability [204].

In many cases, researchers have investigated combinational approaches in which: (i) the general structure of a system is 3D printed using an established technology; (ii) the electronic interconnects are 3D printed via DIW; and (iii) commercial electronic components are physically placed in specified locations at intermediate stages during the 3D printing processes. For example, researchers have demonstrated 3D printed antennas and microwave devices by merging FDM with DIW of conductive inks [205–207]. Similarly, a number of groups have integrated SLA with DIW (while embedding commercial electrical components during the printing process) to fabricate a variety of electronic systems, including motion sensors [208,209] and timer circuits (Fig. 8e) [210]. For example, Fig. 8f shows a six-sided gaming die consisting of a microprocessor, an accelerometer, and light-emitting diodes (LEDs) [211]. One general problem of such methods, however, is that the photocurable materials currently used for SLA processes may be affected by weathering, aging, dimensional changes, and UV exposure doses, and thus, could limit the reliability of SLA-DIW-based 3D printed electronics [177].

4.2. 3D printing of semiconductor and other electronic materials

In addition to polymers and conductors, 3D printed microelectronics can benefit from various materials to construct microelectronic devices of different functionalities, such as semiconductor, magnetic, and piezoelectric materials; however, there are three key issues in producing these materials with high quality via 3D printing processes. First, most

Fig. 9. 3D printed systems comprising semiconductor and additional materials. (a) 3D printed quantum dot LEDs [212]. (b) A 3D printed bionic ear fabricated by DIW of cell-seeded biomaterial and a silver nanoparticle-based polymer [213]. (c) A Li-ion microbattery fabricated by DIW of LTO and LFP [214]. (d) Cuboidal SiC ceramic lattices fabricated by robocasting [222]. (e) Graphene oxide composite structures fabricated by DIW [223].
of these materials are made in the form of nanoparticles to be mixed with solvents and polymers for desirable viscosity and printing properties with respect to specific 3D printing processes. Annealing protocols are generally required to remove the solvents and/or polymers, and the residual material can degrade the properties of 3D printed structures. Second, it is difficult to achieve single crystal structure from the nanoparticles without voids and grain boundaries. Because most high-performance devices are based on single crystalline structures, the characteristics of 3D printed devices are expected to degrade as compared to current state-of-the-art electronic devices. Third, many microelectronic elements, such as transistors, are based on the architecture of 2D structures made of thin films instead of true 3D structures. As such, it is not yet evident that constructing 3D printed microelectronics comprising large out-of-plane thickness is beneficial.

Nevertheless, there have been several recent reports describing functional devices based on 3D printing materials beyond conductive electrodes and interconnects. One notable example is a 3D printed quantum dot LED presented by Kong et al., which was constructed by interweaving five different materials: (i) semiconducting inorganic nanoparticles, (ii) elastomeric matrix, (iii) organic polymers for charge transport, (iv) metal conductors, and (v) a UV transparent substrate (Fig. 9a) [212]. Mannoor et al. demonstrated the ability to create bionic ears by using DIW to 3D print a cell-laden hydrogel matrix and an intertwined conducting silver nanoparticle-based polymer (Fig. 9b) [213]; Sun et al. employed DIW to 3D print Li4Ti5O12 (LTO) and LiFePO4 (LFP) in adjacent architectures to serve as materials for the anode and cathode, respectively, for a Li-Ion microbattery (Fig. 9c) [214].

Researchers have also extended DIW approaches to 3D print a variety of composite materials for microelectronic applications. Although 3D printing of conductive carbon materials was recently reviewed by Fu et al. [215], it is of note that a material of growing interest in the additive manufacturing field is graphene as well as its oxidized and reduced forms, graphene oxide (GO) and reduced graphene oxide (rGO), respectively [216–219]. Graphene-based polymer composites offer substantial increases in thermal stability, conductivity, and mechanical strength all while being relatively inexpensive to synthesize and biocompatible [218]. Researchers have also demonstrated the ability to 3D print structures comprising SiO2 [220], ZnO [221], SiC (Fig. 9d) [222], BaTiO3 [223], ZrO2 [224], and GO (Fig. 9e) [225]. One important caveat, however, is that the efficacy of 3D printing a number of these materials relies on high-temperature post-processing protocols. For example, 3D printed ZnO required sintering temperatures of up to 1500 °C [221], which render its incorporation with other materials difficult.

5. Conclusion

Submillimeter-scale additive manufacturing approaches are empowering researchers to pioneer entirely new classes of microfluidic and microelectronic systems. Although these efforts have generated considerable interest in academia, industry, and the general public, in many ways, the overall field remains in its infancy. At present, state-of-the-art demonstrations of 3D printing-based microfluidic and microelectronic capabilities serve as important first steps towards a longer-term transition of emerging technologies from the lab to real-world uses and commercialization. It is important to note, however, that the utility of additive micro/nanomanufacturing for industrial applications is founded on 3D printing-induced benefits that are unequivocally superior to conventional manufacturing methods. In the case that additive manufacturing protocols continue to suffer from relatively slow fabrication speeds and low production volumes, the aforementioned benefits will instead need to stem from the unparalleled geometric control and/or device customization afforded by distinct 3D printing processes. Thus, it is critical for researchers to focus less on evaluating how 3D printing-based devices can replicate structures and/or functionalities that can be readily produced using conventional means, and instead, focus more on demonstrating new, unique capabilities enabled by additive manufacturing that would be difficult or unfeasible to achieve via traditional microfabrication protocols.

A key challenge to this goal, however, is that while a myriad of additive manufacturing strategies offer the potential to serve as promising alternatives to conventional methods of fabricating solely microfluidic or microelectronic systems, no singular 3D printing approach has thus far exhibited characteristics that would be ideal for the construction of microfluidic devices with fully integrated microelectronics. Specifically, such a technology would enable: (i) simultaneous 3D printing of electrically conductive materials, non-conductive materials, and microchannel structures, (ii) precise resolution of both external and internal features (e.g., for electrodes and microchannels, respectively), (iii) minimal labor before, during, and after the printing process, (iv) high geometric and architectural versatility, (v) a wide selection of printable materials, including materials that are biocompatible and conductive materials that exhibit low electrical resistivity, (vi) rapid fabrication times, and (vii) low costs. Unfortunately, recent works have revealed that current 3D printing techniques that are beneficial for microfluidics manufacturing suffer from numerous limitations in the context of microelectronics fabrication and vice versa.

Researchers have demonstrated that extrusion-based 3D printing methods such as DIW provide significant advantages compared to other additive processes for fabricating microelectronic systems [226], yet such approaches are ill-suited for microfluidics manufacturing [96, 164, 227]. One could employ extrusion-based 3D printing methods to first deposit a combination of electrically conductive materials, non-conductive materials, and fugitive inks to build an integrated multi-material structure, and then execute standard casting and fugitive ink removal protocols [99,130–133] to resolve hollow microchannels that intersect with or run adjacent to the deposited conductive materials. Despite providing a potential means towards microfluidics and microelectronics integration, such a strategy would suffer from considerable post-processing as well as the inherent geometric constraints of extrusion-based 3D printing.

Conversely, SLA and MJM approaches are superior to extrusion-based methods for microfluidics manufacturing [95], and current research into custom SLA resin development and improvements to the 3D printing equipment hardware has begun to improve fabrication of sub-100 μm microstructures [143,144,146]; however, such approaches have not yet been demonstrated for the direct placement and/or integration of electrically conductive materials during the 3D printing process. Instead, such methods typically require extensive post-process metallization protocols [228–230] that continue to be limited by many of the issues associated with conventional microfabrication. As a substitutive route, researchers have demonstrated that 3D printed microfluidic systems can be designed to incorporate the manual insertion of non-3D printed electronic components [139,231]. Yet, such protocols are inherently limited by factors such as labor, precision, and repeatability, and thus, are not ideal for the long-term goals of the field.

Ultimately, we do not expect additive manufacturing to fully replace conventional manufacturing protocols with respect to microfluidics and microelectronics fabrication. Rather, we anticipate that the selection and use of a specific fabrication strategy will be highly dependent on case-by-case factors that directly correlate to the unique capabilities of distinct manufacturing approaches. Consequently, it is paramount that researchers refrain from employing additive manufacturing for cases in which conventional methods would undoubtedly be superior, and instead, take advantage of the distinctive potential afforded by 3D printing to create novel microsystems with beneficial characteristics that would be challenging to achieve through any other manufacturing process. Although it will likely take considerable time to develop 3D printing technologies that are ideally suited for both microfluidics and microelectronics fabrication, researchers have already made significant strides developing and leveraging additive manufacturing methodologies to overcome many of the limitations of traditional clean room-
based microfabrication processes. In the remaining interim, it will be critical for researchers to continue inventing and demonstrating novel strategies to accelerate the advancement of new generations of 3D printed microfluidic systems with full, autonomous microelectronic integration.

**Author contributions**


**References**


