



Direct-ink-writing 3D-printed bioelectronics

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The development of wearable and implantable bioelectronics has garnered significant momentum in recent years, driven by the ever-increasing demand for personalized health monitoring, remote patient management, and real-time physiological data collection. The elevated sophistication and advancement of these devices have thus led to the use of many new and unconventional materials which cannot be fulfilled through traditional manufacturing techniques. Three-dimension (3D) printing, also known as additive manufacturing, is an emerging technology that opens new opportunities to fabricate next-generation bioelectronic devices. Some significant advantages include its capacity for material versatility and design freedom, rapid prototyping, and manufacturing efficiency with enhanced capabilities. This review provides an overview of the recent advances in 3D printing of bioelectronics, particularly direct ink writing (DIW), encompassing the methodologies, materials, and applications that have emerged in this rapidly evolving field. This review showcases the broad range of bioelectronic devices fabricated through 3D printing including wearable biophysical sensors, biochemical sensors, electrophysiological sensors, energy devices, multimodal systems, implantable devices, and soft robots. This review will also discuss the advantages, existing challenges, and outlook of applying DIW 3D printing for the development of bioelectronic devices toward healthcare applications.

Introduction

The rapidly evolving field of bioelectronics is poised for transformative advancements that will revolutionize various aspects of modern healthcare through the implementation of digital health technologies for active monitoring and early diagnosis, personalized medicine for tailored medical treatments, soft robotics for assisted surgery, drug delivery, and smart prostheses [1–4]. Sensors that capture biological signals from various parts of the human body are the heart of this impending technology [5,6]. From monitoring dynamic physical motions and subtle bodily movements to acquiring comprehensive molecular information, these biosensors open new avenues for innovative diagnostic

and healthcare solutions [7–9]. By integrating the Internet-of-Things (IoT) into wearable devices, patients and caretakers can have greater accessibility to monitor, manage and engage in effective medical interventions that safeguard patients' health [10–12]. Indeed, wearable biosensors today have evolved to become increasingly sophisticated owing to the tremendous emphasis on further miniaturizing devices, improving performance with multimodal functionalities, developing soft and elastic electronics, and customizations for better compatibility and personalized point-of-care applications. This has thus led to the diverse use of materials and composites that are engineered to achieve different structures, properties, and functionalities [9,13]. Conventional manufacturing methods are therefore often limited by the materials they can accommodate, the ability to create intricate patterns and geometries, and the complexity and ability for customization of designs.

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Over last years, the adoption of three-dimensional (3D) printing for the fabrication of bioelectronics has attracted significant attention as 3D printing shows promising potential to surpass traditional manufacturing techniques in terms of its versatility for material and design, manufacturing efficiency, process simplicity, and scalability for future mass production [14–19]. Also referred to as additive manufacturing (AM), 3D printing is an emerging technology that is capable of creating complex 3D objects with high precision and flexibility via layer-by-layer construction [20–22]. At present, there are several 3D printing technologies such as fuse deposition modelling (FDM), stereolithography (SLA), digital light processing (DLP), selective laser sintering (SLS), and direct ink writing (DIW) that employ different strategies to pattern and print materials [20]. However, most of the 3D printing technologies usually rely on a certain class of materials, including thermoplastic polymers for FDM, photopolymer resins for SLA and DLP, and powdered polymers or metals for SLS, which limited the customized formulation of inks. Among these approaches, DIW, an extrusion-based AM method using dispensed inks from small nozzles to fabricate 3D structures layer-by-layer has emerged as the most versatile 3D printing technology for the development of bioelectronics (Fig. 1A). Besides being able to encompass a wide range of materials through custom ink formulations, DIW possesses other advantages as well such as low-cost, high printing resolution, fast printing speed and the ability to create of micro- and nanoarchitectures for enhanced functionalities. The operation of DIW is straightforward where an ink is extruded out through a nozzle and directly printed onto a substrate along a pre-determined printing pathway. For the formulated inks, shear-thinning and yield-stress are two crucial features to meet the rheological criteria for the extrusion (Fig. 1B and C) [23]. During the extrusion, the ink exhibits a liquid-like behavior, and it quickly transforms back to a solid-like substance to retain shape until fully solidified once extruded out of the nozzle. The printed resolution of 3D printing process is mainly dependent on the printing parameters, such as the size of the nozzle, printing speed and extrusion pressure. Controlled based on digitally designed models, 3D printing via DIW allows high degrees of freedom for quick prototyping of customized designs. Besides, there are other various types of ink-based printing technologies focusing on the development of bioelectronics such as screen printing that utilizes a stencil with a pre-patterned design and a mesh screen to transfer ink onto a target substrate through physical contact using a squeegee [24], gravure printing that involves direct ink transfer from engraved micrometer-sized recessed cells of the cylindrical roller to the substrate with the aid of an impression cylinder [25], and inkjet printing that uses either a thermal or piezoelectric transducer to eject tiny droplets of ink to create high-resolution patterned images [26]. Each of these printing technologies is differentiated by its unique style for material deposition with its own merits and drawbacks. Compared to these printing technologies, DIW 3D printing, as a promising printing scheme, offers several key advantages, in terms of its versatility for material and design, high resolution with controllable thickness, high efficiency for low-cost fabrication, and good scalability for mass production (Fig. 1D). Furthermore, since deposition is typically done through physical addition of material, different

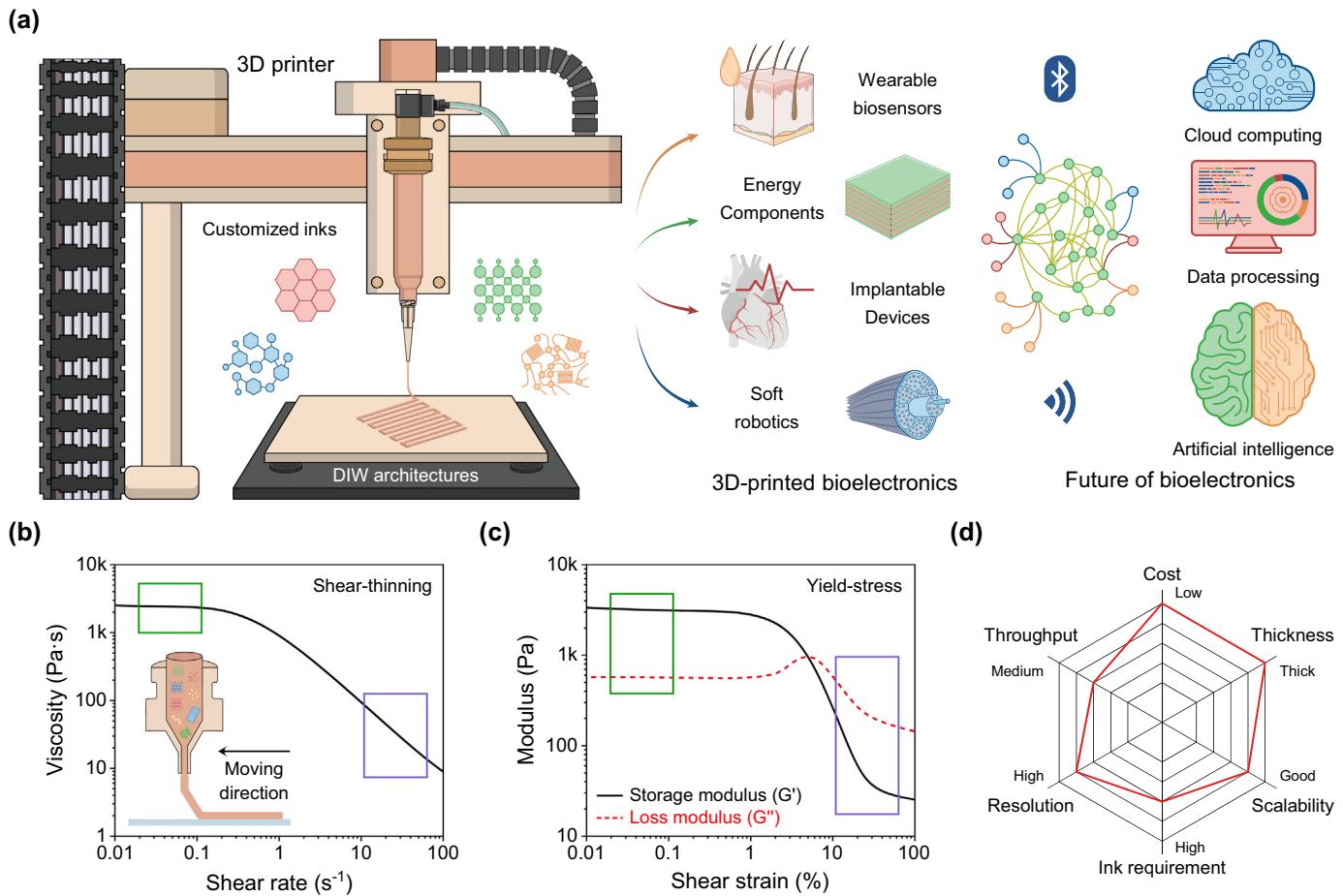
materials can be integrated with ease as they are generally not constrained by chemical compatibility issues. Hence, the employment of 3D printing has thus far spurred the development of novel bioelectronic devices with new functionalities, enhanced sensing performances, improved biocompatibility, seamless interfaces and adherence with soft and customizable features [27–29].

In this review, we will focus on various DIW based 3D printing techniques and discuss the diversity of materials used for ink formulation and the broad range of bioelectronic devices fabricated through DIW including biophysical and chemical sensors, electrophysiological sensors, energy devices, multimodal systems, implantable devices, and soft robotics, highlighting the impact of 3D printing on the design and manufacturing methodologies for these devices (Fig. 1). We will also discuss the prospects and challenges in this fast-growing field of 3D-printed bioelectronics for personalized healthcare and precision medicine.

Design of DIW 3D printable materials for bioelectronics

In the past years, the development efforts in 3D printing mainly focus on the invention and improvement of new types of printers, while the variety of materials that are suitable for 3D printing is still limited. Notably, materials and structural diversity are crucial for the fabrication of functional devices and integrated systems, especially in the realm of wearable devices [15,30,31]. For instance, the versatility to select materials with varied electrical and mechanical properties spanning from highly conducting metals to insulating polymers allows the construction of electronic circuitries [14], engineering of porous materials and incorporation of nanomaterials are critical to enable high-performance physical and chemical sensors [32], and soft and elastic materials are indispensable for the realization of flexible and stretchable functionalities [33]. Combination of these materials enables the creation of wearable devices that can seamlessly adapt to the complexity and dynamics of the human body.

Importantly, functional materials are required to possess certain rheological characteristics, as well as optimal properties for bioelectronics, to be printable via extrusion-based methods [15]. Introducing additives to increase the viscosity and controlling the printing temperature are the primary strategies to obtain inks with distinct shear-thinning behavior, high elastic modulus and shear yield-stress properties. For example, a mixture of PDMS, silica nanoparticles and wax microparticles phase change ink was used to print soft silicone structures via high-operating temperature DIW [34]. In this ink formulation, both the wax microparticles and silica nanoparticles serve as rheological modifiers that increase the moduli and yield stress by creating micro- and nanoscale networks. During extrusion, the nozzle is heated to initiate the melting of wax which leads to a good flow behavior for high-resolution printing. Conversely, most of the developed materials are 3D-printable under room temperature, and the viscosity of customized inks can be enhanced by means of densification. For instance, pristine PEDOT:PSS solution exhibits a dilute dispersion of PEDOT:PSS nanofibrils with low viscosity, while increasing the concentration of PEDOT:PSS enables 3D

**FIG. 1**

Direct-ink-writing (DIW) 3D printing. A, Schematic of DIW 3D printing with customized inks for bioelectronics. B and C, Rheological criteria including shear-thinning (B) and yield-stress features (C) of the customized inks for bioelectronics. D, Radar chart showing attributes of DIW 3D printing.

printable electrically conducting polymer inks [35] (Fig. 2A). The increased concentration led to enhanced entanglements of the PEDOT:PSS nanofibril networks within the solvent causing the suspension to transform into a viscous paste-like printable ink with high electrical conductivity. Alternatively, directly printing a hydrogel-based conductive ink embedded into a block of granular hydrogel supporting matrix that exhibits yield-stress behavior can result in functional materials with reliable mechanical and electrical performance. One method of embedded 3D printing reported the use of a supporting matrix consists of a double network hydrogel with an orthogonal crosslinking mechanism and granular ionically crosslinked hydrogels that allowed it to accommodate the deposition of functional silver-hydrogel ink inside with high conductivity and stretchability [36] (Fig. 2B).

Inorganic materials, such as metal particles, carbon-based materials, and MXenes, have rich and tunable surface chemistry with high conductivity and mechanical robustness, making them suitable for 3D printing as the ink properties can be easily modulated by introducing the gelation of nanosheets [19,37–39]. Recently, the development of more straightforward methods to print additive-free 2D materials are proposed to maintain functionality and control the assembly behavior at different scales. For example, through a facile one-step oxidation treatment, commercial graphene powder can be transformed into highly porous

graphene oxide nanomaterial, which can be made into aqueous ink to construct hierarchically porous architectures through 3D printing [40] (Fig. 2C). In another example, additive-free MXene aqueous inks were prepared following a modified minimally intensive layer delamination route [41] (Fig. 2D). The optimized MXene inks demonstrated desirable rheological and electrical properties, attributed to the large single-layer ratio, high concentration, and narrow flake size distribution, allowing continuous high-precision 3D printing and quick solidification with metallic conductivity.

Although direct printing of nanomaterial inks is a promising direction, introducing scaffolding material into functional soft matter inks results in more controlled 3D-printed structures as the ink rheology and composition can be adjusted [42–44]. Specifically, while it is challenging to pattern pure liquid metal via 3D printing due to its high surface tension, it is feasible to employ platinum-catalyzed polydimethylsiloxane (PDMS) as the silicone support for liquid metal elastomers by shear mixing EGaIn in the PDMS prepolymer [45]. With the increase of loading volume of EGaIn in PDMS, it is possible to develop inks exhibiting shear-thinning and shear-yielding properties that are required for 3D printing (Fig. 2E). Therefore, the presence of silicone serves as a rheological modifier to induce mechanical properties required for 3D printing.

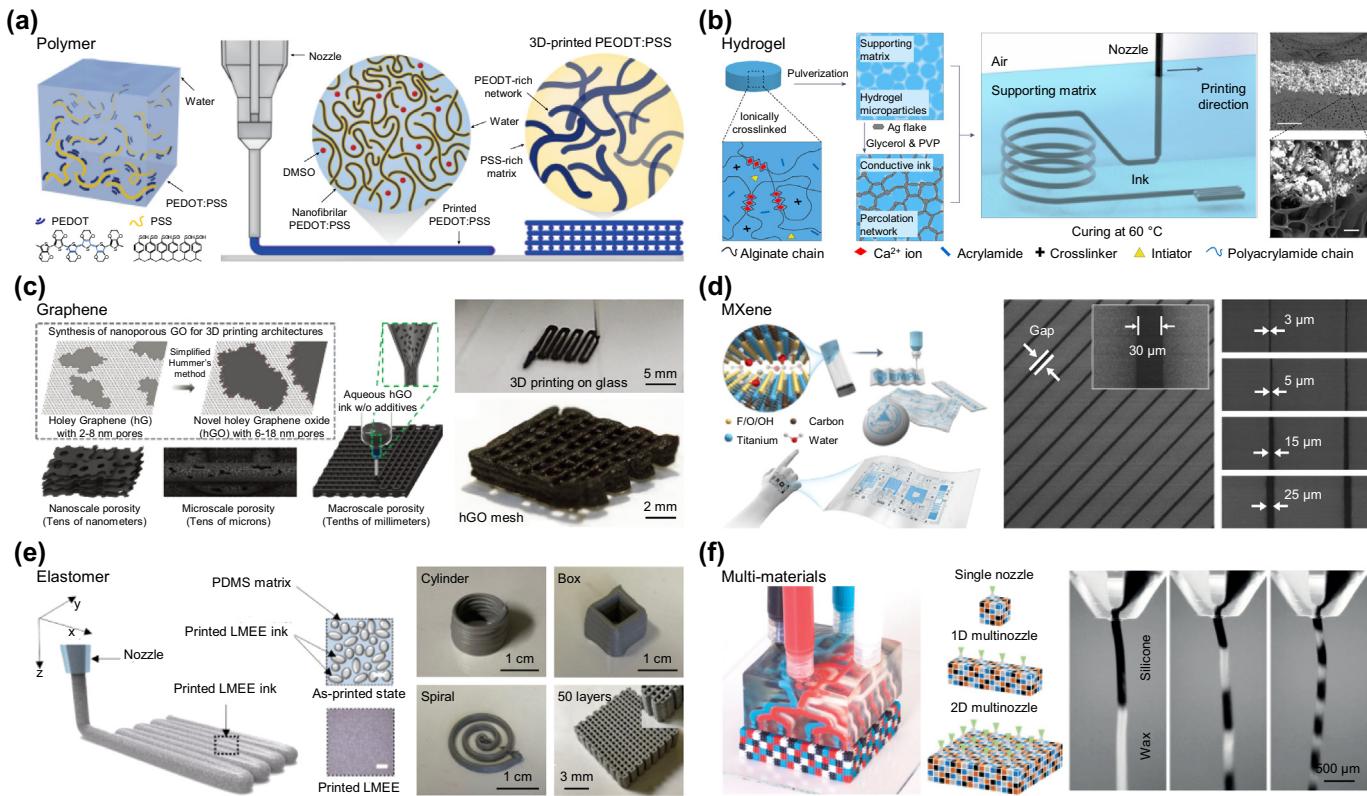


FIG. 2

DIW 3D printable materials for bioelectronics. A, 3D printing of conducting polymers by lyophilization in cryogenic condition and re-dispersion with a solvent. Reproduced with permission [35]. Copyright 2020, Nature Publishing Group. B, Fabrication of hydrogel electronics via embedded 3D printing. Reproduced with permission [36]. Copyright 2022, Nature Publishing Group. C, An aqueous and additive-free 3D printable holey graphene oxide ink for 3D architectures with hierarchical porosity. Reproduced with permission [40]. Copyright 2018, Wiley-VCH. D, Room-temperature high-precision printing of flexible electronics with MXene inks. Reproduced with permission [41]. Copyright 2022, Nature Publishing Group. E, 3D printing of liquid metal embedded elastomers for soft materials. Reproduced with permission [45]. Copyright 2022, American Chemical Society. F, Multinozzle 3D Printing of multimaterials for voxelated soft mater. Reproduced with permission [47]. Copyright 2019, Nature Publishing Group.

3D printing shows great promise to formulate multiple materials into complex structures as it can be used to simultaneously fabricate more than one material in a single geometry while maintaining its structural stability and functionality [46]. The construction of multimaterial architectures generally involves sequentially printing individual materials by laboriously switching out the mounted nozzle for different materials [47]. Addressing this issue, a facile fabrication method that used multiple nozzles simultaneously for 3D printing of multiple materials was reported, in which the composition, function, and structure of the materials are tailored at voxel scale (Fig. 2F). The seamless switching between materials at high frequencies, enabled continuous printing of heterogeneous voxelated filaments and achieved a rapid 3D printing process.

To date, there has been a wide variety of 3D-printable inks that are developed with tailored mechanical and electrical properties for DIW 3D-printed bioelectronics (Table 1) [34–37, 40, 41, 45, 48–56]. These strategies to achieve functional inks have enabled a wide variety of 3D printable materials. However, each method for developing functional inks have trade-offs as adjusting one desired property is coupled to many others. Printing a functional material directly embedded into a supporting material ensures robust mechanical properties but requires a bulky sup-

porting matrix as a scaffold. While additive-free inks maintain high functionality, the mechanical properties of the printed material can be difficult to tune. Moreover, some additive-free inks are limited to planar structures as only thin layers of materials are deposited once the solvent evaporates. On the other hand, mixing in additives enable tunable mechanical properties and can be crucial for enabling the printability of a material, but typically comes at the sacrifice of functional performance, namely electrical conductivity.

The future directions for the design of 3D printing materials lie on the further development of facile methods to print either additive-free inks or optimized ratios between functional materials and supporting matrices to better preserve the functionality. The assembly behavior of the 3D printing materials should be well controlled for the printed structures at the microscale, nanoscale and layer-by-layer configuration. Furthermore, improving the ability to continuously print multimaterial architectures with more precise composition and higher resolution for new composites will translate towards devices with better structural and functional properties. Generally, these techniques to print functional inks can result in materials with soft mechanical properties, which are well-suited for applications in bioelectronic devices that interface with soft tissue.

TABLE 1

Mechanical and electrical properties of various inks for DIW 3D-printed bioelectronics.

Active material	Ink formulation	Elastic Modulus (kPa)	Tensile strength (%)	Electrical conductivity (S cm^{-1})	Resolution (μm)	Applications	Ref
PEDOT: PSS	PEDOT:PSS/water/DMSO	1100	NA	28	30	Flexible conducting electrodes.	[35]
Ag NPs	AgNPs/AgNO ₃ /PAA/DEA/water	NA	NA	1×10^5	10	RF electronics.	[48]
Ag flakes	Ag/TPU/THF/DMF	~2300	up to 240	1×10^4	100	Strain sensor, interconnects.	[37]
Silicone	PDMS/silica NPs/wax MPs	NA	NA	NA	50	Substrate, template material.	[34]
Silicone	Silicone/silica NPs	< 200	up to 2000	NA	260	Substrate, encapsulation, artificial muscles.	[49]
Ag flakes	Ag/PAM	< 5	up to 1800	1.4×10^3	250	ECG, nerve stimulation.	[36]
PAM	AAM/MBAA/APS/SA/CaCl ₂	59.6	450	NA	1800	Biomimetic soft robotics.	[50]
PAA	AA/MBAA/APS/SA/CaCl ₂	NA	200	NA	1800		
PNIPAM	NIPAM/MBAA / SA/CaCl ₂	NA	350	NA	1000		
PVA	PVA/SA/CaCl ₂	NA	380	NA	500		
Graphene	Graphene/PLG	3000	81	8	100	Strain, pressure sensor, implantable electronics.	[51]
GO	GO/NaOH/urea	NA	NA	NA	60	Micro-supercapacitor.	[52]
GO	Holey GO/water	NA	NA	NA	200	Battery.	[40]
rGO/CNT	rGO/SWCNT/SDS/water	NA	NA	$> 2 \times 10^2$	175	Thermoresponsive supercapacitors.	[53]
MWCNT	MWCNT/BuAc/ PDMS	~500	up to ~ 145	7×10^{-2}	100	Strain, pressure sensor.	[54]
MXene	MXene/water	NA	NA	$\sim 6.9 \times 10^3$	120	Antennas, temperature/humidity sensor, supercapacitor.	[41]
hBN	hBN/PVA/water/cellulose	NA	up to 93	NA	400	Bone tissue engineering.	[55]
EGanIn	EGanIn/PDMS	NA	230	6×10^4	180	Triboelectric nanogenerator, thermoelectric generator.	[45]
EGanInSn	EGanInSn/PDMS	NA	100	NA	90	Strain, pressure sensor.	[56]

3D-printed wearable and point-of-care biosensors

The exploitation of soft functional materials enables broad application of biosensors for biophysical, biochemical, and electrophysiological signals [1, 57, 58]. Among the different technologies, DIW 3D printing provides an alternative route for the development of wearable biosensors with widespread options of functional materials and designed structures [16, 29, 59]. Well-prepared biosensors can realize continuous, real-time monitoring of key parameters, which are crucial for personalized medicine and digital health.

Biophysical sensors

Biophysical signals are directly related to human health, such as body temperature, skin condition and blood pressure. To monitor those vital signs continuously and non-invasively, it is still challenging to develop biophysical sensors with soft, comfortable and reliable features. Recently, the use of a wide range of functional materials including MXene, graphene, conductive polymers, and liquid metals for biophysical sensor development has been investigated with optimized layout through 3D printing [60–63].

As we know, the human body operates at an extremely narrow healthy window of approximately 36–37 °C. Irregular deviations could be an indication of various medical conditions such

as infections, inflammatory disorders, hormonal imbalances, heat exhaustion, drugs or other environmental factors [64]. To achieve high sensitivity over a wide working range with a remarkably short response time, MXene bonded polyurethane/polyvinyl alcohol (PU/PVA) hydrogel was developed for high-sensitive and reliable temperature sensing [65] (Fig. 3A). The Raman characterization proves that the peak shifted towards higher frequency with the increasing temperature due to the thermally induced tunnel effect. Furthermore, the addition of MXene enhances the thermal conductivity of the hydrogel and promotes the electron transmission efficiency, allowing more efficient temperature response.

To record the cardiac activity and joint motion, wearable tactile and pressure biosensors have been reported recently based on various working mechanisms through the acquired information from changes in resistive, capacitive, and self-powered electrical signals [66–68]. The balance between the sensitivity and detection range is a crucial concern, and appropriate selection of microstructure and material could substantially improve the performance of sensors. To meet the requirements, an all-3D-printed pressure sensor was proposed with a stretchable elastomer substrate, a double helix interdigital electrode, and a pressure sensing element with hierarchically porous architecture, achieving high sensitivities of 5.54 kPa⁻¹ over a wide working range from 10 Pa to 800 kPa [69] (Fig. 3B). To obtain hierarchical

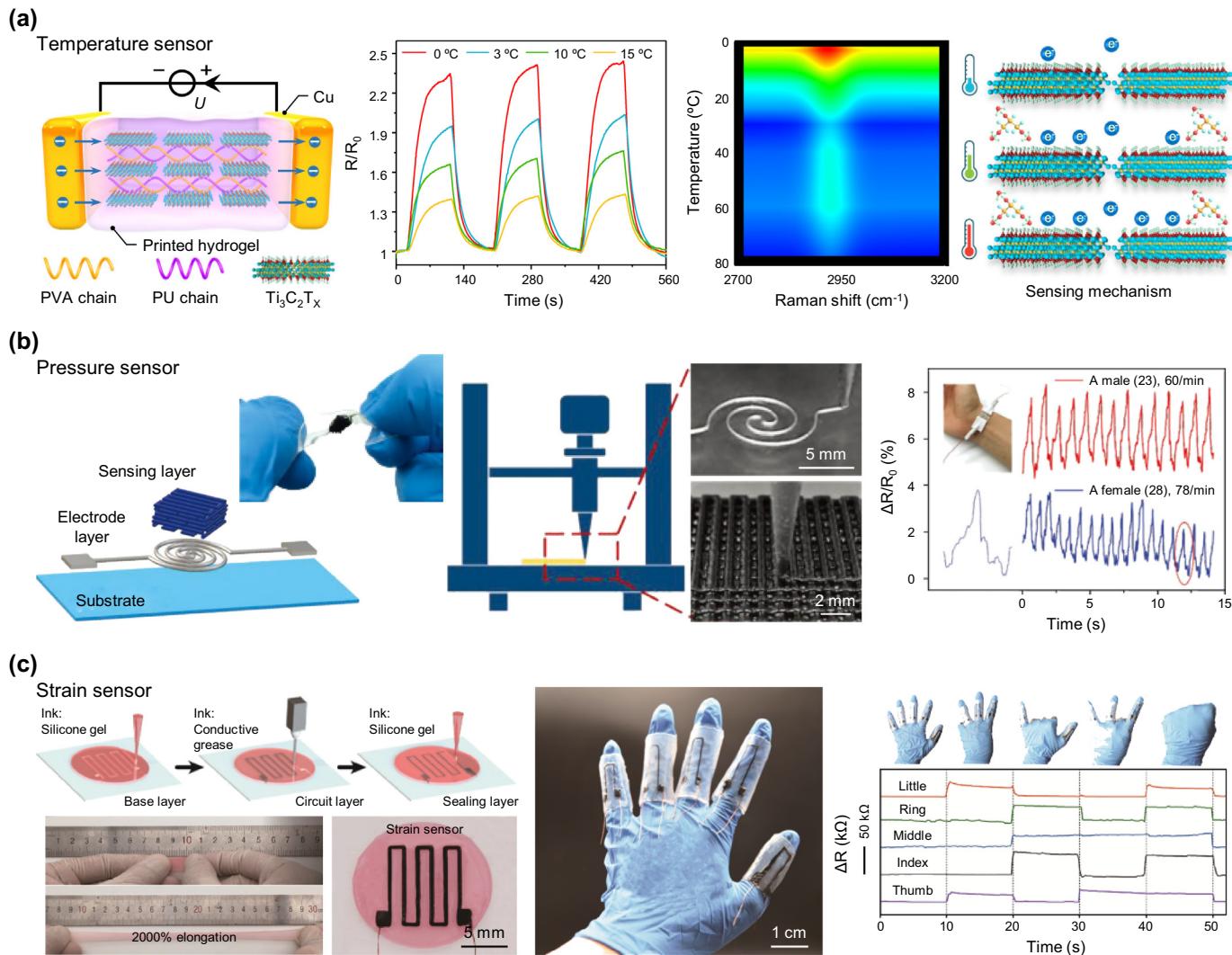


FIG. 3

3D-printed wearable biophysical sensors. A, 3D-printed MXene bonded hydrogel temperature sensor, its corresponding resistance change under different temperatures, the temperature-dependent Raman spectra and temperature sensing mechanism. Reproduced with permission [65]. Copyright 2022, Nature Publishing Group. B, 3D printing of stretchable piezoresistive sensor with hierarchical porosity and multilayer structure for the pulse monitoring. Reproduced with permission [69]. Copyright 2018, Wiley-VCH. C, 3D printing of highly stretchable silicone elastomer as the strain sensor integrated with a glove for the detection of different hand gestures. Reproduced with permission [49]. Copyright 2019, American Chemical Society.

pore sizes varying from macro- to nanoscale, the sensing element was printed via an open mesh design to generate macroscale pores and the composite ink with sacrificial NaCl template was utilized to induce nanoscale pores after the dissolution of NaCl. Owing to the superior sensitivity and signal-to-noise ratio, the pressure sensor was able to monitor the pulse waveform for real-time healthcare.

Additionally, ultrathin skin-like strain sensors have been designed with various materials and strategies. Sensitivity and stretchability are usually the two key factors in designing wearable strain sensors [70]. Along with a comprehensive study covering material configuration, device design, and printing implementation, multimaterial complex structures composed of silicone rubbers and a conductive grease were printed directly to fabricate the strain sensor [49]. Through the modulation of the silicone rubbers with different mechanical properties, super stretchability of up to 2000% was reported and the silicone was

applied into a packaged strain sensor with serpentine layout (Fig. 3C). With a configuration of multiple strain sensors placed on each finger of a hand, various hand gestures were classified by monitoring significant resistance changes corresponding to individual finger movement.

3D printing, as a manufacturing method, is highly complementary to producing soft, stretchable and conformal biophysical sensors for wearable applications. While interesting strategies have been used to engineer hierarchical structures into sensors, improving the resolution of 3D-printed features could further improve the sensitivity of these sensors. Furthermore, while individual standalone sensors have been demonstrated, improving printing spatial resolution will be critical to fabricating dense sensor arrays. There are also many opportunities to explore the use of 3D-printed biophysical sensors operating with different sensing mechanisms, such as thermistor temperature sensors or capacitive pressure sensors for higher sensitivity to

their respective stimuli. These examples of biophysical sensors highlight the versatility of 3D printing for biosensor fabrication, which can similarly be effective for biochemical sensors and electrophysiological sensors.

Biochemical sensors

Besides wearable biophysical sensors focusing on the monitoring of vital signs and physical activities, wearable biochemical sensors are also crucial to access an individual's health state [5,71,72]. Hence, analyzing important biomarkers at the biomolecular level could assist with the diagnosis and monitoring of chronic diseases, such as diabetes, cardiovascular diseases, mental disorders, and infections [73–77]. Different electrochemical techniques, including potentiometry, amperometry, voltammetry, and impedance, allow the real-time analysis of the analytes at different biofluids, such as saliva, sweat, tears, and interstitial fluids, as well as environmental gas conditions [2,78,79]. 3D printing provides an excellent method to prepare biosensors that measure chemical biomarkers levels from pH and electrolytes to metabolites and proteins. Importantly for the formulation of the sensing element, the ink matrices such as the solvents or binders must be appropriately chosen to enable the intended functionality of the biological or sensing component.

For example, the pH in biofluids can provide important health information with applications in infection detection, disease diagnosis, and personalized medicine [68]. Compared to traditional devices with bulky readout instruments and limited flexibility, an integrated and wearable pH sensor is proposed through 3D printing [80] (Fig. 4A). The 3D-printing of nanomaterials on skin-like flexible substrates enables multimaterial and multilayer printing of the sensors. The change in pH is measured potentiometrically where potential change is caused by protonation of the nitrogen atom in polymer chains of the PANI, which allows for on-demand, continuous, wireless and real-time pH measurements of actual sweat with high accuracy. It should be noted that for the formulation of ink, PANI emeraldine base should be involved instead of PANI as it is soluble in organic solvents such as DMSO. To detect other electrolytes, stable ion-selective membranes are necessary for potentiometric sensing of various ions [81]. Specifically, printable ion-selective membrane cocktail recipes are composed of a photocurable structure, a photoinitiator, an ion exchanging salt and a plasticizer [82] (Fig. 4B). Optimizing the composition of the cocktail can result in a printed membrane with the desired thickness and shape once it is cured. The developed ion-selective sensor exhibits great sensitivity with near Nernstian responses and high reproducibility with low deviation.

To develop wearable enzymatic-based sensors for the detection of biomarkers, several factors should be considered, including mechanical flexibility, miniaturization, and scalability. The emergence of 3D printing for the fabrication of wearable enzymatic sensors not only satisfies these requirements but also possesses high throughput, customizability, and high levels of spatial control and accuracy. A representative amperometric glucose sensor was produced by sequentially printing Prussian blue conductive carbon ink and an enzymatic ink containing glucose oxidase immobilized within a sol-gel network matrix to enable a

functional sensing mechanism with suitable rheological properties [83] (Fig. 4C). The 3D-printed enzymatic sensor shows enhanced sensitivity and wide linear range, where the presence of glucose oxidase can react with glucose with amperometric responses.

In addition to enzymatic sensors for metabolite monitoring, 3D printing complements the production of immunosensors for the point-of-care diagnosis of diseases. During the COVID-19 global pandemic, 3D printing provides an alternative solution for the decentralized and on-demand fabrication of various personalized medical devices. Through an approach with a sequence of bottom-up biofunctionalization, COVID-19 recombinant protein can be anchored on 3D-printed graphene/polylactic acid to fabricate point-of-care COVID-19 immunosensor with electronic readout [84] (Fig. 4D). The measurements were conducted impedimetrically through monitoring changes at the electrode/electrolyte interface after interacting with the monoclonal COVID-19 antibody via competitive assay. The screening of the antigen against the SARS-CoV-2 virus has been demonstrated to achieve trace level detection in both buffered and diluted serological samples with a fast turnaround time of just 20 min.

Aside from biomarkers, the monitoring of environmental gases is also significant for daily healthcare. Ammonia (NH_3) is an extremely harmful gas that can damage the respiratory tract, animal epidermis and nervous system [85]. Therefore, it is critical to prepare NH_3 gas sensors with fast response capability at room temperature. Polyaniline (PANI)-gelatin hydrogels are developed through a one-pot synthesis process [86], involving in situ polymerization and formation of the cross-linked network, with excellent viscoelasticity (Fig. 4E). After the modulation of the weight ratio of PANI, the 3D-printed PANI-gelatin ammonia sensor shows fast response time with the varying ammonia concentrations with stable adhesion to skin. In addition, wearable biochemical sensors for breath acetone are in high demand because of its strong correlation with the level of blood glucose, as well as the rate of fat loss in health individuals [87]. 3D-printed acetone sensors consisting of copper nanoparticles and polyethylene oxide showed excellent acetone selectivity after annealing [88] (Fig. 4F).

Preparing biochemical sensors with 3D printing provides a controlled, low-variability and facile method for sensor fabrication without the need for further patterning and electrodeposition process. 3D-printed electrodes can be designed with higher porosity for increased effective surface area, higher catalytic activity, and better entrapment of recognition elements to improve the sensitivity. Meanwhile, additive-free materials are especially important to preserve high functional performance. While the aforementioned strategies have shown promising approaches to monitor certain biomarkers, there are still many opportunities to expand the library of 3D-printed biochemical sensors given the advantages of this technique.

Electrophysiological sensors

Electrophysiological sensors monitor the biopotential changes of targeted organs during cardiovascular, neurological, and muscular activities, which are effective indicators for early diagnostics of disorders [89]. Designing thin, conformal and biocompatible electrodes is crucial to form a stable biotic-abiotic interface that

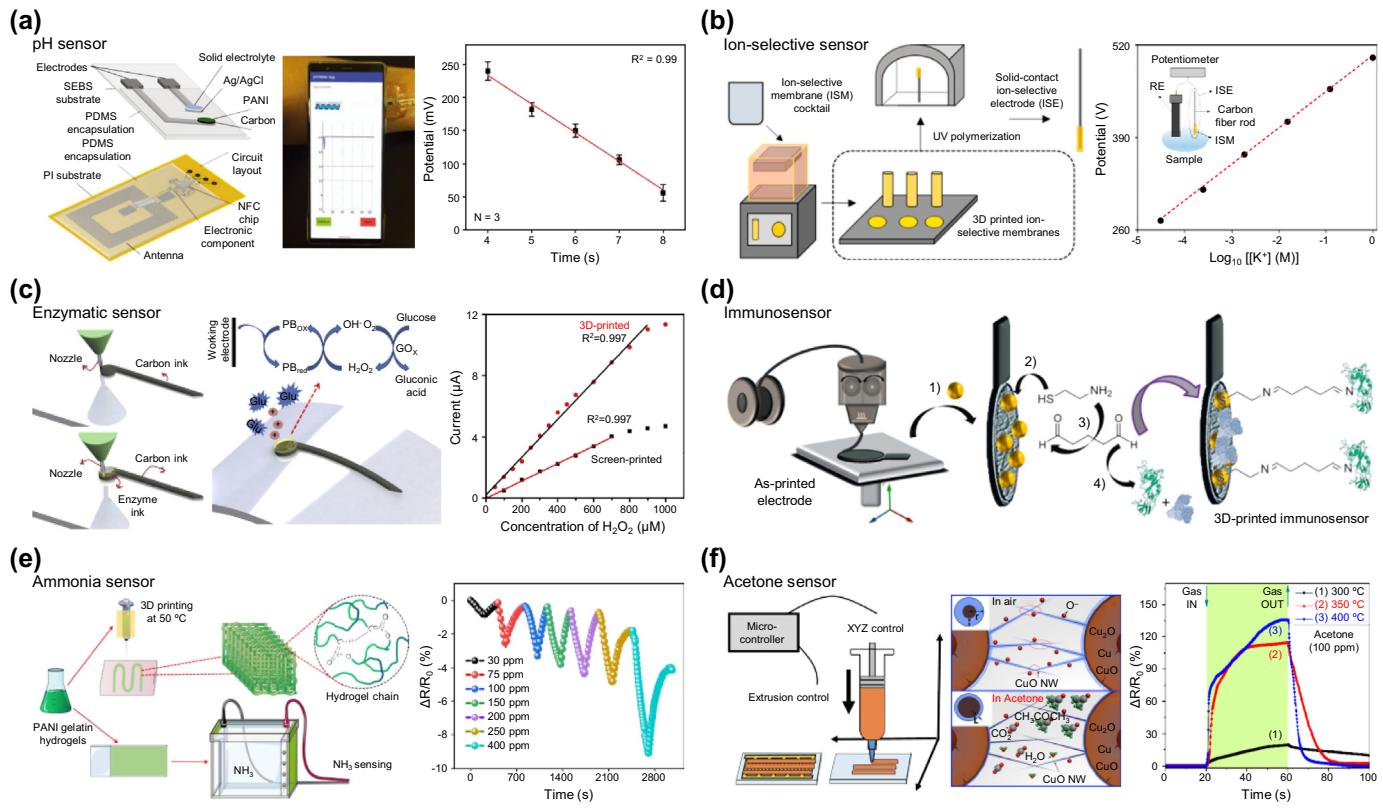


FIG. 4

3D-printed wearable/point-of-care biochemical sensors. A, 3D nanomaterials-printed wearable, battery-free, wireless pH sensor system for the in situ real-time measurement of sweat pH value. Reproduced with permission [80]. Copyright 2023, Wiley-VCH. B, 3D-printed ion-selective membranes for potentiometric sensing of multiple biomarkers. Reproduced with permission [82]. Copyright 2021, American Chemical Society. C, 3D-printing of electrode and enzyme ink to prepare enzymatic biosensor for glucose sensing. Reproduced with permission [83]. Copyright 2018, Elsevier. D, 3D-printed electrochemical COVID-19 immunosensor with COVID-19 recombinant protein on the graphene-based nanocomposite electrode surface. Reproduced with permission [84]. Copyright 2021, Elsevier. E, Schematic diagram of hydrogel formation and 3D-printed ammonia sensor with response for different ammonia concentrations. Reproduced with permission [86]. Copyright 2022, Wiley-VCH. F, 3D-printed chemiresistive sensor for the dynamic response to the acetone. Reproduced with permission [88]. Copyright 2019, American Chemical Society.

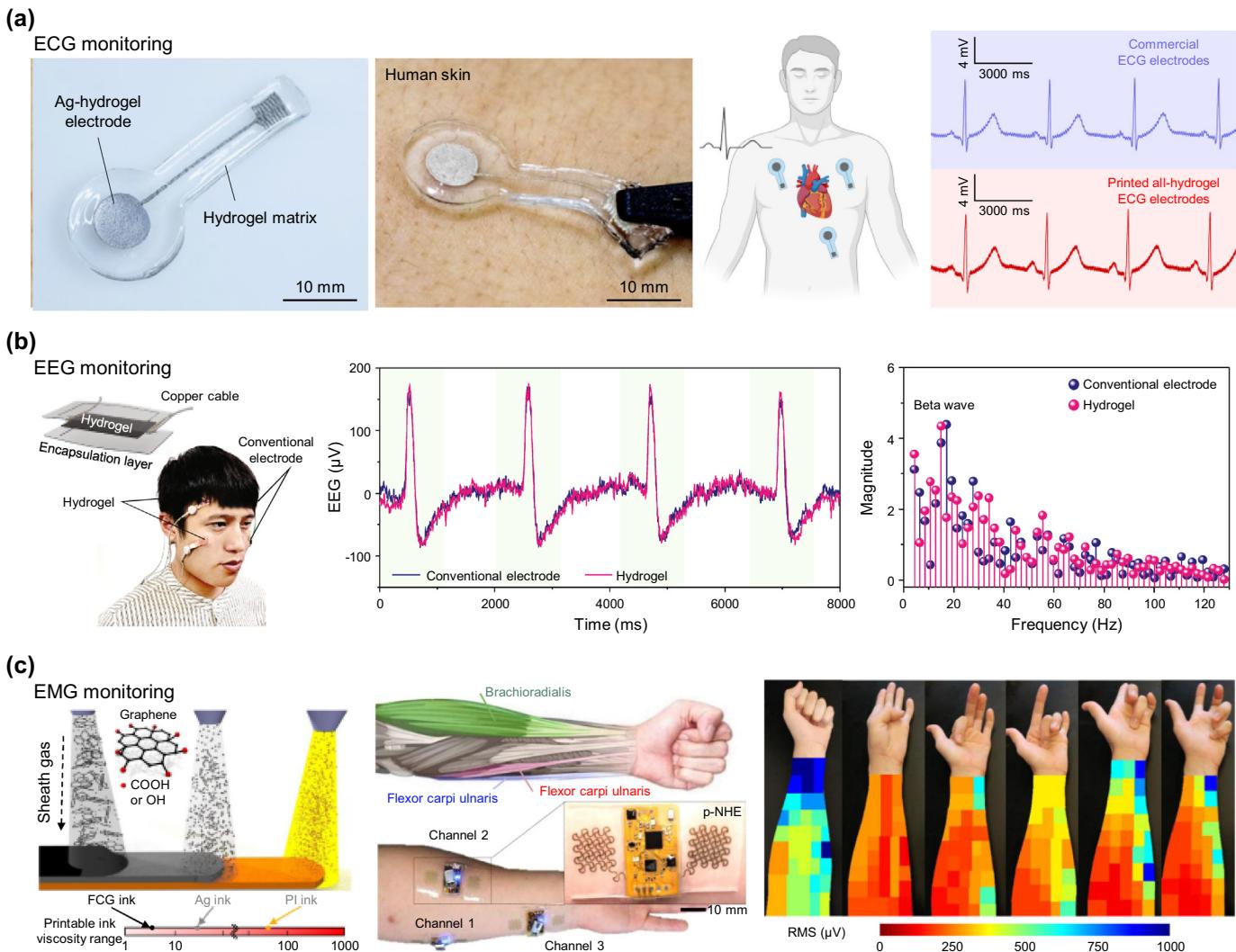
can extract reliable electrophysiological signals and decrease the skin-electrode contact impedance [90–92]. As a developing printing technology, DIW 3D-printed on-skin electrodes are of notable interest for its ability to apply a variety of materials with distinct properties for the continuous monitoring of electrophysiological information [93–95].

Conductive hydrogel electrodes can establish reliable conformal contact with skin surface for reliable electrophysiology recording. An all-hydrogel electrocardiography (ECG) electrode was printed with two exposed pads for human skin attachment and connection of data acquisition [36] (Fig. 5A). To fabricate the encapsulated hydrogel electronics, conductive and stretchable Ag-hydrogel ink was printed directly inside the supporting matrix with two separate crosslinking mechanisms to cure the ink and supports separately. In a three-lead configuration, ECG waveforms measured by the hydrogel-based electrodes exhibited stronger signals than those recorded from commercially available electrodes.

Similarly, another soft, conductive nanocomposite network in hydrogels was used for capturing electroencephalogram (EEG) signals [96]. The printed material displayed ultra-stretchability (2500%), hyper-antifreezing property (-125 °C), extremely low

working voltage (less than 100 μV), and super cyclic tensile stability [96] (Fig. 5B). EEG signals recorded by these electrodes accurately detected subtle changes to the alpha and beta waves in the brain caused by eye rotation and blinking motions with higher resolution compared to commercial metallic electrodes. The remarkable performance of the printed hydrogel electrodes proves that they are promising candidates for human-machine interface with easy fabrication and high-resolution features.

Measuring and decoding electromyogram (EMG) signals can be used to interact with devices in various human-machine interaction applications such as smart rehabilitation and advanced therapeutics [97]. Functionalized conductive graphene with high aspect ratio was DIW printed into electrodes that enabled conformal lamination on human skin and offered gel-free, high-fidelity recording of muscle activities [98] (Fig. 5C). When mounted along the forearm, the EMG sensors can detect multiple hand gestures accurately and enable real-time control of external systems via the EMG signals. Further assisted by an anatomical study with deep learning to create an electrophysiology mapping, EMG recordings captured all finger motions with high accuracy based on the optimal selection of three channels.

**FIG. 5**

3D-printed electrophysiological sensors. A, A 3D-printed hydrogel ECG electrode with conformal attachment on human skin for human ECG waveform recording. Reproduced with permission [36]. Copyright 2022, Nature Publishing Group. B, 3D-printed ultrastretchable, hyper-antifreezing conductive hydrogel for capturing the EEG signal of eye blinking. Reproduced with permission [96]. Copyright 2020, American Association for the Advancement of Science. C, 3D printing of aerosol nanoparticles from polyimide (PI), Ag, and graphene inks to construct multilayered hybrid electronics for EMG recording and hand gestures recognition. Reproduced with permission [98]. Copyright 2020, Nature Publishing Group.

Overall, DIW 3D printing offers the ability to directly print complex wearable and point-of-care sensors with adjustable mechanical and electrical properties for a wide range of applicable scenarios. The ability to customize functional inks based on various materials and to produce versatile 3D structures can further enhance device performance (e.g., sensitivity and skin conformability) for wearable applications.

3D-printed wearable energy devices

To date, wearable energy devices have provided new possibilities to interact with wearable technologies. The research in the field of wearable energy devices can be categorized into energy storage devices (such as batteries and supercapacitors) [99–101] and energy harvesters (such as solar cells, biofuel cells, piezoelectric and triboelectric nanogenerators) [81,102–104]. These compact and portable energy devices supply sustainable power for prolonged utility and greatly enhance the convenience and mobility

for active usage. Besides improving performance, the key design objectives include softness, biocompatibility, and high integration with other components. 3D printing provides a versatile strategy to address those requirements, with the advantages of multidimensional structure, high resolution, mass production and high throughput [105–107].

In ideal scenarios, energy harvesting allows for the operation of devices with low energy storage capacity requirements. Based on different working mechanisms, several approaches have been specifically tailored for wearable platforms. Triboelectric generators offer an alternative means for harvesting biomechanical energy, which can produce electrical charges by contact electrification and electrostatic induction during the contact of two surfaces with different polarity of charge separation [108–110]. The efficiency is greatly dependent on the differences in the electron-attracting ability of the materials and the morphology of the contact surfaces, to achieve high output power density and energy

conversion efficiency. Among different configurations, electronic textile has drawn attention and can be developed by employing a 3D printer equipped with a coaxial spinneret to simultaneously print CNT ink and silk fibroin ink as core-sheath fibers [111] (Fig. 6A). The 3D-printed pattern can be optimized by maximizing the effective area and the prepared electronic textile can harvest biomechanical energy from human motion with a high-power density as high as 18 mW m^{-2} .

Other than human kinematic energy, thermoelectric generators exploit the Seebeck effect to harvest energy from the temperature difference between the skin and ambient environment [112]. Although the power density harvested is relatively low due to modest temperature gradients, this approach yields continuous and stable power generation, which is suitable for long-term monitoring of biophysiological information. The performance mainly depends on the selection of materials and design of the structure. By manipulating various characteristics of thermoelectric particles, including size, size distribution and surface charge states, thermoelectric inks with high viscoelasticity can be created without further organic modifiers [113]. Microthermoelectric generators have been developed by printing vertical arrays of alternating of n- and p-type 3D filaments with high aspect ratios in a well-controlled manner (Fig. 6B). The freestanding 3D geometries is crucial to achieve large thermal gradient and obtain enhanced power output.

Energy storage devices, in the form of batteries and supercapacitors, comprise the majority of power sources for bioelectronics [114–116]. To address the requirements of energy storage in applications ranging from miniaturized electronics to medical devices, battery-based devices in bio-integrated platforms have been developed with high specific energy densities, and excellent cycling stability [117]. The application of such batteries mainly relies on soft materials, biocompatible electrolytes and design optimization. Recently, a facile effective strategy is introduced to fabricate stretchable electrodes and separator for Li-ion battery via 3D printing of active materials mixed with nanofibrillated cellulose [118] (Fig. 6C). The 3D-printed Li-ion battery showed robust mechanical and electrical performance of up to 50% reversible stretchability with negligible degradation over prolonged stretching cycles, which are attributed to its high aspect ratio, strong interactions and printed serpentine patterns. The facile 3D printing of battery leads to low-cost manufacturing of high-performance energy storage devices and enables stretchable battery for wearable electronics.

Additionally, supercapacitors show several key advantages over batteries including rapid charging capability, and promising power density, which are of interest to wearable devices [119]. Particularly, fiber or fabric-based supercapacitors are highly desirable with high surface areas, wide materials selection and favorable mechanics [120]. To overcome the persistent restrictions in fabrication procedures, scalability and mechanical durability, an all-in-one coaxial fiber-shaped asymmetric supercapacitor is proposed by a coherent multi-ink 3D printing method [121] (Fig. 6D). With the electrodes and gel electrolytes printed simultaneously into a single fiber, this supercapacitor delivers a superior electrochemical performance and outstanding mechanical stability due to the compact coaxial structure and reduced charge

carrier diffusion path. After the integration with other mechanical units, it is promising to realize self-powered wearable platforms by applying these energy storage devices.

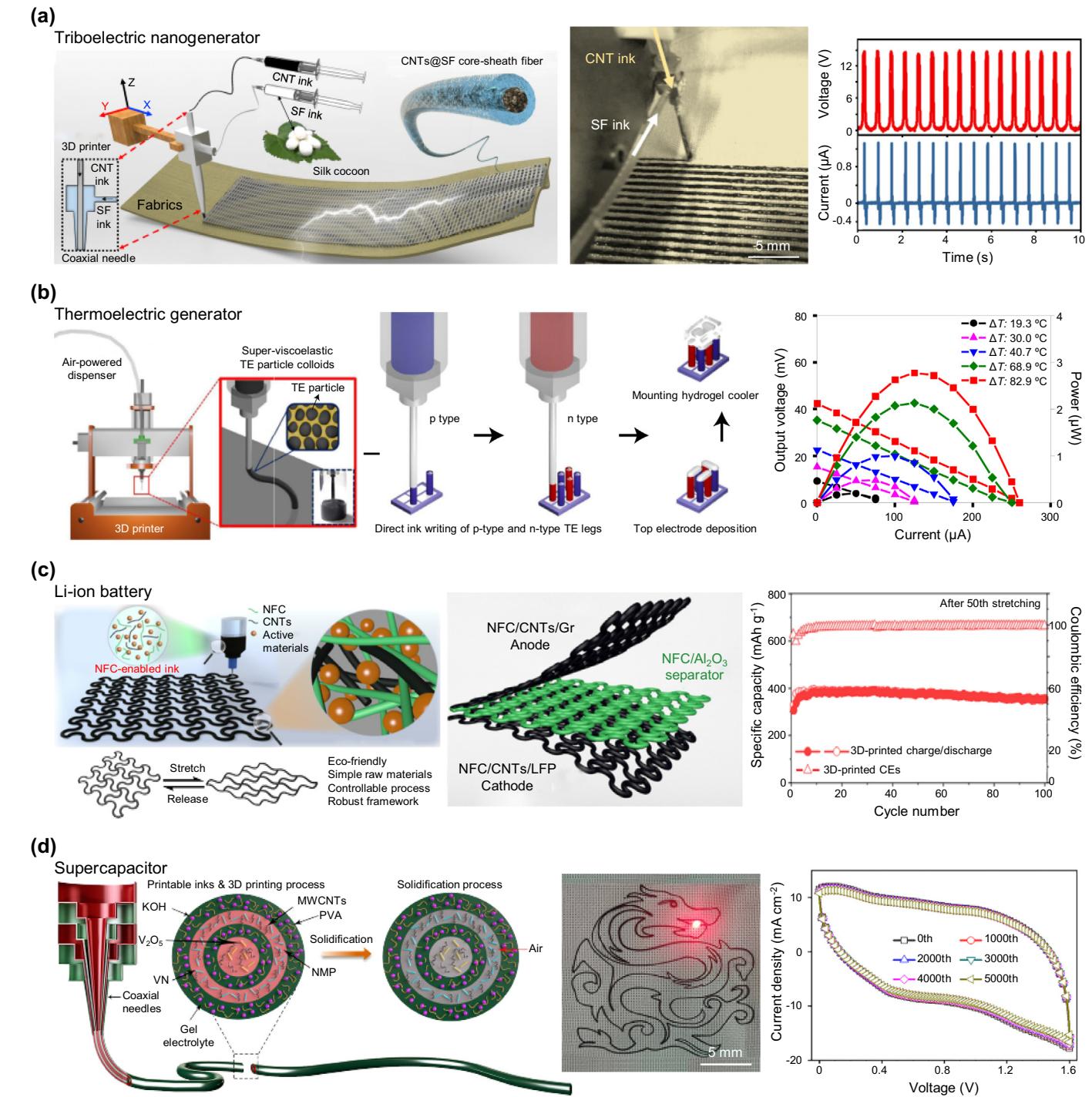
High-throughput 3D printing technology has been successfully used to construct complex structures because of its advantages such as continuous manufacturing capability, scalability, and low cost. Although the use of soft materials typically makes wearable energy storage devices less efficient than conventional energy storage materials, the ability to fabricate these complex structures have opened avenues of producing high-performing stretchable batteries, interesting fiber-based energy storage devices for textile electronics, and wearable energy harvesting devices improved by 3D geometries. This promising approach shows great potential in the field of wearable energy devices.

3D-printed wearable multimodal systems

With the rapid development of wearable bioelectronics, the demand for integration and miniaturization is increasing. Inspired by the function of human skin, flexible bioelectronic devices are designed with different functions, such as detecting the information of vital signs or biomarkers, and harvesting and storage energy [122–124]. Developing wearable multimodal systems that integrate biosensors with energy devices are interesting for broad applications in human-machine interfaces, robotics, prostheses, and healthcare [125–127]. Multimodal systems based on active materials and delicate structures can readily respond to multiple external stimuli [8,128,129]. Among different processing techniques, 3D printing can pattern active materials, delicate structures, complex geometries and integrated connections, accelerating the development of wearable multimodal systems [18,130,131].

Engineering complex multimodal systems with various materials and devices necessitate the development of simplified fabrication processes and multimaterials printing. One interesting approach recently reported [132], allows selective volumetric depositions of single metals and also diverse active material combinations, including ceramic, semiconducting, magnetic and colloidal materials, into site-specific 3D topologies. In a single integrated manufacturing process, a 3D-printed all-in-one embedded self-sensing device was successfully fabricated as a smart prosthesis, seamlessly combining structural and functional materials to provide human-like sensing capabilities (Fig. 7A). The proposed device with 3D electronic interfaces was used for tactile sensing, internal wave mapping and shape self-sensing. Such simultaneous sculpting, patterning and deposition of different materials showcases the possibilities to fabricate various multimodal systems.

In addition to wearable multimodal biosensors, energy devices and data transmission are also essential in integrated wireless sensing electronics [133]. In the era of the Internet of things, high performance integrated antennas are indispensable in flexible, portable electronics for wireless data transmission and energy harvesting. Near-field communication (NFC) is a short-range wireless technology that allows simultaneous power and data transmission between devices through inductive coupling, offering a versatile platform for battery-free miniaturized sensing electronics. Based on excellent wireless sensing and

**FIG. 6**

3D-printed wearable energy devices. A, 3D-printing of core-sheath fiber-based patterns on fabrics for energy-management smart textiles and its output performance as energy harvester. Reproduced with permission [11]. Copyright 2019, Elsevier. B, 3D printing microarchitectures for microthermoelectric generator and its output voltage and power at various temperature differences. Reproduced with permission [113]. Copyright 2021, Nature Publishing Group. C, 3D-printed deformable electrodes and separator enabled a stretchable battery with great performance stability after stretching-releasing cycles. Reproduced with permission [118]. Copyright 2022, Elsevier. D, 3D printing extrusion process of the printable coaxial fiber-shaped asymmetric supercapacitor and its electrochemical performance as energy storage device. Reproduced with permission [121]. Copyright 2021, American Association for the Advancement of Science.

outstanding power/data transmission properties, an all-MXene-printed flexible wireless integrated sensing system composed of a temperature and humidity sensor, micro-supercapacitors for energy storage and antennas for wireless communication was

developed [41] (Fig. 7B). After coupling with a flexible printed circuit board as the control module, wireless communication with smart phones were used for collecting sensor data and transmitting energy.

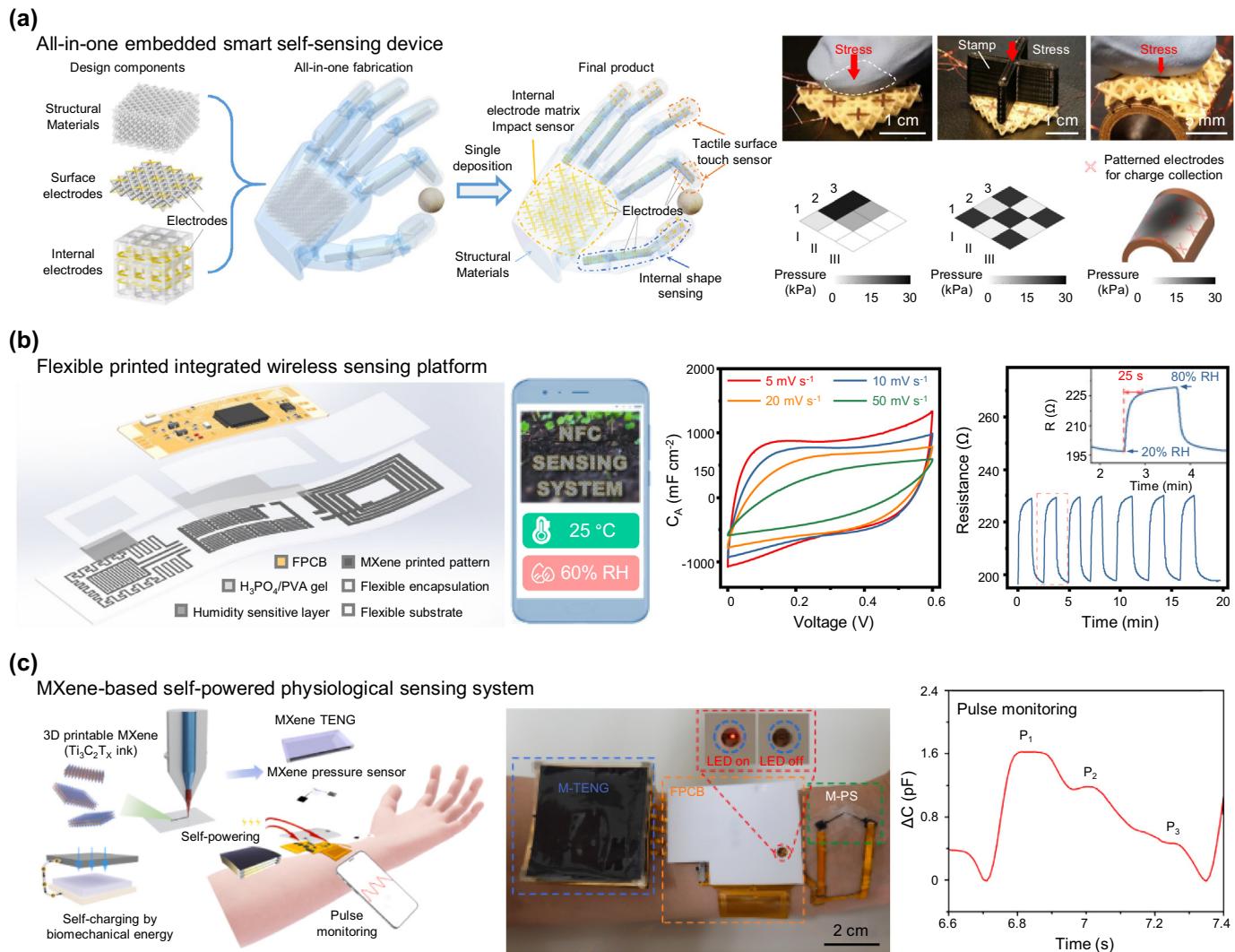


FIG. 7

3D-printed wearable multimodal systems. A, All-in-one embedded smart self-sensing device using 3D printing of multi-materials, showing the corresponding pressure map when the conformal tactile sensor applied with the pressure. Reproduced with permission [132]. Copyright 2020, Nature Publishing Group. B, Flexible 3D-printed integrated wireless sensing electronics with all MXene-printed functional modules, including a temperature sensor, humidity sensor, micro-supercapacitor and NFC. Reproduced with permission [41]. Copyright 2022, Nature Publishing Group. C, MXene-based self-powered physiological sensing systems via 3D printing with inks modified for the detection of wrist pulse using biomechanical energy. Reproduced with permission [135]. Copyright 2022, Elsevier.

Furthermore, sustainable, self-powered wearable devices that record physiological signals are essential in personalized health monitoring [134]. A novel MXene-based, 3D-printed self-powered physiological sensing system was recently proposed and validated. The system utilizes MXene as active electrodes for the power-efficient triboelectric nanogenerators, a capacitive pressure sensor and multifunctional circuit [135] (Fig. 7C). It exhibited high power output and fast response time to external stimuli, enabling continuous pulse monitoring and wireless data transmission to a mobile device. Fully powered by human motion, such a self-powered sensing system shows powerful potential for real-time continuous monitoring of physiological information.

Over the past decade, the innovation of 3D printing has revolutionized conventional fabrication and manufacturing technology. The scope of 3D printing has expanded from simple

mechanical structures to functional devices, providing easy tailoring and fast prototypes of customized designs. While multimodal sensors are sensitive to various input signals, it is of vital importance to decouple sensing mechanisms to achieve high selectivity of respective targets without any effects from cross-sensitivity. The potential for 3D printing to fabricate various combinations of multimodal systems with multiple sensors that respond to a wide variety of stimuli, integrated powering solutions, and data transmission capabilities, presents exciting possibilities.

3D-printed implantable devices

In addition to wearable devices that primarily continuously monitor health from the skin for better awareness, implantable devices have also been widely developed to provide monitoring and treatments inside the human body [136–138]. 3D printing

technology is playing an increasingly important role to produce implantable devices with complex shapes that solve the design and manufacturing problems [139–141]. Furthermore, high material utilization and precision of customized 3D-printed implantable devices allow them to be applied to various parts of the human body, including soft electrodes for electrophysiological recording and nerve stimulation, biomedical devices with complex mechanical architectures, such as vascular stents, contact lenses, wound dressings, and artificial joint [28,142,143].

For example, microphysiological systems, also known as organs-on-chips, which recapitulate the structure and function of native tissues *in vitro*, have emerged as a promising alternative approach to animal models to study diseases, treatment efficacy, and more. However, current microphysiological devices typically lack integrated sensors, which are difficult to implant onto small pieces of tissue, and require multi-step lithographic processes for fabrication. A facile route for fabricating the instrumented cardiac microphysiological devices was introduced through multimaterial 3D printing [144] (Fig. 8A). With six customized functional inks, the soft materials with piezo-resistive, highly conductive and biocompatible features allow for the integration of strain gauges within micro-architectures to guide the self-assembly of physio-mimetic laminar cardiac tissues. For example, the thickness of cantilever layers and strain gauge wire were minimized within 6.5 μm using highly diluted polymer-based ink, and micro-structured grooves were constructed by printing 60 μm width filaments with viscous PDMS ink. Such cardiac microphysiological device can provide readouts of tissue contractile stress inside cell incubator environments and show potential in the study of drug responses and the contractile development of human stem cell-derived cardiac issues.

As discussed for 3D printable materials, owing to the unique combination of electrical conductivity and tissue-like mechanical properties, conducting polymer hydrogels have emerged as a promising candidate for bioelectronic interfacing with biological systems [145,146]. Enabled by the favorable *in vivo* biocompatibility and stability, the 3D-printed all-hydrogel bioelectronic interfaces can demonstrate stable long-term electrophysiological recording and nerve stimulation [146].

Recently, a bi-continuous conducting polymer hydrogel was proposed and achieved high conductivity without sacrificing its mechanical properties [147] (Fig. 8B). This multimaterial 3D printing allowed a flexible choice of designs and fast manufacturing of the all-hydrogel bioelectronic interfaces for various target organs with a rapid fabrication process. The miniaturized hydrogel-based device comprising of micrometer-scale electrodes was printed at a high-resolution of 100 μm with an adhered interface of less than 5 mm² provided successful *in vivo* electrophysiological recording of rat hearts up to 28 days post-implantation. Notably, the signal-to-noise ratio of electrophysiological recording by the all-hydrogel bioelectronic interfaces improved over time, indicating successful integration of the device with tissue and proper healing with minimal chronic immune reactions following surgical implantation.

Besides electrophysiological recording, hydrogel electronics that have soft mechanical properties matching biological tissue has the potential for various biomedical applications. A millimeter-scale all-hydrogel electrode was designed and printed

for *in vivo* electrical nerve stimulation [36] (Fig. 8C). The advantageous flexibility and stretchability allowed the hydrogel electrode to stably wrap around the sciatic nerve without additional bioadhesives to trigger the movements of its hindlimb. The all-printed hydrogel demonstrated superior electrical-stimulating capability over conventional ionically conductive electrode, which can be attributed to both the high conductivity of the hydrogel and tight, conformal contact between tissues and the 3D-printed electrode.

As a new type of digital printing technology, 3D printing has many advantages and promising applications in bioelectronics, especially for implantable medical devices. Compared to the conventional cleanroom fabrication process, 3D printing offers more efficient and customized scheme, which enables quick prototyping and iterative design improvement. In addition, based on the formulation of customized inks, it is feasible to print and pattern biocompatible materials with tailored properties and structures, which is paramount for precision medicine. To further develop the versatility of 3D printing towards different applications, it is essential to formulate various 3D printable raw materials, such as high conductive hydrogels with excellent mechanical properties. 3D-printed implantable devices should meet the gold standards of the industry, as well as state-of-the-art devices made by alternative fabrication method. In that respect, 3D printing must improve the resolution of 3D-printed features, as photolithographically patterned electrode arrays can achieve significantly higher densities, which is in critical demand for neural interfacing applications. Otherwise, the combination of novel functional materials and advanced printing technology is the basis and direction for the future biomedical field regarding personalized medical care.

3D-printed soft robotics

Soft robotics has received increasing attention due to their advantages over conventional rigid robots, including adaptability, resilience, soft manipulation and safety for human operators, among other reasons [4,148,149]. However, it is still challenging to fabricate soft robotics in a facile and integrated method. The development of 3D printing has provided an alternative fabrication technology with high quality and wide selection of materials at the same time [30]. Notably, functional soft materials are particularly well suitable for soft robotics due to their ability to respond to a wide range of stimulants, large actuation strain and deformations, various complex actuation motions and multiple functionalities [20]. Therefore, 3D-printed soft robotics has an interesting potential for applications in various fields such as soft grippers, actuators, and biomedical devices [50,150,151].

For soft robotics, the involvement of flexible and stretchable electroluminescent electronics provides more possibilities for practical applications [152,153]. Advancing on traditional manufacturing techniques that remain laborious and cost-prohibitive, a facile and easily accessible route for fabricating electroluminescent devices-integrated soft robotics is proposed through a 3D printing process [154] (Fig. 9A). The means of using multimaterial inks including ion conductive elastomer, electroluminescent elastomer, and insulating dielectric elastomer, enables the on-demand creation of flexible and stretchable electroluminescent

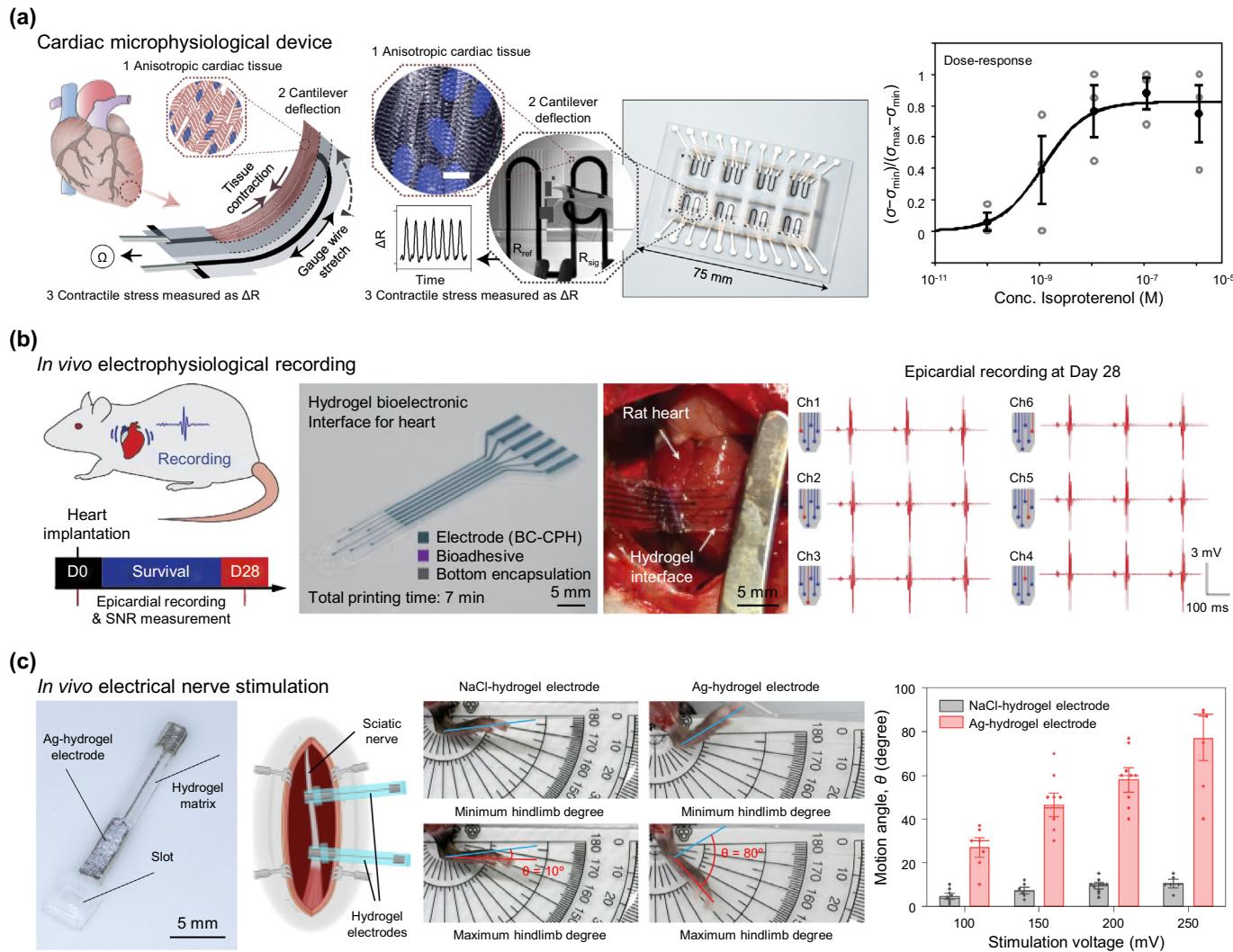


FIG. 8

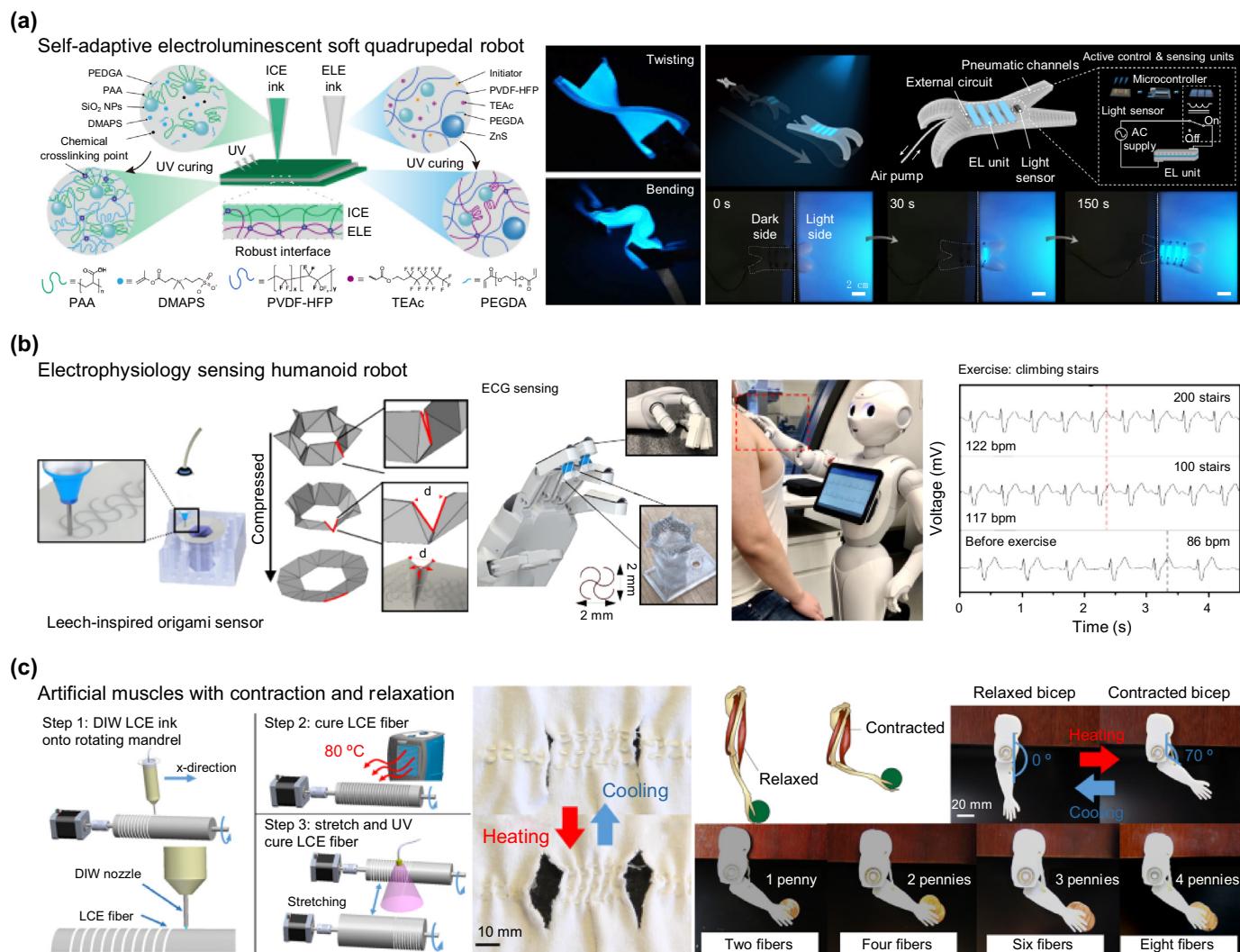
3D-printed implantable devices. A, Instrumented cardiac microphysiological devices via multimaterial 3D printing with the dose–response for isoproterenol. Reproduced with permission [144]. Copyright 2016, Nature Publishing Group. B, 3D printable high-performance conducting polymer hydrogel for all-hydrogel bioelectronic interfaces to realize long-term *in vivo* electrophysiological recording. Reproduced with permission [147]. Copyright 2023, Nature Publishing Group. C, 3D-printed hydrogel electrode for *in vivo* electrical nerve stimulation and the angle change of a mice hindlimb in response to stimulation voltage using different types of electrodes. Reproduced with permission [36]. Copyright 2022, Nature Publishing Group.

devices with high fidelity. Through the integration of 3D-printed electroluminescent devices with a soft quadrupedal robot and sensing units, a self-adaptive artificial camouflage is created, which can instantly change its surface color to match the environment and open new avenues for creating next generation flexible and wearable bioelectronics.

In the last few decades, robotics has found important applications in biomedical fields. The emergence of soft matter in robotics enables the design at different scales and opens new possibilities for bioelectronics [155]. Different levels of biocompatibility and biomimicry are required for soft materials in robotics depending on the level of interaction with humans. To further reduce the risk of secondary infection and improve the efficiency, remote monitoring system of human healthcare has been widely studied, and soft robotics offers a promising approach to mitigate risk and improve patient care effectiveness and quality [156]. Among the crucial biomarkers, blood pressure is an essen-

tial medical diagnostic tool that is highly related to several chronic diseases, and high blood pressure is a preexisting symptom of disorder or indicator of possible infections in patients [153]. To monitor blood pressure remotely and reliably, a 3D-printed leech-inspired origami sensor is proposed, which can be integrated to the fingertips of a humanoid robot [157] (Fig. 9B). The leech-inspired suction mechanism generates a local soft vacuum to facilitate strong contact with human skin, enabling the collection of ECG signal and blood pressure information accurately with a low signal-to-noise ratio.

In addition, soft robotics can be designed to perform muscle-like contraction as an actuator-based artificial muscles [158]. Within the field of soft robotics, numerous pneumatic actuators have been developed since 1950 s to achieve multiple possible deformations, lighter weight, cost reduction, improved compactness, and reduced radial size [159]. To further realize the miniaturization and customization of the artificial muscle, a class of

**FIG. 9**

3D-printed soft robotics. A, 3D printing of flexible electroluminescent devices and soft robots with ion conducting elastomer layers and electroluminescent elastomer layer to realize spatially instantaneous color-changing ability. Reproduced with permission [154]. Copyright 2022, Nature Publishing Group. B, 3D-printed leech-inspired origami dry electrodes for the electrophysiological measurement on the humanoid robot fingertip. Reproduced with permission [157]. Copyright 2022, Nature Publishing Group. C, 3D-printed artificial muscles using liquid crystal elastomer fibers with contraction and relaxation, enabling a lifting motion for soft robotics. Reproduced with permission [160]. Copyright 2019, American Chemical Society.

3D-printed biomimetic artificial muscles consisting of a liquid crystal elastomer (LCE) fiber is proposed without any strain-limiting elements [160] (Fig. 9C). Upon heating, the LCE fiber contracted causing the arm to achieve angle of 70°, meanwhile, by increasing the number of woven fibers, the activation force increases with the increase of lifted pennies. The LCE fiber could lift 250 times its weight, and twisted bundles of LCE fibers enabled more damage-tolerant muscles for soft robotics.

Overall, 3D printing has become a common and widely used technology for the fabrication of soft robotics, which enables the formation of complex structures in a relatively simple manner. Meanwhile, 3D-printed soft robotics for bioelectronics faces different challenges regarding the choice or development of materials depending on the applications and associated requirements. The controllability and tunability of mechanical properties, the response reliability to external stimuli, and the adaptability are crucial factors for the materials of soft robotics to meet the

demands of bioelectronics. Importantly, it is promising to develop materials tailored for various printing technologies and multimaterial printing for fully functional soft robotics without post-printing assembly.

Since the emergence of the field, soft robotics have had an increasing number of biomedical applications, such as in a soft prosthetic arm [161], interfaces that deploy electrodes implanted into the body [162], and as a robotic sleeve [163] that actuates to support pumping of the heart. Adapting 3D-printed soft robotics for such medical devices will further open the possibilities for improved and innovative soft medical robotics.

Conclusion and perspective

The application of DIW-based 3D printing technology to bioelectronics holds great promise for advancing the development of innovative and customized healthcare devices such as multimodal wearable biosensors, miniaturized energy storage and har-

vesting modules, biocompatible implantable devices, and autonomous soft robotics. The ability to construct intricate electronic circuitries and complex geometries, incorporate multiple materials, and customize designs for personalized applications makes DIW 3D printing an exceptionally viable manufacturing tool for next-generation bioelectronics. As described in this review, many recent works have demonstrated the successful implementation of DIW to create wearable and implantable bioelectronics with much-improved functionality, flexibility, and biocompatibility. All types of bioelectronics benefited from DIW 3D printing approach in different ways. First, with phase-elimination process, 3D printing could induce porous structures in micro to macroscale, which greatly enhance the operational capabilities of bioelectronics for biosensing, energy harvesting, and energy storage. Second, the formulation of customized inks under the rheological criteria allows the development of bioelectronics with specific materials, achieving the printing of digitally designed patterns with high resolution. Third, the performance of bioelectronics can be well modulated through the optimization of printing parameters, including pressure, speed, temperature, and number of printing layers.

However, to incorporate the 3D-printed devices for practical utilizations and clinical practices, several challenges remain to be addressed especially for the bioelectronics requiring multimaterial printing in sequence. Overall, formulation of customized inks, printing parameters, alignment among printing various materials, and post-printing processes (curing temperature and drying conditions) are critical for the development of bioelectronics. First, integration of miniaturized low-power devices is essential to enhance packing density and long-term sustainable use, which necessitates reliable printing at high resolution, preparation of highly efficient energy devices, and combination of energy harvesters and energy storage devices. Second, it is desired to develop scalable and compatible fabrication procedure to incorporate other functional modules and device components. Third, efficient wireless communication platforms must be established for rapid acquisition, transmission, and storage of data, which is key for bioelectronics with remote operations. Last, acquisition and analysis of comprehensive information with the aid of artificial intelligence would be beneficial to ensure accurate translations and predictions for diagnostic assessments.

It is well anticipated that the next phase of development is trending towards the construction of all-compatible 3D-printed integrated systems, where fabrication processes can be further streamlined to incorporate more devices to achieve the eventual goal of mass production and commercialization [164]. This necessitates the formulation of novel and multifunctional inks, development of scalable designs, and establishing new printing protocols that accounts for material compatibility during printing and post-printing processes. Importantly, ensuring the scalability, reproducibility, and regulatory compliance of 3D-printed bioelectronics will be crucial for their translation towards clinical practice, which are highly dependent on the consistency and stability of the customized inks. Meanwhile, the storage and variability in printing conditions should be well considered and established during ink preparation. Moving forward, the future of 3D printing holds many exciting opportunities in the field of biomedical engineering. The rapid advancement in the devel-

opment of new inks through the incorporation of nanomaterials and biocompatible conductive inks will enhance device performance and enable new functionalities. Critically, multimaterial printing through high-precision sequential or multi-nozzle printing will facilitate the construction of more sophisticated multimodal and integrated systems. Skin-interfaced wearable biosensors with highly sensitive physiochemical sensing capabilities will enable real-time monitoring of a diverse range of biomarkers for continuous health surveillance. Integration of wearable energy harvesting and storage modules will enable sustainable and long-term utility. Most of all, through coupling the information collected with machine learning algorithms and data analytics, these systems will be able to better predict an individual's health condition and offer more efficient and accurate healthcare interventions.

Data availability

No data was used for the research described in the article.

Declaration of Competing Interest

The authors declare that they have no known competing interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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