Skin-inspired soft bioelectronic materials, devices and systems

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Abstract

Bioelectronic devices and components made from soft, polymer-based and hybrid electronic materials form natural interfaces with the human body. Advances in the molecular design of stretchable dielectric, conducting and semiconducting polymers, as well as their composites with various metallic and inorganic nano-microscale materials, have led to more unobtrusive and conformal interfaces with tissues and organs. Nonetheless, technical challenges associated with functional performance, stability and reliability of integrated soft bioelectronic systems still remain. This Review discusses recent progress in biomedical applications of soft organic and hybrid electronic materials, device components and integrated systems for addressing these challenges. We first discuss strategies for achieving soft and stretchable devices, highlighting molecular and materials design concepts for incorporating intrinsically stretchable functional materials. We next describe design strategies and considerations on wearable devices for on-skin sensing and prostheses. Moving beneath the skin, we discuss advances in implantable devices enabled by materials and integrated devices with tissue-like mechanical properties. Finally, we summarize strategies used to build standalone integrated systems and whole-body networks to integrate wearable and implantable bioelectronic devices with other essential components, including wireless communication units, power sources, interconnects and encapsulation.

[H1] Introduction

Wearable and implantable bioelectronic devices are revolutionizing biomedical sciences by providing multimodal physiological monitoring and treatment in real time[1-7]. Bioelectronic devices interface with biological systems to monitor or stimulate physiological processes. These systems integrate with the human body to provide timely prevention strategies, early diagnosis and medical therapies[8-10]. Moreover, new bioelectronic devices can mimic, restore and even enhance human capabilities[11-14]. Coupled with the rapidly progressing 'internet of things', the field of bioelectronics is positioned to enable next-generation digital healthcare by monitoring physiological conditions and sharing real-time data with healthcare providers.

Conventional bioelectronic devices are stiff and inextensible, whereas tissue and organs are soft and dynamic. Mechanical mismatch between bioelectronic devices and tissue can lead to tissue damage, immunological responses and chronic inflammation (**BOX 1**)[4,5,8,10]. Furthermore, mismatch in stiffness often results in non-conformal contact, poor adhesion and delamination, hindering the efficient transmission of electrical, chemical, mechanical and optical signals to or from the body[8,10]. Soft bioelectronic devices can circumvent these limitations[1,6,7,13] by using functional electronic polymers (and composites of insulating polymers embedded with particulate nano-microscale inorganic materials) with low elastic moduli (<1–10 MPa). Moreover, by geometrically patterning thin inorganic (<1 micron) device layers into serpentine geometries, low bending stiffness and stretchability with an otherwise intrinsically inextensible material, can be achieved[15,16]. Using such strategies, functional organic and hybrid materials can be designed to mimic the properties of skin, such as softness, stretchability, self-healing ability, biodegradability and permeability[1,12] (**Figure 1, BOX 1**). Incorporation of such materials and devices into bioelectronic systems could ultimately enable multifunctionality similar to skin, including the ability to mimic the tactile sensitivity of skin for advanced prosthetics, the ability to encode and transmit sensory information through artificial neuromorphic devices and eventually even the ability for transient implantable devices to degrade in the body without producing toxic by-products.

In this Review, we first discuss strategies to achieve materials and devices with skin-inspired properties, with a focus on organic polymer-based materials. Based on these materials and device engineering approaches, we discuss sensors and actuators for wearable and implantable applications. Operating individual bioelectronic sensors and devices often requires extensive wiring and external bulky equipment, which greatly limits their application outside laboratories and hospitals. Integrated standalone systems also require soft or flexible power sources, measurement circuits, wireless communication, interconnects and encapsulation. Therefore, we also discuss strategies for integrating soft bioelectronic devices, from wired bulky instruments to customized printed circuits board (PCB)-based hybrid systems, strain-engineered soft integrated circuits to intrinsically soft systems (**Figure 1**). Finally, system integration aspects are discussed, including wireless communication strategies, power sources, displays, interconnects and encapsulation layers.

[H1] Approaches to skin-inspired devices

Like conventional electronics, bioelectronic devices include passive and active components such as interconnects, resistors, capacitors, electrodes, diodes and transistors[6,14]. The first four passive components are typically composed of conducting and insulating materials, which are used in soft sensors and actuators (**BOX 2**)[6,17]. For example, biological signals can be electrically measured using sensing components that exhibit changes in resistance, capacitance or impedance in response changes in mechanical or chemical signals. Diodes and transistors (such as organic field-effect transistors (OFETs)), which enable versatile electronic functionality such as amplification, filtering and modulation of analog and digital signals, also rely on semiconducting materials. Through the integration of these and other components, multimodal wearable and implantable bioelectronic devices have been designed to interface with different body parts for health monitoring and therapeutics (**Figure 1**).

Molecular engineering concepts can also be used to develop semiconducting and conducting polymers that are intrinsically soft and stretchable, including molecular design and synthesis of polymers and multi-component networks[18,19] (**Table 1**). These strategies alter the chemical structures of semiconducting polymers, such as systematic modifications of the conjugated backbone or the side chains; however, there are trade-offs between favorable mechanical properties (such as stretchability), generally associated with amorphous polymer films above the glass transition temperature, and electrical performance (such as field-effect mobilities), mainly associated with polymer films containing long-range semicrystalline order[18,20-26].

Multi-component networks involve introducing secondary components in semiconducting or conducting polymer networks[27-29]. Promising approaches for multi-component systems include blending with elastomers and incorporating small molecule additives[27,28,30,31]. An important breakthrough was the discovery that when blended with thermoplastic elastomers in solution and cast into thin films under certain conditions (such as the solvent used, the degree of immiscibility between blended polymers and their composition in solution during spin coating or solution shearing), the semiconducting polymers phase segregate into interpenetrating nanoconfined fibrillar structures which exhibit high stretchability while maintaining or enhancing the electronic performance relative to the neat polymer films[23,27,31]. The phase segregation process results in the alignment of the polymer chains along the long axis of the nanostructures and π−π stacking perpendicular to the long axis[23,27,31]. However, it is still difficult to predict the combination of semiconducting polymer, thermoplastic elastomer and solution processing parameters that yield optimal nanofiber morphologies; therefore, systematic empirical optimization is needed for each system[32,33]. Another limitation of the blending approach is that thermoplastic elastomers are susceptible to creep or inelastic deformation; however, this shortcoming can be mitigated using covalent cross-linking strategies (such as azide/C−H insertion and azide/C=C cycloaddition)[18]. Importantly, the blending strategy enables the incorporation of multifunctionality into organic semiconductors[18,34]; for example, a bioadhesive semiconducting polymer blend of semiconducting poly(3,3′-bis(2-(2-(2-methoxyethoxy)ethoxy)ethoxy)-2,2':5′,2”-terthiophene) (p(g2T-T)) and brush-architectured polymer containing a polyethylene backbone with tetra(ethylene glycol) side chains terminated by carboxylic acid and N-hydroxysuccinimide ester functional groups showed strong adhesion to wet tissue while maintaining a high field-effect mobility (~1 $cm^2\ V^{-1}\ s^{-1}$), biocompatibility and stretchability[35].

For devices and materials that do not have intrinsic skin-like properties (such as inextensible materials with high elastic moduli (>1 GPa), like silicon), device-level engineering could be performed using structural design approaches.[16,36] Typical structural design routes include devices with patterned structures[15,37], micro-structured thin film[36,38,39] and nanocomposite networks[40,41] (**Table 1**). One limitation of strain-engineered devices is a sacrifice in spatial resolution of components owing to the larger areal footprint required by complex geometric designs[42,43]. For example, serpentine patterns, which are used for converting global strains of stretchable substrates into flexion of the inextensible functional components[44]. The low device densities can be a limitation for certain biomedical applications, such as electrophysiological signal mapping in the brain[42].

[H1] On-skin soft bioelectronic devices

Skin, the body's largest organ, is the interface through which we interact with the external environment[17]. Extensive secretion occurs from the skin to maintain thermal homeostasis through perspiration, which contains ions[45], metabolites[45] and proteins[46]. Thus, skin provides a vital interface to extract physical and chemical biomarker information. In this section, we start by discussing devices for on-skin sensing and signal conditioning, where information is transmitted from the skin to devices. We then move to systems of interest for prosthetics, including sensors which mimic tactile sensation of the skin, neuromorphic devices for transmitting information and haptic on-skin actuators, where skin functions as a hub to receive and process information.

[H2] On-skin sensing. Current medical equipment in hospitals typically require extensive wiring and bulky measurement units, making them difficult to use outside of hospitals for continuous monitoring applications[47]. For example, patients with symptoms such as palpitations, dizziness and chest pain might require continuous 7-day electrocardiography[48]. Commercially successful wearable devices, such as the Apple Watch (~5 cm × 4 cm × 1cm) and Fitbit (4 cm × 2 cm × 1 cm) can provide real-time vital sign monitoring without limiting wearers' daily activities[49,50]. However, these rigid electronic devices often suffer from motion artifacts caused by their non-conformal interface with the skin, limiting their recording accuracy[51]. To improve accuracy of signal recording (and stimulation), conformal and reliable interfaces between wearable devices and skin are needed[52,53]. For example, accurate electrophysiological recordings, such as electrocardiogram (ECG) and electromyography (EMG) monitoring, require low interfacial electrical impedance (1–100 kΩ at 1kHz), for which conformal contact is needed (**Box 2**)[9,17]. Similarly, other physical and chemical signal recordings also require conformal contact for reliable signal transduction, such as optical signal transmission for photoplethysmography (PPG) sensors and mass transport (sweat and biomarkers) for chemical monitoring[9,17,54].

Several soft wearable physical sensors have been fabricated to monitor vital signs with high fiedelity[6]. For example, a soft multimodal system was developed using serpentine Au as stretchable interconnects for rigid commercial sensors (temperature, PPG and ECG sensors) (**Figure 2, top left**)[55,56]. However, the device-level engineering approaches used in these works are not suitable for multi-channel sensing with high spatial resolution over large areas, which is desirable for future electroencephalogram (EEG) and EMG recording devices. Alternatively, intrinsically stretchable materials can provide conformal interfacing with skin and high spatial resolution[31,57-59]. For example, an intrinsically stretchable, highly conductive poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS) enabled low interfacial impedance (~50 Ω cm^2) and high surface (density down to 100 µm electrode widths), whereby clinical devices typically have resolutions of ~5 mm or larger[6,31] **(BOX 2)**. In this system, a photo cross-linkable supramolecular additive was developed for PEDOT:PSS, in which interlocked mobile junctions of polyrotaxanes provide a stretchable network, and the polar polyethylene glycol methacrylate (PEGMA) network induces nanoscale phase separation of PEDOT chains, enabling high conductivity within physiological environments, even in a strained state (~6000 S/cm under 100% stain)[6,31]. Other on-skin physical sensors, including pressure[60], strain[61,62], temperature[63] and skin conductance[6], have also been developed. Soft interfaces are also advantageous for monitoring signals through the skin transmitted by acoustic waves[64,65]. For example, a wearable ultrasound imaging system made from a robust bio-adhesive hydrogel made of chitosan-polyacrylamide interpenetrating polymer networks provided continuous imaging of different internal organs for 48 h[64,65]. Importantly, the examples discussed still need to be connected to bulky equipment for measurement, limiting their application outside of laboratories or hospitals.

In addition to these physical sensors, wearable chemical biosensors can measure chemical biomarkers non-invasively from sweat and minimum-invasively through interstitial fluids (ISF) in real time[2,3,54,66]. These sensors are useful for monitoring health conditions and early detection of diseases[67-69]. A conformal contact with skin is favorable for sweat stimulation and collection, making flexible and soft bioelectronic devices ideal for wearable chemical sensing[3,68,70-72]. Flexible electrochemical biosensor arrays have been integrated to monitor metabolites (such as glucose and lactose) and ions (such as K^+ and Cl^-) in real time (**Figure 2, top left**)[2,3,73]. Furthermore, electrochemical sensing can be used to monitor other clinical biomarkers, such as hormones and cytokines[67,74,75]. For example, the stress hormone cortisol can be sensed using a molecularly imprinted polymer[75], antibody[76] and aptamerantibody-based[67] approaches. Similarly, a stretchable epidermal sweat-sensing platform for glucose and lactate was integrated using high-throughput screen printing methods[77]. The stretchable composite inks were robust enough to withstand 1,500 stretching cycles at 20% strain. With the commercialization of continuous glucose monitoring (CGM) devices, continuous chemical sensors are gaining attention[2,66,78]. However, most biosensors still suffer from signal drift and low accuracy against gold-standard measurements, especially when exposed to biofluids where protein and other biomolecules are present[3].

[H2] Epidermal signal conditioning. Sensing signals obtained from wearable devices often require signal processing, such as amplification and filtering. Current wearable sensor systems typically include separated sensors and mixed-signal circuits for signal conditioning, signal processing and data acquisition[79]. However, the interconnects between soft sensors and rigid electronics are often fragile and susceptible to influence by external noise and motion artifacts, which leads to a low signal-to-noise ratio (SNR)[80]. These challenges have been addressed by engineering system designs[80-82]; however, near-sensor signal conditioning (where conditioning units such as amplification and filtering circuits can be designed and fabricated together with sensors on the same substrate) is preferred to achieve high-fidelity signal recordings. This approach suppresses noises from traces and wires when external processing devices (such as printed circuit boards) need to be connected to sensors. High-density and stretchable OFET arrays are suitable for developing intrinsically stretchable signal conditioning modules[30]. For example, an EMG sensor array was integrated with a stretchable organic amplifier circuit using a stiffness-patterned elastomer approach to enable strain-insensitive performance, including a gain of >120 and enhanced EMG signals[83]. Similarly, the amplifier circuit improved the signal quality in pulse sensation by amplifying voltages across the resistive strain sensors (**Figure 2, bottom left**). Moreover, these signal conditioning circuits can reduce interference from strain induced by movement. In another example, a soft temperature sensor based on differential circuits minimized the interference from external strain by performing on-chip compensation. Here, stretchable circuits and sensors that experience a similar level of strain as were fabricated on the same substrate to improve accurate and perform real-time substraction[84].

On-skin signal conditioning strategies have also been reported using organic electrochemical transistors (OECT). For example, an OECT-based complementary inverter was developed with co-facial vertical OECT structures and ambipolar organic mixed ionic-electronic conductors (OMIEC) material exhibiting both p-type and n-type OECT behavior. These materials enable complementary

OECT inverters with lower power consumption and better noise tolerance than monopolar devices. These unique configurations enabled downscaling of device dimension (within 10 μm of length). The ECG signal was amplified through an inverter device showing a gain of ~10 compared to commercial ECG electrodes[85]. Moreover, the design of an OECT device supported by a nano-mesh membrane enabled the integration of breathability with on-skin amplification and recording with a SNR up to 25.9 dB[86].

Advances have also been made in near-sensor digitalization of signals[87]. Recorded analog biosignals (such as amplitude signals) can be transmitted to the receiving ends (for example, computers) for digitization; however, these analog signals are more susceptible to environmental noise (such as motion artifacts) than digitized signals (such as frequency signals), resulting in lower fidelity of data transmission[88,89]. Alternatively, near-sensor circuits can digitize analog signals prior to transmission, leading to recordings with high SNR; for example, by integrating ring oscillators with sensors (such as pressure sensors) on single chips[87]. However, such near-signal digitization circuits typically require complex design and fabrication steps. Advances in the design and fabrication of soft organic transistors will enable higher density and operation speed, and the development of more complicated circuits such as a high-speed operational amplifier and analog-to-digital converter (ADC) that can be integrated with e-skin for advanced digital signal processing.

[H2] Tactile sensation. The somatosensory system enables the human body to perceive the external world and infer physical properties of objects including stiffness, texture, roughness and temperature (**Figure 2, bottom middle**)[1]. Soft tactile sensors enable artificial sensation with applications in robotics and prosthetics. To gain natural and realistic sensation, multimodal mechanical sensors are necessary to mimic various types of mechanoreceptors on skin[1,90,91]. Accurate multi-point sensing and large-area mapping require soft and deformable sensors with skin-like mechanical properties. For example, an electronic skin that simultaneously monitors and differentiates thermal and mechanical stimuli was designed by using an ionic-liquid-containing polymer gel made of poly(vinylidene fluoride-co-hexafluoropropylene) mixed with 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide (EMIM TFSI). The impedance in this material can be decoupled based on differences in the dependence of ion relaxation dynamics on temperature and mechanical strain[92]. Moreover, simultaneous differentiation of multi-axial input such as normal stress, shear stress and bending, is essential in tactile sensors to resemble realistic human tactile sensations. Multi-axial inputs are typically decoupled using multi-arrays of tactile sensors and protruding structures. For example, micro-pyramidal subtructures[93] can decouple different axial forces such as pressure versus strain or normal versus shear forces. With patterned stiffening microelectrodes underneath each pyramid, the interfacial capacitance depends only on pressure while remaining unchanged under in-plane stretching. Furthermore, a self-decoupling mechanism with a sinusoidally magnetized film enabled decoupling between normal and shear force by incorporating multiple pairs of north-south magnetic poles. In this sensing mechanism the magnitude of the magnetic field depends only on normal force, and the ratio of the magnetic field along two perpendicular directions depends only on shear force[94]. However, building a multimodal soft tactile system with similar spatial resolution and sensitivity to human skin is still challenging. Device density and robustness need to be improved towards large-area multimodal sensors for prosthetic and robotic applications, such as surgical robots and assistive technologies[1,12,95].

[H2] Artificial nervous system. The perception of touch at the brain's somatosensory cortex instructs muscle movements through the motor cortex. In patients with damaged spinal cords or motor neurons, their sensory and perception loops cannot be completed. The reconstruction of these loops is essential for prosthetic applications. Soft organic artificial afferent (sensory) and efferent (motor) nervous systems have been developed to mimic the sensorimotor systems (**Figure 2, right**)[87,96-98]. By combining mechanical sensors (such as pressure and strain sensors), ring oscillators (to convert amplitude information to frequency signals) and synaptic transistors (for combining sensing signals into pulse train patterns), the artificial nervous system can transduce external artificial skin sensory signals into electrical pulse patterns and post-synaptic current[87,97]. However, most artificial nerves still need to be connected to rigid modules for signal processing, limiting their abilities to integrate the entire system with the human body. To overcome this challenge, an integrated soft e-skin was developed that combines multi-modal sensors with signal conditioning and closed-loop actuation[87]. In this integrated circuit, low voltage operation (~5 V) of OFETs was achieved through the design of a dielectric trilayer, including nitrile butadiene rubber (NBR) with a high permittivity of ~28[87]. Practical considerations, such as durability, reliability, scalability and biocompatibility, are important next steps for future artificial nerves[1,12].

[H2] On-skin actuators. Human–machine interfaces include receiving information and sending feedback to the human body through skin. Information from bioelectronic devices can be conveyed in real-time to users through on-skin haptic devices[99,100]. Virtual reality has further boosted the interest in haptic devices that provide a natural feeling of objects within virtual or augmented reality. For example, integrated soft actuators can induce spatially programmed tactile sensation through mechanical vibrations from electromagnetic fields and electrotactile systems (**Figure 2, bottom right**)[13,99,101,102]. Other stimulation systems, such as piezoelectric, hydraulic and ultrasonic actuators have also been developed for flexible actuators for haptics[101,103]. However, these systems often adopt rigid materials and complex mechanical design, limiting their actuation efficiency and wearing comfort. Dielectric elastomer actuators (DEA), which function through an electrostatic stress mechanism, are more suitable for soft robotics and haptics. For example, an 18-μm-thick soft DEA can provide vibrotactile feedback generation from 1 Hz to 500 Hz on skin[104]. Combined with soft tactile sensors, these on-skin actuators can also be used for closed-loop haptic displays, including tactile displays and remote surgeries[105-107].

[H1] Implantable soft bioelectronic devices

Soft bioelectronic technologies can also be applied as implantable devices. Although several proofs-of-concept for implantable devices in animal models (typically rodents or porcine) have been demonstrated, there are still challenges for their clinical translation, such as device manufacturing and reliability, as well as satisfying stringent requirements for regulatory approval. Despite these limitations, new concepts and capabilities for implantable devices need to be demonstrated for fundamental and translational applications.

[H2] Soft bioelectronics for the brain. Brain-machine interfaces have gained considerable interest in fundamental and translational research owing to their application in diagnosis and treatment of brain diseases[5,108-110]. Despite exciting advances, a major challenge is the mechanical mismatch between the brain and rigid probes, which causes damaged tissue, scar formation and degraded sensing and stimulation performance over time[111-113]. To form a conformal interface that fits the curvature of the brain, a common device-level strategy is to decrease film thickness[114-118]. For example, an ultrathin polyimide Au electrode array was developed using silk fibroin as a sacrificial layer (**Figure 3, top row, left**), whereby the 2.5-µm-thick devices showed higher SNRs than the 76-µm ones (mean root mean square 5.7 over 3.6)[115]. However, Au or Pt electrodes often suffer from higher interfacial impedance with ionic solution, limiting the recording with lower noise levels[119]. Thus, OMIECs have been proposed to measure electrophysiological signals (**BOX 2**); for example, a 256 channel soft and conformable neural interface array was developed with PEDOT:PSS as interface materials to measure both action potentials and local field potential without penetrating the brain surface[116]. Similarly, PEDOT:PSS based organic electrochemical transistors can measure electrophysiological signals with further amplification[120].

Moreover, intrinsically stretchable PEDOT:PSS systems offer conformal and seamless interfaces with the brain while providing low interfacial impedance[121]. For example, soft and stretchable PEMGA-based PEDOT:PSS electrode arrays were used for neural stimulation in the brain stem of a rodent model[31] (**Figure 3, top row, middle**). The interfacial impedance of these electrodes is three orders of magnitude lower than that of microcracked gold electrodes with similar dimensions owing to the volumetric capacitance of the organic mixed ionic-electronic conducting layer. Here, the capacitance scales linearly with the volume linearly owing to the uniform distribution of charge within the PEDOT:PSS films [31] (**BOX 2**). More importantly, these electrode arrays do not induce observable brain tissue damage when implanted at the brainstem region, whereas the commonly used flexible polyimide substrate with similar thickness caused severe damage to brain tissue. This difference is likely due to mechanical interactions between soft, pulsating brain tissue and rigid substrates with higher elastic modulus (2.5 GPa) for polyimide compared to soft (~1 MPa) for SEBS used in the PEDOT:PSS electrodes[31,111]. Notably, these experiments were performed in small animal models (such as rodents), whereas the human brain typically experiences much larger head motions (4–10% in humans compared with 2–3% in rodents)[122]These electrodes (such as PEDOT:PSS) are moving into human clinical trials to treat neurological diseases, such as the suture-like neural probes developed by Neuralink Co[123] [31,111].

In addition to electrophysiological recording, neurochemical monitoring is vital to understand and regulate brain functions and neural circuits[124]. However, few tools are available to monitor chemical signaling in the brain. Using laser-induced graphene electrodes with catalytical Fe_3O_4 nanoparticles, a tissue-like stretchable and implantable neural probe, NeuroString[125] (**Figure 3, top row, right**), enabled simultaneous monitoring of multiple neurotransmitters (serotonin and dopamine) using fast-scanning cyclic voltammetry (FSCV) in brain and intestine with high selectivity and minimal tissue damage. Other soft biosensors such as enzymatic and aptamer-based sensors have also been developed for neurotransmitter monitoring in vivo[126-129] [126,130]. Among these methods, FSCV-based approaches have higher reversibility than receptor-based (such as enzyme and aptamer) approaches, which is advantageous for continuous monitoring with high temporal resolution (<100 ms). However, FSCV methods are limited to electroactive neurotransmitters (such as serotonin and dopamine). Moreover, sensing in complex brain cerebrospinal fluids, where different neurotransmitters have similar and often overlapping electrochemical redox potentials, is challenging. To improve selectivity, custom waveforms (such as square waves and N-shape waves[131]) and different electrode materials (such as adding catalytic nanomaterials[125]) are being explored. By contrast, enzymatic and aptamer sensors have higher selectivity owing to their specific recognition mechanism. However, enzymatic approaches are limited to enzymatically active neurotransmitters (such as glutamate). Aptamer-based sensors are more universal because they rely on conformational changes of aptamers, which are independent of the chemical nature of target neurotransmitters. However, the stability of aptamers in biofluids, when used in vivo, is still low and requires coatings (such as hydrogels[132]) to prevent biofouling. For aptamers with high binding affinity (<100 nM), the ability to regenerate remains challenging for continuous monitoring. In next-generation soft neurochemical probes, multimodal and multiplexed sensors that combine two or more sensing mechanisms could be of great interest in overcoming the shortcomings of a single sensing approach.

In addition to electrophysiological and neurochemical monitoring, soft probes with multimodal sensors and actuators further enable closed-loop sensing and modulation[133-136]. For example, a multifunctional fiber was integrated with optogenetics, electrophysiology, fluid delivery and thermometry for bidirectional recording and modulation of the mesolimbic reward pathway in the mouse brain[137]. Soft probes with multimodality will be important for building a more complete picture of how the brain processes information.

[H2] Soft bioelectronics for cardiac monitoring. Monitoring cardiac electrophysiology with high spatiotemporal resolution provides important information for understanding, diagnosis and treatment of cardiovascular diseases such as atrial fibrillation (AF)[42,138]. Owing to the constant volumetric contraction and expansion cycles with cardiomyocyte deformation of up to 20%, bioelectronic devices that can accommodate high strains without constraining or interfering with normal cardiac functions are needed[113]. Unique geometric or structural designs are therefore needed to increase electrode stretchability for cardiovascular applications, such as honeycomb-structured multielectrode arrays[139]. For example, a three-dimensional and multimodal elastic membrane was developed with serpentine structures and rigid islands using mainly inorganic materials (Au, Si, InGaN and IrO_x) to form a stable interface with the heart (**Figure 3, top row, right**)[140]. Multimodal cardiac sensors and actuators were developed using this approach, including electrodes for electrophysiological recording and stimulation, mechanical strain sensors, temperature sensors, pH sensors, heaters and LEDs for thermal and optical stimulation (~2 sensors per 0.25 cm^2). To further increase device stretchability and maintain their conductivity during stretching, nanocomposite-based stretchable electrodes were developed. For example, a serpentine structured cardiac mesh using Au–Ag nanocomposites embedded in an elastomeric block-copolymer (SBS) matrix, resulted in an optimized stretchability of 266% and maximum of 840% with similar device density (~2 sensors per 0.25 cm^2) (**Figure 3, middle row, left**)[141].

However, in these serpentine-based devices, there is a trade-off between array stretchability and electrode density. Therefore, intrinsically stretchable bioelectronics devices are better suited for high-resolution recording and modulating dynamic cardiac activities[113,121,142]. For example, a tissue-like, high-density, stretchable electrode array has been developed based on a soft PEDOT:PSS hydrogel[143] with a Young's modulus of ~10 kPa, resembling that of cardiac tissue (**Figure 3, middle row, middle**). The low interfacial impedance between PEDOT:PSS hydrogels and tissue led to a high electrocardiogram (ECG) recording SNR of 102.7 ± 9.4 compared with 19.6 ± 1.8 for conventional ionic hydrogels in porcine and rabbit models (64 sensors per 0.25 cm^2).

To increase recording densities, an epicardial bioelectronic patch was developed with rubbery transistor arrays using poly(3-hexylthiophene-2,5-diyl) nanofibrils (P3HT-NFs)/PDMS as stretchable semiconductors (a 5×5 array in a porcine model with a density of ~1 sensor per cm^2), which improved ECG recording resolution with soft transistors despite the low device density[144]. Moreover, soft and bioresorbable bioelectronic devices enable temporal monitoring and support of cardiac functions after cardiac surgery without requiring an additional operation to retrieve the device[113,138,145,146].

[H2] Soft bioelectronics for the nerve interface. The peripheral nervous system, the bridge between the central nervous system and the rest of the body, provides essential bidirectional communicating functions for sensing and perception[113,147]. Closed-loop implantable bioelectronics with stimulation and recording functions could help understanding and modulating the peripheral nervous systems[148]. Peripheral nerves are cylindrical and thin (~0.1–10 μm in diameter), making them difficult to closely contact rigid devices[149]. Moreover, the regions near peripheral nerves undergo constant movement caused by the motion of their surrounding muscles, making the attached devices susceptible to motion artifacts, electrical noise and delamination[136]. Structural designs that combine rigid components with system level flexibility to conform to nerve tissues are suitable in this case. For example, an implantable cuff system was designed by integrating serpentine traces, a microscale inorganic LED, a microfluidic system and an elastomer encapsulation ((**Figure 3, bottom row, right**). These structural engineered systems provide stable and multimodal sensing and modulation to nerve tissues, including electrical, optical, pharmacological and thermal neuromodulation.[113,147].

A broad range of soft and stretchable bioelectronic devices have been developed for nervous system recording, including microcracked Au devices, nanocomposite-based probes and devices based on intrinsically stretchable materials[24,40,59,121,150]. For example, microcracked Au electrodes on soft elastomeric substrates are used as interconnects[150]. With a similar microcracked Au strategy, an ultrathin (~1.3 μm thick) and stretchable electrode enabled nerve stimulation and recording with high SNRs down to mV levels (**Figure 3, bottom row, left**)[59]. Similarly, a soft and stretchable neuromorphic device with synaptic transistors combined with hydrogel electrodes enabled neuromodulation with low power consumption (~1/150 of a typical microprocessor system), which is important for the design of stand-alone self-powered systems with wearable batteries[96].

Even though stretchable bioelectronics can accommodate strain cycles, challenges remain in adapting them to developmental tissue growth, which might cause substantial stress accumulation[24,151]. To overcome the limitation of bioelectronics interfacing with dynamic tissue and organs, 'morphing electronics' (MorphE) that undergo irreversible deformations over a long-time scale (8 weeks) of tissue growth while remaining elastic and conformal within short time scale (daily body movement, estimated to be second to minute levels) dynamic movements, have been proposed[24] (**Figure 3, bottom row, middle**). MorphE consist of conductive viscoplastic polymers (VP) made with a PEDOT:PSS/glycerol composite supported on a soft viscoplastic polymer substrate containing weak hydrogen bonding interactions, which show near-zero stress at a low strain rate of 0.05% s^{-1}. The MorphE concept demonstrates how self-healing materials which behave like viscoelastic liquids can be used in bioelectronics, including for nerve interfaces[152,153].

[H1] System-level architectures

In addition to sensors and actuators, a standalone bioelectronic system requires power sources, data acquisition and communication strategies. An ideal body-area soft bioelectronic network (bodyNET) would consist of multimodal wearable and implantable skin electronics that can be operated independently and are connected through wireless networks to provide real-time feedback to wearers. Wireless strategies, power solutions, on-skin displays and practical considerations such as interconnects and encapsulation therefore need to be addressed.

In this regard, we discuss three types of soft bioelectronic wireless strategies: passive tag systems, near-field communication (NFC) based systems and Bluetooth-based systems. Batteries are often required to power electronics for contemporary wireless protocols such as Bluetooth and WiFi, therefore flexible and stretchable power systems would be ideal for on-skin bioelectronic systems. In addition to wireless data transmission, the on-skin real-time displaying of information using stretchable LEDs and on-skin projectors, are discussed. Finally, we review efforts for building complete and integrated systems, such as interconnects with commercial PCBs and encapsulation.

[H2] Passive tag systems. Antennae are electronic components designed to transmit or receive electromagnetic waves and are commonly used for wireless communication systems in the form of passive tag systems. Information obtained from the sensors can be wirelessly accessed from an external reader[154]. The sensing tags are composed of only passive components, including serial or parallel connections of inductors, resistors and capacitors, in addition to passive-component-based sensors (typically resistive or capacitive sensors). Owing to the simplicity of the components, soft and stretchable passive tag systems have been fabricated using entirely stretchable materials, or biodegradable materials, which makes them attractive for skin-mounted and implantable sensing applications[155,156]. These systems have a characteristic resonance frequency denoted as

$$f_r = 1/2\pi\sqrt{LC} \tag{5}$$

where f_r, [Hz], L, [H], and C [F] represent the resonance frequency, inductance and capacitance, respectively. Information from a sensor device can be wirelessly read from the external reader through a change of resonance frequencies or the electromagnetic energy dissipation of the passive tag[154]. Sensors based on capacitive sensing modulate resonance frequencies by capacitance changes correlated with external stimuli[154,157-159].

Passive sensor systems have been explored for biosensing applications[90,159]; for example, capacitive pressure sensors, whose capacitance is correlated with hydrostatic pressure, have been implanted in rats to monitor blood flow post-operatively through surgically reconstructed arteries for early detection of vascular anastomosis complications such as occlusion[159] **(Figure 4, top left**). In addition, passive capacitive pressure sensors have also been implanted for monitoring elevation in intracranial pressure[157], which is a common complication of brain injury leading to cerebral ischemia, brain herniation and even death[160]. Moreover, resistor-based strain sensors have been used to develop soft and stretchable passive wireless tags placed at multiple locations on the human body to simultaneously track movement, heart rate, temperature and breathing[155] (**Figure 4**, **top right**). These passive wireless sensor tags contain only a few active components and are simple to fabricate, but the signals must also be read in close proximity (~1 cm). Furthermore, the sensor signals can be influenced by body motion and the misalignment and distance between the sensing antenna tag and the reader. More advanced passive sensors could be incorporated into the bodyNET for addressing some of these challenges for improved and versatile sensing capabilities[161].

[H2] Passive NFC-based systems. Radiofrequency identification (RFID) systems transfer information to an external reader, which can also wirelessly power the communication device. Near-field communication (NFC)-based RFID devices (which enable wireless information transfer up to 1 m with compliance of ISO/IEC 15693 and of 4 cm or less in bioelectronics) are becoming more prevalent for wearable and implantable sensing applications[162-164]. These bioelectronic systems typically use a hybrid configuration that combines soft sensors with commercial NFC chips for wireless communication[162-164]. For example, a wireless smart bandage combines soft hydrogel electrodes with an NFC chip for wireless impedance monitoring and electrical stimulation to accelerate wound healing[57] (**Figure 4**, **middle left**). Similarly, a soft multimodal system for neonatal intensive care was developed using NFC systems (**Figure 4**, **middle left**)[56]. With additional front ends, the NFC-based systems are compatible with most sensing and stimulating systems, thereby being suitable for a broad-range of applications[162,165]. Moreover, NFC-based systems are relatively compact compared with Bluetooth-based systems as they do not require batteries; nonetheless, commercial NFC modules are rigid which prevents manufacturing entirely soft and stretchable systems.

By contrast, OFETs enable building soft and stretchable RFID transponder systems; for example, a fully stretchable diode (which converts wirelessly transmitted alternating current (AC) power into direct current (DC) electricity for powering the system) can operate at 13.56 MHz, matching the wireless signal transfer frequency of commercialized NFC devices[166]. Stretchable circuits containing OFETs have also been realized, including ring oscillators[83], amplifiers[30,83] and logic gates[30,83,167]. Further advances will result in stretchable RFID systems containing circuits and sensors to develop fully soft and wireless electrophysiological recording and stimulating devices.

[H2] Active wireless communication systems. Unlike passive systems that can only send signals when powered by external devices, active wireless communication systems, such as Bluetooth Low Energy (BLE) and Wi-Fi, can continuously communicate with external devices or cloud servers[163,168]. For example, BLE modules have been integrated with stretchable conductors and encapsulated into elastomer substrates (**Figure 4**, **bottom left**)[55]. High-bandwidth wireless communication protocols such as Wi-Fi can facilitate real-time streaming of high-volume datasets from bioelectronics and direct access to cloud server through a local router[169,170]. Most physiological biosensors (such as electrical, optical, mechanical and chemical sensors) require sampling frequencies below 1 kHz[171], which can be handled through passive NFC-based systems (bandwidth of <400 kbps) or BLE communication systems (bandwidth of <1Mbps). However, some biosensing systems, such as piezoelectric and ultrasonic sensors, require high-frequency data sampling (>1 MHz) that can only be transmitted via high-bandwidth communication protocols. For example, a wearable ultrasound sensors used Wi-Fi (bandwidth of up to hundreds of Mbps) to transmit high-bandwidth data (6 MHz) for real-time blood-pressure monitoring[170]. High-density mapping and multimodal monitoring can further increase the required bandwidth for wireless communication. Nonetheless, the form factor and duration of operation of these bioelectronic systems are limited owing to the high-power consumption (~10 milliwatts in BLE and up to several watts in Wi-Fi) of wireless communication and limited capacity and compactness of batteries. The device densities and circuit complexity required for wireless communication applications are still too challenging to be realized based on capabilities of current soft integrated circuits. We envision that a hybrid architecture with rigid ICs will still be needed for wireless communication bioelectronic systems in the short-term.

[H2] Flexible and stretchable power. Power solutions are additional, but essential components for fully integrated bioelectronic systems. Commercial batteries, even flexible ones, are still too thick and rigid, therefore, soft and stretchable batteries are being investigated[172,173]. For example, a supramolecular lithium-ion conductor made of ion-conducting polymer poly(propylene glycol)-pol(ethylene glycol)-poly(propylene glycol) (PPG-PEG-PPG) and dynamically bonded 2-ureido-4-pyrimidone (UPy) backbone unit was developed for stretchable Li-ion batteries with a capacity of 1.1 mAh/cm^2 with 70% strain[173]. Moreover, a stretchable Ag_2O-Zn battery integrated with a stretchable epidermal sweat sensing platform powered 14,000 sensing acquisitions over a week[77] (**Figure 4**, **top right**). Similarly, a fiber-shaped zinc ion battery powered a wearable system on clothing with stable charging/discharging for more than 500 hours[174].

Battery-operated systems provide efficient and reliable power supply for most bioelectronic systems; however, conventional batteries need to be recharged or replaced over time and they are still too rigid and bulky compared with other bioelectronic components. Current battery-free strategies include wirelessly powered systems[175,176] and self-powered systems[176-178]. Wireless systems (such as passive NFC-based systems) are powered by external transmitters through electromagnetic or acoustic waves[56,175,179] and can deliver energy with higher intensity (for example, <10 mW in electromagnetic and <0.2 mW in acoustic waves) than self-powered systems[176]. However, the impact of irradiated waves on biological tissue (such as elevated temperature) limits the maximum power[175,176], and the need for external transmitters limits their applications outside hospitals during daily activities. Alternatively, self-powered systems can scavenge energy from the external environment (such as sunlight, electromagnetic waves, temperature, metabolites, mechanical motion). For example, a self-powered sensor used power generated from electrochemical oxidation reactions in sweat metabolites (such as, lactate)[180,181]. Other self-powered systems include piezoelectric nanogenerators, triboelectric nanogenerators, photovoltaics and thermoelectric generator (**Figure 4**, **top right**)[177]. However, low power capacity (for example, <0.5 mW from triboelectric nanogenerators and ~1 μW in biofuels) limits their application in physiological recording and stimulation (~10 μW per channel for electrical recording and ~10 mW for optical recording)[176].

[H2] Stretchable displays

Soft and stretchable displays can provide real-time information to users[182,183]. For example, all-polymer light-emitting diodes (APLEDs) have high brightness and minimal changes in brightness under 100 cycles with a strain of 40%[184] (**Figure 4**, **middle right**). Besides intrinsically stretchable materials, soft displays have also been explored using structural design approaches, including nanocomposites (such as quantum dots[185]) and serpentine designs (such as rigid islands[186,187]). However, these displays often suffer from limited device density to achieve the required stiffness and stretchability, therefore leading to limited display resolution. Other concepts have also been proposed, including a pico-projector with interactive elements to be rendered on the skin, whereby an external projector needs to be worn all the time[188] (**Figure 4**, **middle right**) [189,190]. On-skin displays can be used in health monitoring, prosthetics, consumer electronics and virtual reality applications[191,192].

[H2] Interconnects. Many existing soft bioelectronic prototypes rely on flexible or rigid PCBs for reading sensor signals, wirelessly transmitting information and supplying power[193,194]. In these systems, interconnects between soft components and PCBs are often the failure point—modulus mismatch can lead to concentration of stress at interfaces and result in delamination[195]. Moreover, conventional interconnects, such as anisotropic conductive film and silver paste, often exhibit low SNRs and signal artifacts caused by motion[80].

Metal-polymer composites are a widely used strategy for forming interconnects[15,196]. In particular, 'microcracked gold' interconnects (and electrodes) formed by evaporating gold directly onto stretchable polymer substrates through a shadow mask have proved to be a useful strategy owing to high conductivity, elastic stretchability and simplicity in pattering features (~100-micron line width)[15,59,197]. For example, a plug-and-play assembly strategy using interpenetrating metal-polymer nanostructures (formed by the evaporation of ultrathin (~90 nm) gold nanostructures onto the self-adhesive, thermoplastic elastomer, styrene ethylene butylene styrene (SEBS)) enabled laminating stretchable interconnects without the need for adhesive paste[80] (**Figure 4**, **bottom right**). With this approach, an ultrathin layer containing conformable electrodes can be directly laminated to a thick film containing robust interconnects[80]. The interconnects can be laminated to a rigid PCB—the thickness of the interconnect layer increases the film stiffness preventing localized strain at the interface, thus mitigating delamination and motion artifacts[80]. Notably, the conductivity of microcracked Au electrodes (especially with ultrathin layers) often depends on the level of strain (higher strain results in lower conductivity), which might influence the device performance when used as an interconnect in bioelectronic devices.

In addition to solid metal composites, liquid metals, such as eutectic gallium indium (EGaIn), are promising materials for interconnects in stretchable electronics owing to their high stretchability and conductivity[142,198]. However, the resolution of current EGaIn patterning approaches (such as screen printing) is usually >100 microns owing to the feature size limitation of masks and the high surface tension of EGaIn, limiting their translation to high-density and complex circuits. Combining conventional lithography techniques (such as photolithography and electron beam lithography) and adhesion layer such as Au) with soft lithography could overcome these limitations by enabling sub-micron patterning of EGaIn[199]. However, these approaches are not yet widely applied owing to their high cost and limited process compatibility introduced by lithography steps. Moreover, the liquid form of these materials makes them easily smeared, requiring an additional barrier layer for protection.

Liquid metal–elastomer composites have also been developed as stretchable interconnects[200,201]. For example, an acoustic field-assisted method enabled the assembly of stretchable and highly conductive EGaIn micro and nanoparticle networks for elastic printed circuit boards[200]. A key feature of these composites is a near-zero change in resistance at 100% strain (thanks to the size-dependent deformation of the multiscale liquid metal inclusions), which is crucial for stretchable interconnects[200,201].

[H2] Encapsulation. The protection of soft electronic devices from degradation and damage using suitable encapsulation layers is vital for translational applications. Bioelectronic devices with stable and reliable performance in inert environments (such as inside nitrogen glove box) or ambient conditions might not function in biologically relevant environments. For example, wearable devices are designed to work in ambient environments, where oxygen and moisture molecules are present, whereas implantable devices are designed to function in harsher environments where body fluids (such as sweat, blood and cerebrospinal fluid) and tissues are present. Nonetheless, many semiconducting polymers suffer from degradation or instability in these environments caused by moisture and oxygen leading to the formation of traps[202,203]. These traps restrict charge transport and decrease carrier mobilities, therefore decreasing the device performance and reliability. To tackle this challenge, material design strategies have been used to improve the environmental stability of organic materials. For example, OFETs with crosslinked organic semiconductor films have higher stability in ambient environment than neat films[29,204].

However, these molecular design strategies are not universal to all material and device systems, and extra synthesis and fabrication steps are often required. A more feasible approach is to apply an additional layer(s) to encapsulate the entire device. These encapsulation layers must have similar mechanical properties to other parts of the devices to maintain overall device softness and stretchability. For example, PDMS-based elastomers are often used in soft electronic systems for encapsulation[205]. However, elastomers tend to have higher water permeabilities than dense plastic and inorganic materials owing to the free volume present between polymer chains[206]. Among elastomers, butyl rubbers usually have lower water and air permeability than silicone and nitrile rubbers, but their permeabilities are still orders of magnitudes higher than metal and inorganic materials[206]. Therefore, encapsulation layers with both high stretchability and low air and water permeability are needed. One promising direction is to combine elastomers with inorganic and metallic materials to decrease their permeability. For example, stretchable EGaIn-based elastomer encapsulation have low gas permeability, although not optically transparent[207]. In addition to micrometer-scale encapsulants, molecular-level encapsulation approaches can be used; for example, by functionalizing fluorinated molecules onto semiconducting polymer composites presenting vinyl groups, which show improved stability of OFET in highly humid air (85–90% humidity) and artificial sweat environment over a month[204].

Besides protecting bioelectronic devices from environmental effects, these encapsulation layers could also serve as barriers to prevent chemical leakage, contamination and electrical shock risks from human subjects. Moreover, the encapsulation layers are in direct contact with human skin or other tissue and organs, which can trigger foreign body responses. Therefore, systematic biocompatibility and reliability studies should be conducted for encapsulation materials to address safety concerns.

[H1] Outlook

Soft bioelectronic devices with skin-like properties provide exciting opportunities for seamlessly interfacing with the human body. In this Review, we discussed approaches to whole-body soft bioelectronic systems, from fundamental molecular designs of soft electronic materials, device fabrication strategies, to considerations of system-level requirements.

Although there are now have a handful of skin-inspired materials available, the biomedical applications of soft electronic materials are still in the early stages. Matching the physical properties required for different biomedical applications is essential and should be accounted for before device development. For example, bioelectronic devices for skin, brain, heart and nerve have different mechanical properties, such as the maximum strain a device can withstand. Alongside softness and stretchability, which have been extensively demonstrated at the material level, device performance and system stability should also be improved. Current intrinsically stretchable semiconductors are still limited by low charge carrier mobility (~1 $cm^2 V^{-1} s^{-1}$) compared with well-established inorganic materials (such as Si with mobility >100 $cm^2 V^{-1} s^{-1}$). Further development of molecular design strategies (such as semiconducting polymer blends with higher carrier mobilities) are needed to construct high-density, high-performance transistors and integrated circuits. Building next-generation soft circuits also requires processing control and device engineering, such as device configurations with smaller channel lengths, interface engineering between dielectric and semiconductors with less charge traps. Moreover, the processibility of each layer needs to be considered when fabricating multilayer devices (such as transistors and diodes), including patterning resolution, solvent compatibility and alignment accuracy.

Developing manufacturing approaches with high throughput and low cost, preferably leveraging established tools for semiconductor manufacturing processes, is an important step towards translational applications. Moreover, stretchable encapsulation materials with low water and oxygen permeability are essential. It is crucial to develop strategies to address common mechanical failures between soft and rigid interconnects for device assembly and system integration. In the long-term, development of soft systems based entirely on stretchable materials will require further material and device developments.

For clinical applications, the risks associated with materials' biocompatibility and user comfort during extended wear must be addressed[208 209]. For example, continuously wearing skin-mounted sensing devices can cause irritation due to allergic reaction to materials and the accumulation of moisture and perspiration, which can be examined according to the patch test criteria of the International Contact Dermatitis Research Group (ICDRG)[210].

Importantly, the requirements for mitigating hazards and improving device performance can be contradictory. Materials and devices designed to be highly permeable to gas and water vapor can prevent occlusion of perspiration and promote user comfort; however, such designs might render the device more susceptible to degradation—especially if the materials are sensitive to moisture or oxygen, such as organic semiconductors[211]. For example, biodegradable devices are often more sensitive to moisture compared to non-biodegradable ones owing to their swelling and dissolution behavior within a physiological environment, leading to trade-offs in device stability in mid/long-term usage[212,213]. Developing permeable materials with more sophisticated electronic functionality—which are also insensitive to degradation caused oxygen and water vapor—is therefore essential. Developing next generation bioelectronic devices should be tailored to specific applications, where a trade-off between different functionalities and performance can be balanced through rational design.

In summary, the field of soft bioelectronics provides unprecedented opportunities to improve human healthcare. With concerted interdisciplinary efforts from chemical science and engineering, soft bioelectronic networks can be built to interface with humans and provide real-time, body-distributed physiological monitoring.

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Author contributions

C.Z., J.P., S.E.R., and Z.B. co-wrote the manuscript. All authors approved the final version of the manuscript.

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Key points

- Bioelectronic materials and devices with skin-inspired properties, including soft, stretchable, self-healing, biodegradable and permeable, form natural interfaces with the human body.
- Molecular engineering approaches provide flexibility in designing dielectric, conducting and semiconducting polymers with desired mechanical, electrical, chemical and physical properties.
- Skin-like soft bioelectronic devices can be used for on-skin health monitoring and epidermal signal conditioning with high fidelity, reliability and user comfort.
- Tissue-like soft bioelectronic devices interface with organs and tissue seamlessly for signal recording and modulation with minimal tissue damage and immunological response.
- Translational applications of soft bioelectronic devices require system-level consideration, including wireless communication units, power sources, interconnects and encapsulation.

Table 1 Materials for soft bioelectronic devices and systems.

Materials/composite		Mechanical properties: Effective Young's modulus	Electrical properties: Conductivity, impedance[b] / Mobility/Dielectric constant	Examples	Refs
Conductors[a]	Patterned structures	0.1-10 MPa	<4×10^7 S/m, ~2kΩ @1kHz	Serpentine Au, buckled Au on elastomer	15,56,140
	Conducting polymers	0.1 MPa−1 GPa	<6×10^5 S/m, <30kΩ @1kHz	PEDOT:PSS (with additives), polypyrrole	5,24,31,58
	Nanocomposite networks	10 kPa−10 MPa	<2×10^7 S/m, ~50kΩ @1kHz	AuNW/PDMS, AgNW networks	5,214,196,215,216
	Micro-structured thin films	1−100 MPa	<5×10^7 S/m, 600-700kΩ @1kHz	Micro-cracked Au	15,31,59,217
	Liquid metals	1−100 MPa	<5×10^7 S/m	Ga, EGaIn, Galinstan on elastomer	142,200,218,219
Semiconductors	Patterned structures	10−100 GPa	50-100 $cm^2 V^{-1} s^{-1}$	Si nanomembrane, GaAs nanoribbons	220,221
	PSC	0.1−1 GPa	0.5−2 $cm^2 V^{-1} s^{-1}$	IDTBT, DPP-PDCA, DPP-8TVT	22,222-224
	PSC/elastomer blends	0.1−1 GPa	0.25-1.4 $cm^2 V^{-1} s^{-1}$	DPP-TT/SEBS, DPP-TT/BAN2200/PU, P3HT/PDMS	27,29,225-227

	Nanomaterial network	0.1−100 MPa	10−30 $cm^2 V^{-1} s^{-1}$	S-CNT on elastomer	228-231
Dielectrics	Polar elastomers	1−10 MPa	9-27	NBR, PVDF-HFP	87,232,233
	Non-polar elastomers	0.1−10 MPa	2-6	PDMS, PU, SEBS	230,234,235
	Ion gels	1−10 kPa	~7	EMIM-TFSI/PDMS	236,237

(a) Effective elastic modulus and conductivity vary depending on ratios between conducting and matrix/substrate material. Effective elastic modulus is defined as modulus measured with the fabricated devices.

(b) The impedance values vary depending on electrode sizes.

(c) All values are ranges obtained from cited references to show the range obtained in literature.

AuNW, gold nanowires; AgNW, silver nanowires; BA, a precursor consisting of perfluorophenyl azide end-capped polybutadiene; NBR, nitrile butadiene rubber; PSC, polymer semiconductor; PEDOT:PSS, poly(3,4-ethylenedioxythiophene) polystyrene sulfonate; PDMS, polydimethylsiloxane; M-CNT, metallic carbon nanotube; PU, polyurethane; SEBS, styrene-ethylene-butylene-styrene; EGaIn, eutectic gallium-indium; IDTBT, indacenodithiophene-co-benzothiadiazole. DPP, diketopyrrolopyrrole. PDCA, 2,6-pyridine dicarboxamide. TVT, thienylenevinylene. TT, thienothiophene DPP-TT, poly-thieno[3,2-b]thiophene-diketopyrrolopyrrole. P3HT, poly(3hexylthiophene). S-CNT, semiconducting carbon nanotube. PVDF-HFP, poly(vinylidene fluoride-co-hexafluoropropylene). EMIM-TFSI, 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide.

Figure captions

Figure 1 | A whole-body health monitoring system based on soft and stretchable organic electronic materials and devices. Molecular-level materials design enables a variety of skin-inspired properties, such as softness (that is, tissue-like moduli), stretchability, self-healing ability, biodegradability and permeability (left column). These organic materials facilitate the development of a soft bioelectronics system through skin-inspired device, such as stretchable electrodes, transistors and sensors (mid-left column), to interface with different parts of the body (schematics on the right). Soft bioelectronic devices have been applied to monitor multimodal biomarkers from neuronal, muscular and physiological activities. Real-time data can be acquired and wirelessly transferred from wearable and implantable bioelectronics to the cloud (such as mobile devices and healthcare providers) to provide personalized information for early diagnosis or monitoring. **Bottom**:

evolution of integrated standalone soft bioelectronic systems, where a system is defined as a device that can be independently operated, including bulky equipment wired systems, flexible printed circuit board (PCB)-based hybrid systems, strain-engineered soft systems and intrinsically soft systems. HF, high frequency; ECD; electrochromic devices; SWCNT, single walled carbon nanotubes. Part 'Stretchable electrodes' reprinted with permission from ref. 31, AAAS. Part 'Stretchable transistors' adapted from ref. 22, Springer Nature Limited. Part 'Stretchable sensors' adapted with permission from ref. 87, AAAS. Part 'Strain engineered soft systems', image courtesy of Rogers Research Group. Part 'Intrinsically soft systems', reprinted from ref. 166, Springer Nature Limited.

Figure 2 | On-skin soft bioelectronic devices. Applications of soft on-skin bioelectronic devices: **On-skin health monitoring**: soft bioelectronic devices for high-quality monitoring of physical and chemical biomarkers for health monitoring applications through improved skin-device interfaces. **Epidermal signal conditioning**: soft on-skin circuits for high-fidelity signal conditioning to minimize noise level and signal distortion. **Tactile sensation**: skin-like strain, pressure and temperature sensors to perceive the external stimulus for tactile sensation. **Artificial neuromorphic devices**: bio-mimetic artificial nerve systems for neurorehabilitation applications, including synaptic transistors to mimic the information processing in biological neuron networks. **On-skin actuation**: sensory feedback through a soft on-skin actuators, including vibrational, electrotactile and dieletric elastomer-based actuators. ECG, electrocardiogram; EMG, electromyography. Part 'Artificial neuromorphic devices' adapted with permission from ref. 87, AAAS. Part 'On-skin health monitoring' adapted from ref. 77, Springer Nature Limited. Part 'Tactile sensation' adapted with permission from ref. 92, AAAS. Part 'On-skin actuation' reprinted from ref. 13, Springer Nature Limited and adapted with permission from ref. 104, Wiley.

Figure 3 | Implantable soft bioelectronic devices. Examples of implantable soft and tissue-like bioelectronic devices interfacing with the brain, heart and nerves to provide functions such as electrophysiology, biochemistry monitoring, microfluidics for drug delivery, optogenetics, and thermometry. **Top row (brain neural interfaces)**: brain-machine interface to record and modulate brain activities with seamless conformal contact (left, surface devices) and minimal tissue damage (right penetrating devices). Left: A photograph of Au electrodes on ultrathin polyimide substrates (2.5 μm thick) for in vivo brain electrophysiological monitoring. Middle: A photograph of soft and intrinsically stretchable PEDOT:PSS electrode arrays on the brain stem for electrophysiological stimulation. Right: A photograph (left) and X-ray CT of graphene-based stretchable electrodes for neurotransmitter sensing for the brain-gut axis. **Middle row (cardiac monitoring)**: soft bioelectronic for stable electrophysiological monitoring and mapping during cardiac cycles. Left: A photograph of an epicardial mesh wrapped around a rabbit heart, which uses Au-Ag core-sheath nanowire composites embedded in styrene−butadiene−styrene rubber, and the inserted schematic shows the structures of Au shell around Ag nanowires. Middle: A photograph of a high-density, stretchable electrode array based on soft PEDOT:PSS hydrogels on a porcine heart. Right: Photographs of multi-modal serpentine structured electrode arrays, including electrophysiological recording electrodes and stimulators, pH sensors, temperature sensors, strain sensors, light-emitting diodes (LEDs) and heaters. **Bottom row (nervous interface)**: nerve interfacing devices for neural modulation. Left: A photograph of 1.3-μm-thick microcracked Au/PDMS probes wrapped around a rat nerve. Middle: A photograph of conductive viscoplastic polymer-based neural electrodes for long-term neuronal recording in growing tissue environments bottom. Right: Photographs of multimodal and stretchable cuff devices based on serpentine designs, including μ-LEDs for optogenetics and microfluidics for drug delivery. ECG, electrocardiogram; ECoG, electrocorticography; EEG, electroencephalogram; LAD, left anterior descending; LV, left ventricular; PDMS, polydimethylsiloxane; PEDOT:PSS, poly(3,4-ethylenedioxythiophene) polystyrene sulfonate; RV, right ventricular. Part 'Thin metal electrodes' adapted from ref. 115, Springer Nature Limited. Part 'Conducting polymer electrodes' adapted from ref. 116, Springer Nature Limited. Part 'Soft neurotransmitter sensors for brain-gut axis' adapted from ref. 125, Springer Nature Limited. Part 'Au-Ag nanowire composites' adapted from ref. 141, Springer Nature Limited. Part 'Elastic electrode arrays' adapted with permission from ref. 143, Proceedings of the National Academy of Sciences. Part 'Multimodal cardiac monitoring' adapted from ref. 140, Springer Nature Limited. Part 'Microcracked Au/PDMS neural interfaces' adapted from ref. 59, Springer Nature Limited. Part 'Viscoelastic electrodes' adapted from ref. 24, Springer Nature Limited. Part 'Multimodal neural cuffs' adapted with permission from ref. 241, AAAS.

Figure 4 | Strategies for wireless communication and system-level integration in skin-inspired bioelectronic devices. Passive tag systems: soft passive tags used for wireless monitoring of physical biomarkers. On the left, wireless capacitive pressure sensors for post-operative monitoring of blood flow. On the right, soft and stretchable passive wireless tags for multi-modal monitoring including movement, heart rate, temperature, and breathing. **NFC (near-field communication)-based system**: NFC transponder chips used in wireless digital signal transfer. A hybrid form includes soft electrodes with flexible NFC tags, as shown on the left, for wound monitoring applications. On the right, NFC-based stretchable platforms were used for wireless physical biomarker monitoring in pediatrics. **Bluetooth-based system**: high-functional system-on-chip devices with Bluetooth chips included were used for real-time wireless data streaming. A stretchable module for monitoring multimodal physical markers in pediatrics (left) and a three-dimensional stretchable electronic circuit (right) were shown as examples. **Power solutions**: examples of a stretchable battery device and self-powering module based on triboelectric mechanism. **On-skin displays**: examples of intrinsically stretchable organic light-emitting diode (OLED) devices and projection devices for the bidirectional user interface on skin. **Interconnects and encapsulation**: examples of strategies to connect soft sensors with rigid read-out electronics and encapsulation strategies for improved wearability, biosafety, and robust electronic performance. BIND, Berkeley Internet Name Domain; BLE, Bluetooth Low Energy; IC, integrated circuit; FPCB, flexible printed circuit board; NFC, near-field communication; RFID, radiofrequency identification. Part 'Bluetooth-based systems' adapted from ref. 55, Springer Nature Limited. Part 'Stretchable batteries' adapted from ref. 77, Springer Nature Limited. Part 'Self-powered systems' adapted with permission from ref. 181, AAAS. Part 'Stretchable LEDs' adapted from ref. 184, Springer Nature Limited. Part 'On-skin projectors' adapted with permission from ref. 188, Association for Computing Machinery.

BOX 1 FIGURE

Moduli and maximum strain of materials and organs. Top row: moduli of common materials and organs. Bottom row: reported maximum strain of common materials and maximum strain of different organs during daily activities.

PDMS, polydimethylsiloxane. SEBS, styrene-ethylene-butylene-styrene. PU, polyurethane. PI, polyimide. PET, Polyethylene terephthalate.

BOX 1 Properties of skin-inspired bioelectronic materials

Softness: Softness is a relative term describing a material's tendency to deform in response to an applied force. In the context of materials for organic bioelectronic devices, softness typically refers to materials with low elastic moduli (<1-10 MPa). For example, the elastic modulus, also known as Young's modulus (E [Pa]), quantifies the relationship between tensile or compressive stress, σ [Pa] (force per unit area), and axial strain, ε [m/m] (proportional deformation), within the linear elastic regime:

$$E = \frac{\sigma}{\varepsilon} \tag{1}$$

Typically, materials with tensile moduli less than a few MPa are considered soft. For example, silicon has a tensile modulus of ~200 GPa, polydimethylsiloxane (PDMS) and typical thermoplastic elastomers such as poly(styrene-ethylene-butadiene-styrene) (SEBS) have a tensile modulus of ~1 MPa, hydrogels have tensile moduli of ~10 kPa, and tissue has tensile moduli ranging from 1 kPa–30 MPa[11,244,245] (**BOX Figure**).

In addition to the elastic modulus, the bending stiffness quantifies the ability of a structure to resist bending deformation under an applied force. The effective bending stiffness k [N m] depends on both the Young's modulus of a material, E [Pa], and its thickness, t [m], in the case of devices with rectangular cross-section:

$$k \propto Et^3 \quad (2)$$

Histological studies show that devices with a lower bending stiffness induce less of an immune response[115,129]. Because bending stiffness is proportional to the third power of thickness, ultrathin devices provide a low bending stiffness and the ability to conform to curved organs and tissue[115,246]. For example, the effective bending stiffness of ultrathin polyimide devices (<10 μm) are ~10×10^{-8} N·m, which is less than that of thicker elastomers (*e.g.*, ~2×10^{-7} N·m for 100-μm PDMS)[115,151,247].

Stretchable: Stretchability describes a material's ability to be deformed without breaking or losing its structural integrity. Elastically stretchable materials can undergo reversible deformation (that is, they return to their original shape when the external force is removed) without fracture or plastic deformation. This property can be advantageous for bioelectronic devices because many organs and tissue undergo dynamic movement and strain during daily life[1,113,248-250] (**BOX Figure**). For example, human skin undergoes 10-15% strain during running activities, whereas the heart undergoes 20% strain during cardiac cycles. Even in brain tissue, constant micro-motion in the ~10-μm range is produced through respiration and vascular pulsation[251-253]. Therefore, stretchable bioelectronic devices are needed to maintain conformal contact with dynamic movement of tissue for high-quality recording and stimulation.

Self-healing: Self-healing materials, like living tissue, can be repaired from some forms of damage and restore device functionality; these materials are designed to mimic the regenerative abilities found in living organisms (such as the skin). Dynamic bonds comprising reversible inter- and supra-molecular interactions can be incorporated within flexible polymer backbones to design self-healing polymers[254,255]. Incorporation of these materials within bioelectronic devices can extend their lifetime by providing mechanism for damage-repair and provide new forms of dynamic functionality such as the ability to wrap around and grow with living tissue[254,255,256]. Moreover, these thermoplastic elastomers are compatible with scalable and sustainable manufacturing techniques such as melt processing. However, there are trade-offs between self-healing ability and elasticity in these materials—that is, viscoplastic flow is required for self-healing, but can limit the operational and mechanical stability of devices made from self-healing polymers.

Biodegradable: Biodegradability is a loosely defined term which indicates materials or devices that undergo degradation under physiological or natural conditions[90,257-259]. In the context of implantable bioelectronic devices, byproducts after degradation should be biocompatible or of low toxicity to human body and the environment. The term 'biodegradable' is often used interchangeably with 'bioresorbable' in the field of bioelectronics—the latter refers to complete degradation within the human body without leaving any remaining foreign material or producing a persistent inflammatory response[260]. Biodegradable bioelectronic devices are of great interest for implantable applications[90,257-259]. Existing implantable medical devices (such as pacemakers) are most useful for chronic situations in which they can be left in the body permanently (caused by risks associated with subsequent surgical removal)[261]. Biodegradable devices, which do not require surgical removal, can have broader applications, such as in acute conditions (for example, monitoring of postoperative intracranial pressure)[262]. Polymers with cleavable chemical linkages, such as ester and imine chemistry, are biodegradable[257,263]. However, degradability can vary depending on pH and temperature. Fully bioresorbable devices have been reported for in vivo electrophysiological recording and stimulation using materials such as metal (Mg, Fe), semiconductor (Si) and substrate (silk fibroin, polylactic-co-glycolic acid (PLGA))[146,260,264,265].

Permeability: Permeability, or ‘breathability’, describes the ability for gas or vapor to pass through a material and is an important property for wearable and implantable electronics to prevent occlusion of perspiration and promote user comfort. The water vapor transmission rate (WVTR) of bioelectronic devices should be comparable to human skin (WVTR of 22-28 g/m^2/h) to be considered breathable[266-268]. The inherently low water vapor transmission of plastics or elastomers (WVTR of <<5 g/m^2/h) can be increased to match the evaporation rate of moisture from skin in the resting state by introducing micro-scale pores or using ultrathin membranes[266-268]. Moreover, membranes with high electrical conductivity and gas permeability can be designed using ‘nanomesh’ electrodes (that is, random networks of gold nanowires) without substrates, which exhibit high electrical conductivity (~10^{-6} Ω m) and high gas permeability (40 mm/s of air permeability)[269,270] with water vapor transmission rates similar to control experiments with no membrane[269]. Despite these advances, permeable bioelectronic components have been rarely used in electrodes and resistive sensors. Developing permeable materials with more sophisticated electronic functionality—which are also insensitive to degradation due to oxygen and water vapor—is an important research area.

BOX 2 Electronic materials for bioelectronic devices

There are three classes of electronic materials used in skin-inspired bioelectronic devices: conductors, insulators and semiconductors. Although these materials exist as a spectrum when compared in terms of their resistivity, they exhibit distinct functionalities.

Conductors: Conductors are substances that facilitate the flow of electrical current. They can be classified as electronic conductors, which allow the movement of electrons (or holes), and ionic conductors, which enable the migration of ions.

Electronic conductors can be used as interconnects to fixed resistors for electronic circuitry or as variable resistors for transducing physical and chemical signals. Interconnects facilitate the flow of electronic current between distinct circuit components, whereas electrodes establish contact with nonmetallic circuit elements. Biological tissues such as the brain, heart and nervous system can be monitored or stimulated by recording or providing electrical potential and current through electrodes[31,143,271,272]. For both electrodes and interconnects, low values of resistance and minimal change in resistance with applied strain are preferred to minimize signal attenuation and distortion caused by energy dissipation (that is, Ohmic loss).

Ionic conductors, in particular, exhibit frequency-dependent conductivity (that is, impedance) within the frequency window of interest in bioelectronics (<1 MHz), which arises due to the movement of ions within the material[272]. Electrical impedance (Z, [Ω]) refers to an electrical resistance to both alternating current (AC) and direct current (DC), and is defined as a complex number:

$$Z = R + iX \tag{3}$$

where R [Ω] is the resistance and X [Ω] is the reactance, and i is an imaginary number. The reactance, the imaginary part of impedance, is a frequency-dependent response arising from the capacitive behavior of the materials and interfaces. For example, the reactance of an ideal capacitor is inversely related to both capacitance and frequency. For bioelectronic interfaces, the motion of charged ions can be confined by bi-phasic or multi-material interfaces such as solid-solid and liquid-solid interfaces, which leads to complex frequency-dependent behaviors referred to as polarization (for example, electrical double-layer capacitance)[273]. This interfacial behavior between electrodes and tissue is particularly important because a low interfacial capacitance results in a high contact impedance, resulting in limited transfer of electrical energy across liquid-solid interfaces[271,272]. Thus, improved charge injection properties can be achieved by increasing the conductivity of electrodes and the interfacial capacitance.

Organic mixed ionic-electronic conductors (OMIECs), such as the widely used poly(3,4-ethylenedioxythiophene) polystyrene sulfonate (PEDOT:PSS), have emerged as promising candidates for many bioelectronic applications owing to their excellent electrical properties (hole mobilities of 1 to 10 $cm^2\ V^{-1}\ s^{-1}$) and high ionic conductivities ($10^{-2}\ S\ cm^{-1}$)[274-276]. These blends of semiconducting polymers (PEDOT) with ion-conducting polymers (PSS, which also acts as a dopant for PEDOT) convert ionic currents from an external electrolyte to modulations in charge carrier densities of the conjugated polymer. The amount of charge modulation for a given change in potential scales linearly with the volume of these films, giving rise to the volumetric capacitance ($F\ cm^{-3}$), leading to low interfacial impedance at tissue interfaces and high transconductance in organic electrochemical transistors[274,277].

Semiconductors: The most important feature of semiconductors is that their conductivity can be modulated to switch between a resistive and conductive state through the application of an electric field (or through chemical doping). This phenomenon forms the physical basis for the field-effect transistor, a solid-state electrical switch. In synthetic polymers, extended pi-conjugation along the backbone gives rise to semiconducting behavior. These rigid polymers often contain flexible side chains, which makes them processable from solution using various printing and patterning processes to fabricate devices. The electrical performance of these materials, typically quantified by the field-effect mobility μ [$cm^2\ V^{-1}\ s^{-1}$], is defined by the transfer equations for a field-effect transistor operating in the saturation regime:

$$\mu = \frac{2L}{WC_i}\left(\frac{\partial\sqrt{|I_D|}}{\partial V_G}\right)^2, V_D > V_G - V_T \qquad (4)$$

where I_D [A] is the current between source and drain electrodes of a transistor, C_i [$F\ cm^{-2}$] is the capacitance per unit area of the dielectric layer, W [cm] is channel width, L [cm] is channel length. V_T [V] is the threshold voltage, V_G [V] is the gate voltage.

The field-effect mobility of semiconducting polymers is highly dependent on the morphology and packing of these polymers and is generally worse than established silicon semiconductor technology. Nonetheless, moderately complex electronic devices can be configured with these polymers to achieve versatile electronic functionalities, such as signal amplifiers, oscillators, filters or switches by combining diodes and transistors as well as passive components (such as resistors, capacitors, inductors). Moreover, amplifiers and filters can be developed with combinations of diodes and transistors, which have been widely used in skin electronics for bioelectric signal amplification and conditioning[30,84].

Dielectric: Dielectric or insulating materials impede the flow of electrical current. Rather than allowing current to flow, dielectric materials are instead polarized by an applied electrical potential. Dielectric materials are typically used as an electrical insulator to impede dissipation of energy or electrical interference between conductors or from the surrounding environment. Insulators are often used to form a substrate of electronic devices or encapsulation conductors. Encapsulating materials are crucial for soft electronics, especially when these electronics are designed to work in environments with body fluids[278,279]. Typical elastomers (such as PDMS) have relatively high water and air permeability owing to their amorphous morphology (WVTR of ~1 $g/m^2/h$), whereas conventional encapsulation materials (such as SiN_x, SiO_x, Al_xO_y, parylene) with low permeability (WVTR of <1 × 10^{-5} $g/m^2/h$) are rigid[279].

Electrical dipoles induced by or oriented by electric fields in dielectric materials can store electrical potential energy, such as in a parallel plate capacitors. The ability of an insulating material to form electrical dipoles is quantified by the dielectric constant (k):

$$k = \varepsilon/\varepsilon_0 \tag{5}$$

where ε is the permittivity of materials and ε_0 is the permittivity of vacuum (8.854×10^{12} F/m). When used as dielectrics in transistors, insulating materials with high resistivity, dielectric constant and breakdown voltage are generally preferred. Polymer dielectrics with high dielectric constants lead to low-voltage operation of transistors, which are ideal for wearable and implantable applications[280]. The dielectric constants of elastomers (for example, ~2 for PDMS, ~10 for PVDF based dielectric) are normally lower than inorganic dielectrics (such as ~25 for HfOx)[280]. Efforts towards high-*k* polymer dielectrics include molecular modification (such as introducing polar groups) and blending with nanofillers (such as Al_2O_3)[280,281]. However, high-*k* dielectrics often introduce traps at the semiconductor/dielectric interface, leading to electrical hysteresis during device operation; therefore, multilayer strategies with passivated interfaces could be a more suitable alternative[280].

Short summary

Soft bioelectronic devices are made from polymer-based and hybrid electronic materials that form natural interfaces with the human body. In this Review, we present recent developments in soft bioelectronic sensors and actuators and discuss system-level integration for wearable and implantable medical applications.

Fig 1

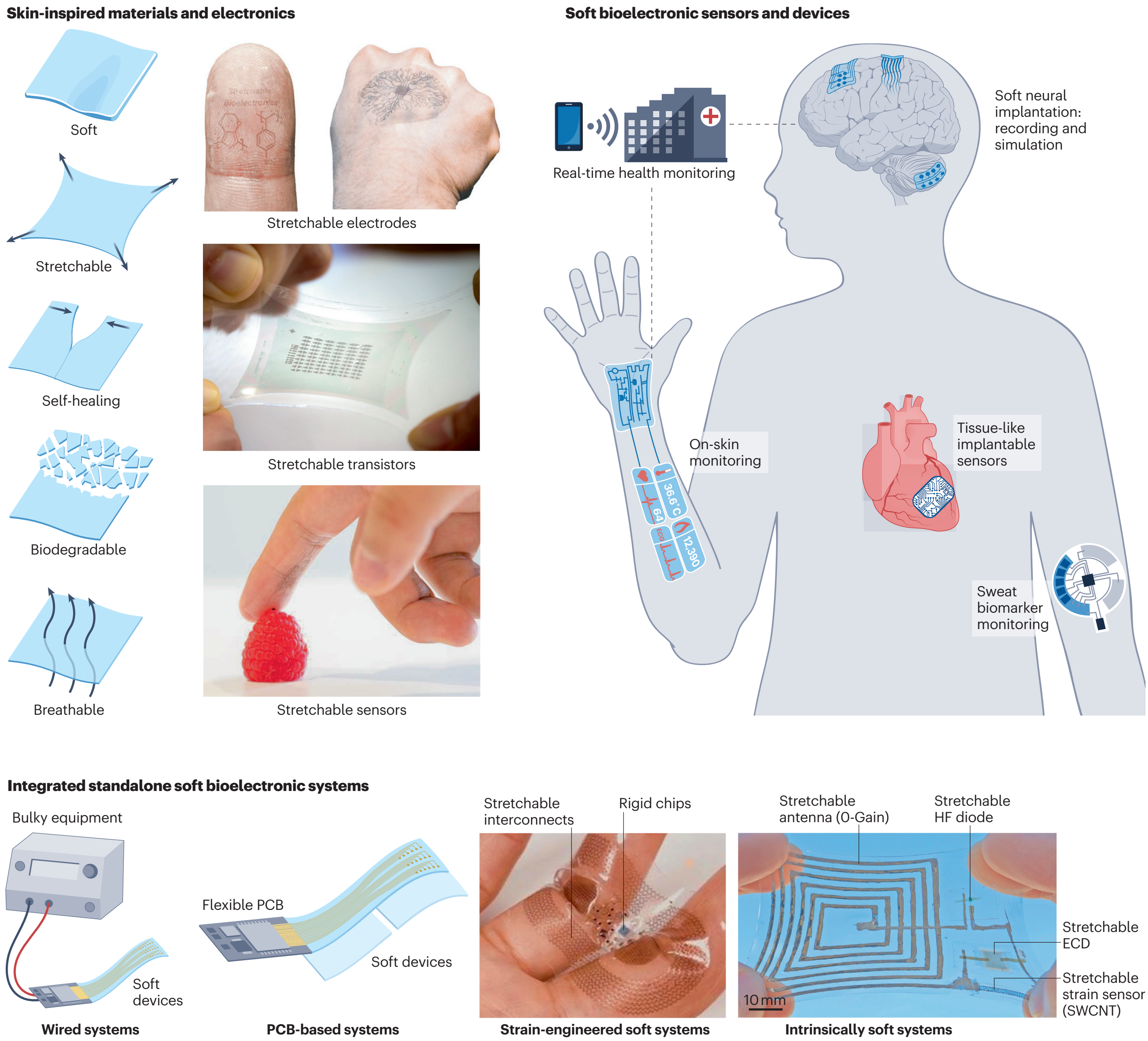

Skin-inspired materials and electronics
Soft
Stretchable
Self-healing
Biodegradable
Breathable
Stretchable electrodes
Stretchable transistors
Stretchable sensors
Soft bioelectronic sensors and devices
Real-time health monitoring
Soft neural implantation: recording and simulation
On-skin monitoring
Tissue-like implantable sensors
Sweat biomarker monitoring
36.6°C
64
12,390
Integrated standalone soft bioelectronic systems
Bulky equipment
Soft devices
Wired systems
Flexible PCB
Soft devices
PCB-based systems
Stretchable interconnects
Rigid chips
Strain-engineered soft systems
Stretchable antenna (O-Gain)
Stretchable HF diode
Stretchable ECD
Stretchable strain sensor (SWCNT)
10 mm
Intrinsically soft systems

Fig 2

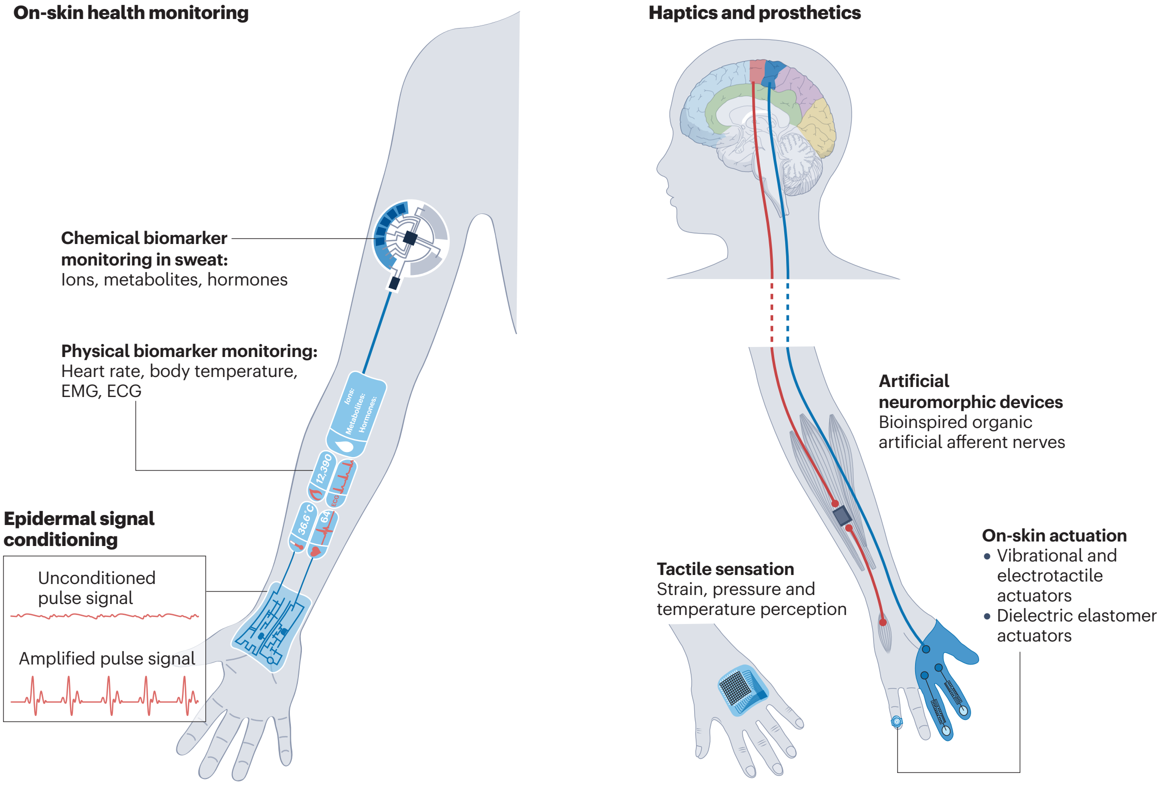

On-skin health monitoring
Chemical biomarker monitoring in sweat:
Ions, metabolites, hormones
Physical biomarker monitoring:
Heart rate, body temperature, EMG, ECG
Epidermal signal conditioning
Unconditioned pulse signal
Amplified pulse signal
Haptics and prosthetics
Artificial neuromorphic devices
Bioinspired organic artificial afferent nerves
On-skin actuation
• Vibrational and electrotactile actuators
• Dielectric elastomer actuators
Tactile sensation
Strain, pressure and temperature perception

Fig 3

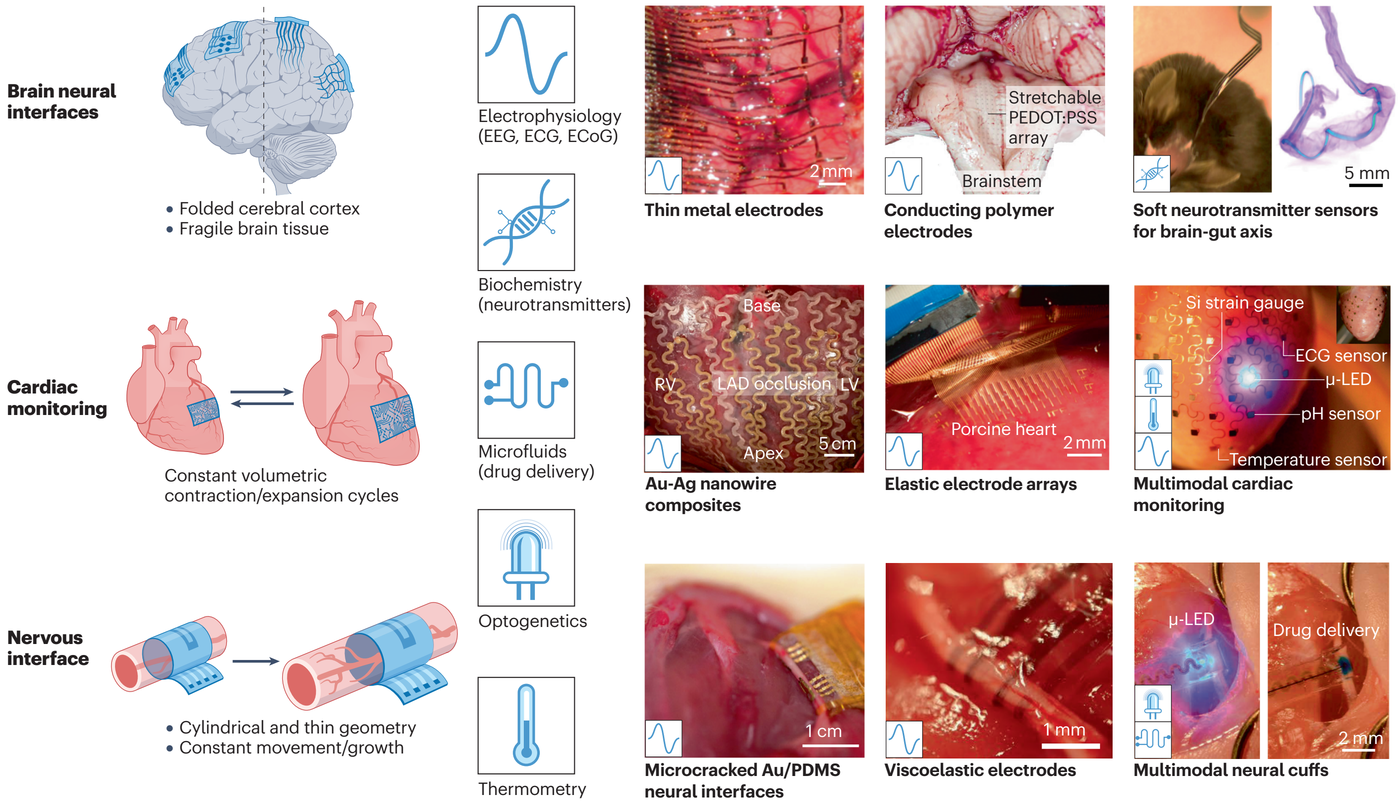

Brain neural interfaces
• Folded cerebral cortex
• Fragile brain tissue
Cardiac monitoring
Constant volumetric contraction/expansion cycles
Nervous interface
• Cylindrical and thin geometry
• Constant movement/growth
Electrophysiology (EEG, ECG, ECoG)
Biochemistry (neurotransmitters)
Microfluids (drug delivery)
Optogenetics
Thermometry
2 mm
Thin metal electrodes
Stretchable PEDOT:PSS array
Brainstem
Conducting polymer electrodes
5 mm
Soft neurotransmitter sensors for brain-gut axis
Base
RV
LAD occlusion
LV
Apex
5 cm
Au-Ag nanowire composites
Porcine heart
2 mm
Elastic electrode arrays
Si strain gauge
ECG sensor
μ-LED
pH sensor
Temperature sensor
Multimodal cardiac monitoring
1 cm
Microcracked Au/PDMS neural interfaces
1 mm
Viscoelastic electrodes
μ-LED
Drug delivery
2 mm
Multimodal neural cuffs

Fig 4

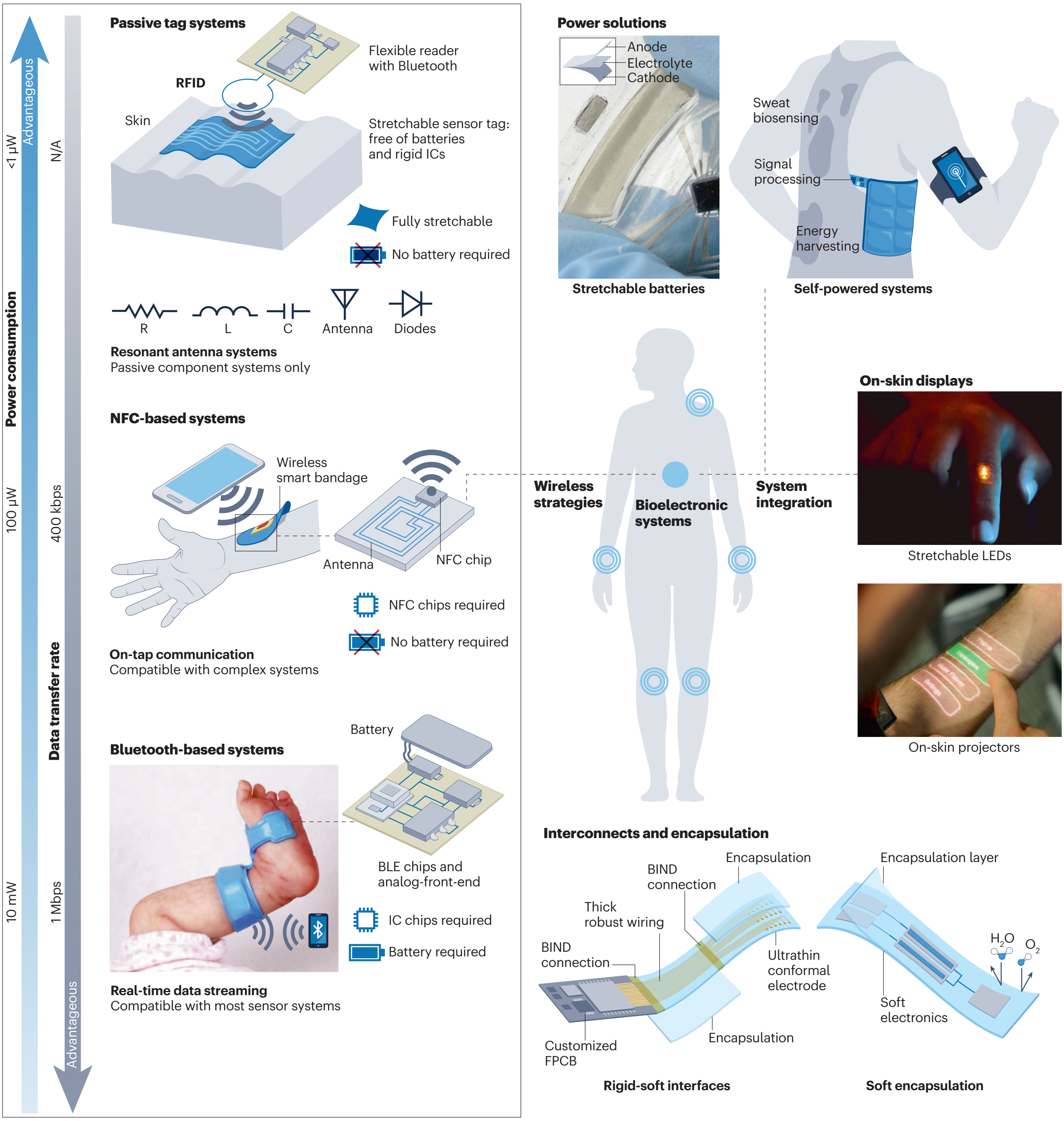
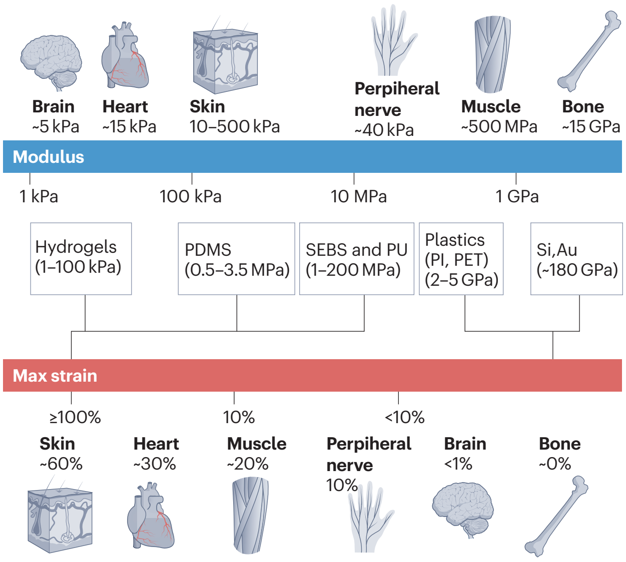

Power consumption
<1 μW
100 μW
10 mW
Advantageous
Data transfer rate
N/A
400 kbps
1 Mbps
Advantageous
Passive tag systems
RFID
Skin
Flexible reader
with Bluetooth
Stretchable sensor tag:
free of batteries
and rigid ICs
Fully stretchable
No battery required
R
L
C
Antenna
Diodes
Resonant antenna systems
Passive component systems only
NFC-based systems
Wireless
smart bandage
Antenna
NFC chip
NFC chips required
No battery required
On-tap communication
Compatible with complex systems
Bluetooth-based systems
Battery
BLE chips and
analog-front-end
IC chips required
Battery required
Real-time data streaming
Compatible with most sensor systems
Power solutions
Anode
Electrolyte
Cathode
Stretchable batteries
Sweat
biosensing
Signal
processing
Energy
harvesting
Self-powered systems
Wireless
strategies
Bioelectronic
systems
System
integration
On-skin displays
Stretchable LEDs
On-skin projectors
Interconnects and encapsulation
BIND
connection
Encapsulation
Thick
robust wiring
BIND
connection
Ultrathin
conformal
electrode
Customized
FPCB
Encapsulation
Rigid-soft interfaces
Encapsulation layer
H_2O
O_2
Soft
electronics
Soft encapsulation

Fig 5


Brain
~5 kPa
Heart
~15 kPa
Skin
10–500 kPa
Perpiheral nerve
~40 kPa
Muscle
~500 MPa
Bone
~15 GPa
Modulus
1 kPa
100 kPa
10 MPa
1 GPa
Hydrogels (1–100 kPa)
PDMS (0.5–3.5 MPa)
SEBS and PU (1–200 MPa)
Plastics (PI, PET) (2–5 GPa)
Si, Au (~180 GPa)
Max strain
≥100%
10%
<10%
Skin
~60%
Heart
~30%
Muscle
~20%
Perpiheral nerve
10%
Brain
<1%
Bone
~0%