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Abstract

Recent technological advances of soft functional materials and their assembly into wearable (i.e., on-skin) biosensors lead to the development of ground-breaking biomedical applications ranging from wearable health monitoring to drug delivery and to human-robot interactions. These wearable biosensors are capable of unobtrusively interfacing with the human skin and enabling long-term reliable monitoring of clinically useful biosignals associated with health and other conditions affecting well-being. Scalable assembly of diverse wearable biosensors has been realized through the elaborate combination of intrinsically stretchable materials including organic polymers or/and low-dimensional inorganic nanomaterials. In this Chapter, we review various types of wearable biosensors within the context of human health monitoring with a focus of their constituent materials, mechanics designs, and large-scale assembly strategies. In addition, we discuss the current challenges and potential future research directions at the end of this chapter.

Keywords: advanced functional materials, wearable biosensors, health monitoring systems, stretchable electronics, sensor technology

1. Introduction

Wearable sensor technology has evolved from traditionally fundamental measurement technology across science, engineering, and industry, and is now increasingly significant as a core method to advance human healthcare. To meet the requirements allowing for preventative health monitoring, diagnosis, and treatment, various types of wearable biosensors have been developed to capture the physical and electrophysiological biosignals (e.g., temperature, heart rate, respiration rate, electrodermal activity, and body motion) or biochemical responses (e.g., biomarkers in biofluids). Many of these wearable biosensors are required to remain in contact with the human skin for a prolonged period throughout the continuous monitoring of the biosignals. In this field, the largest continuing challenge is that rigid or semi-flexible forms of biosensors, particularly when integrated with wireless communication unit, are not compatible with the soft and irregular skin surface [1]. This mechanical mismatch results in discomfort to users as well as considerable noise signals during data collection. Recent advances in soft functional materials and assembly techniques have led to the development of mechanically stretchable and flexible biosensors that can be unobtrusively integrated into the human skin in
a manner that complies with the natural motion of the wearer [2, 3]. The thin and flexible nature of these biosensors allows their conformal, seamless contact to the skin while simultaneously providing (i) excellent breathability and deformability for user comfort and (ii) durability to allow repeated attachment and detachment to the skin without irritating the wearer and damaging the devices. These aspects play a critical role in achieving high-fidelity recording of biosignals during long-term use in many clinical applications [4, 5].

According to the report by Grand View Research, Inc, the global market for wearable (i.e., on-skin) biosensors is anticipated to reach USD 2.86 billion by 2025 [6] at a phenomenal Compound annual growth rate (CAGR) of 38.8% during the forecast period (Figure 1) [6]. The wearable biosensors are a key component of electronic medical platform systems used by consumers as interest in real-time motion detection activity tracking grows. Furthermore, the wearable biosensors are emerging as a promising revolution that captures clinically important parameters form a distance and thereby reduces the patient’s overall hospital cost. The manufacturers have incorporated contextual information and data to determine motion detection activities. Additionally, this analysis provides users with results that can be used to define their health and fitness goals [6]. This rapid interest over this market is likely to drive industry growth over the forecast period into advanced stages. The market of wearable biosensors in the field of health and fitness monitoring and diagnosis is gaining more attention due to their potential number of applications.

The wearable biosensors demand the following requirements. First, they require the ability to interface with the human skin with high compatibility, durability, and abrasion-resistant for the recording of biosignals with high-fidelity. Therefore, the conventionally-used semiconducting materials (e.g., silicon) remain impracticable. Second, they require an accurately operatable sensing system (‘selectivity’) that can differentiate between various environmental stimuli including mechanics, temperature, humidity, and various mechanical components such as atmospheric pressure, lateral deformation, shear, flexion, torsion, and vibration. Lastly, they require an affordable ‘sensitivity’ to detect the tiny biological signals through an appropriate amplification.

In this Book chapter, we overviewed various types of wearable biosensors tailored for the monitoring of mechanical, optical, and biochemical responses for human healthcare. We categorized the wearable biosensors according to their formfactors. In Section 3, we overviewed the functional materials used for these
biosensors, such as carbon-based nanomaterials and inorganic nanostructured materials, that provide tailored mechanical, electrical, or electrochemical properties. We also described the basic sensing mechanisms (e.g., piezoresistive, piezocapacitive, iontronic, and piezoelectric sensing) of the wearable biosensors. In addition, we discussed organic field-effect transistor type of wearable biosensors, which can amplify small biological signals into large-signal information. In Section 4, we described various transduction systems according to their sensing mechanisms (e.g., electromechanical, optoelectrical and chemical sensing). In Section 5, we reviewed recently-reported assembly strategies to construct the wearable biosensors in a cost-effective manner. In Section 6, we discussed about future opportunity to further facilitate the commercialization of these wearable biosensors at a wider scale.

2. Types of wearable biosensors

Several human biosignals and stimuli should be concerned to display user’s health conditions. For example, the assessment of biochemistry in biofluids (e.g., sweat, interstitial fluid, and blood) can provide fruitful information about personal health status and disease progression. In addition, both electrical and non-electrical biosignals such as electrooculography (EOG), mechanomyogram (MMG), electrocardiogram (ECG), electromyogram (EMG), galvanic skin response (GSR), magnetoencephalogram (MEG), and electroencephalogram (EEG) are useful indicators to offer the biosignal and info of a special tissue, organ, brain, or cellular system, such as the nervous system.

In addition to these internal vital signs, the on-skin detection of external harmful stimuli with a biosensor is also a critical issue. When it comes to, the realm of wearable biosensing applications can be extended to motion detection, hazardous gas monitoring, disease diagnosis, and harmful UV-light detection (Figure 2). The sensing mechanisms of these sensors are diverse. In this Section, we will discuss several examples of chemical, optoelectronic and mechanical biosensors.

2.1 Wearable chemical biosensors

Sweat and sebum are representative human skin secretions that originate from the sweat glands in the dermal layer of the epidermis and therefore in-situ detection of these secretions on the skin is critically important for health monitoring. Sweat, a physiological aid for regulating body temperature, is secreted from the external glands. For example, sweat is a particularly useful sensing target due to the ease and presence of biomarkers associated with critical health conditions such as dehydration, physical exhaustion, mental stress and illness [13–15]. Sebum is secreted to lubricate human skin from Sebaceous glands. When sebum spreads up along the hair shaft, it is distributed over the surface of the skin, lubricating, and waterproofing the stratum corneum, the outer layer of the skin. It consists mostly of lipids. Those secretions can reflect the human health condition indirectly. Sebum provides antioxidant and antimicrobial lipids to the skin surface. Thus, proper secretion of sebum on the human skin surface increases the skin permeable barrier function. However, excess sebum frequently results in acne vulgaris. The acidic state of the skin pH is an essential factor in retaining the integrity of the skin-permeable barrier. It is reported that skin pH can be changed in skin diseases such as atopic dermatitis [16].

Wearable chemical biosensors that non-invasively analyze biofluids such as sweat, sebum, saliva, tears, and intermediate fluids provide the potential to...
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dramatically improve health condition evaluations by tracking changes in metabolic processes [17]. The sweat sample collection can be performed using an absorbent pad or a plastic microtube [18]. However, these methods are not compatible with remote monitoring and on-site use because they depend on cumbersome multi-step expensive benchtop hardware for sample preparation procedures and analysis. Recent advances in soft microfluidics, stretchable/flexible chemical sensing technologies form a basis of a new wearable sensor system that overcomes the limitations of this conventional approach [19]. The wearable sweat sensors are promising tools for continuous health and physiological monitoring. Among the various types of sweat sensors, optical detection utilizes photo-transmission techniques such as chromaticity, fluorescence, and light detection to provide an attractive strategy for measuring integrated chemical sensors due to cost efficiency and simplicity. Colorimetric sensors are also widely adopted in wearable sensor platforms, especially in case of the integrated microfluidic systems. Koh et al. demonstrated that a soft, flexible microfluidic platform based on silicon elastomer was recently developed, using colorimetric dyes to detect lactate, chloride, glucose, pH and loss of sweat [7]. The dye was located on top of the filter paper inserted into the micro reservoir. The lactate and glucose measurements were achieved by integrating enzymes into chromaticity-inducing reagents to enable the colorimetric readout sensing.

In terms of the detection of hazardous gases to human, Lee et al. demonstrated a flexible and transparent biosensor on polyethylene terephthalate (PET) that can detect 255 ppb NH₃ using spray-deposited single wall carbon nanotube (SWCNT) with Au nanoparticles in a reproducible manner [20]. The AuNP decoration of transparent SWCNT film through the use of an electron beam (e-beam)
evaporation enhanced the performance of the gas sensor, which exhibited a high uniformity of the sensing behavior. The enhancement of this sensing performance was resulted from the carrier depletion zone control enabled by the combination structure of the AuNPs and the SWCNTs. The proposed sensor had a fast response time regarding NH$_3$ gas but did not fully recover at room temperature.

Lee et al. developed a patch-based, integrated system that combines non-invasive sweat glucose monitoring with microneedle-assisted therapy (Figure 3) [21]. The patch-based wearable/strip type single-use integrated systems include large-area porous metal based electrode, minimized sensor designs for stable sweat detection from small amounts of sweat, design patchable and disposable sensors to achieve practical application, multicycle operation of the sweat measuring control and absorption layer to collect efficiently sweat samples, a porous Au nanostructure film to maximize the surface-to-volume ratio to detect a tiny amount of glucose in sweat. This sweat sensor exhibited high performances in terms of sensitivity, multimodal sensing, and accuracy.

Figure 3.
(A) Optical camera image (top; dotted line, edges of the patch) and schematic (bottom) of the wearable sweat monitoring patch. A porous sweat-uptake layer is placed on a Nafion layer and sensors. (B) Optical camera image (top) and schematic (bottom) of the disposable sweat monitoring strip. (C) Optical camera image (top; dotted line, edges of the patch) and schematic (bottom) of the transdermal drug delivery device. Replacement-type microneedles are assembled on a three-channel thermal actuator. Adapted from Ref. [21].
2.2 Wearable optoelectronic sensors

Photodetector is a key device attached to the front end of the optical receiver that converts input optical signals into output electrical signals [22]. Especially in medical applications, optoelectronic devices are very useful as they are able to detect biometric signals and other clinical information non-invasively. Organic optoelectronic devices including organic light emitting diodes (OLEDs), organic photodetectors (OPDs), and organic phototransistors are in the spotlight in the area of medical devices as they provide a wide absorption spectrum and high photogeneration yield with easy-to-fabricate, lightweight, and flexible features [23].

Recently, OLEDs [24–30], polymer light-emitting diodes (PLEDs) [31–34], and OPDs [35–38] were fabricated on glass or plastic substrates, implementing a muscle contraction detector and transmission mode pulse oximeter. Moreover, OLEDs and organic photovoltaics were manufactured on 1-μm-thick ultra-thin films but were operated in N₂ box atmosphere [39, 40]. Realizing ultra-flexible optical sensor with an extended stability of surrounding conditions, allowing the sensors to integrate intimately and unnoticed on the skin, and to enable the application’s cornucopia [10].

A representative non-invasive measurement system using pulsed oximetry characterizes peripheral oxygen saturation evaluated by oxyhemoglobin in the blood is shown in Figure 4 [10]. An organic pulse oximeter with polymer LEDs and Si-based photodetectors were implemented based on pulse sensing and display on the human skin. The reflective pulse oxygen system used green and red LEDs to generate two wavelengths through fingers, and a light detector later measured the change in absorbance on the same side of the LED to determine peripheral oxygenation [10].

Choi et al. demonstrated an array of ultra-high-density curved MoS₂-graphene light detectors using a single lens optical unit [9]. The high-density MoS₂-graphene curved structure of the photodetector array was fabricated using an ultra-thin, soft material and strain-isolating/-releasing device architectures. The photodetector array and ultrathin neural-interfacing electrodes were embedded onto the soft flexible printed circuit board, accomplishing a human eye-inspired soft implantable optoelectronic device. The proposed device offered minimal mechanical deformation to the eye model, which were demonstrated by both experiments and finite element analysis (FEA) simulations. The wearable photodetector array and ultrathin neurointerference system reduced mechanical distortion of the retina and effectively stimulated the retinal nerve responded by optical input signals.

Ng et al. developed organic bulk heterojunction photodetectors having dark current as low as <1 nA cm⁻² and efficient charge collection behavior. The development of a 4 μm-thick sensor layer using amorphous silicon TFTs provided a highly flexible image sensor operation with excellent performance as high as > 35% external quantum efficiency and noise equivalent power of 30 pW cm⁻² at the applied reverse bias voltage of −4 V [41].

Figure 4. Ultraflexible organic pulse oximeter. (A) Device structure of the pulse oximeter. (B) Operation principle of the reflective pulse oximeter. Adapted from Ref. [10].
2.3 Wearable electromechanical sensors

Various types of wearable electromechanical sensors have been developed by exploiting different sensing mechanisms such as piezoresistive, piezoelectric, capacitive and iontronic methods (Figure 5) [5, 42].

One of the simplest electronic devices is a piezoresistive, where a variation in resistance is recorded when the resistor is in contact with the human skin. In this piezoresistive mechanism, not only the value of the resistance but also several other parameters are assessed, including response time, recovery time and sensitivity. Since the resistors can be easily manufactured and characterized, they represent the most-widely-studied-device-structure for application detection, including flexible and wearable sensors [43].

Wearable capacitive sensors measure the change in the capacitance of a capacitor. The fabrication of these capacitive sensors is relatively simple (consecutive vertical stacking of metal/insulator/metal) and can detect various forms of mechanical force, such as strain, pressure, and touch.

Piezoelectricity defines as the accumulation of electrical changes in piezoelectric materials under mechanical stress. The piezoelectric-based sensors measure voltage change when electrical polarization induced by strain or pressure is generated.

Iontronic sensors are to form ionic-electronic interface at the nanoscale distance between the electrode and the electrolyte. When voltage is applied at each positive and negative electrodes, the corresponding counter ions accumulate at the interface of electrodes, resulting in an ultrahigh capacitance per unit-area. The capacitance of these iontronic sensors is at least 1000 times larger than that of metal oxide-based parallel plate capacitors. Thus, iontronic capacitance-type sensors are on spotlight suitable for wearable electromechanical sensors due to its intrinsic high value of capacitance. The detailed working principle will discuss at Section 4 in detail.

Park et al. reported an array of ultra-thin consistent tactile detectors based on MoS$_2$ film of 2.2 cm × 2.2 cm. The integrated sensor with a graphene electrode provided excellent mechanically flexible endurance and optical transmittance in the visible light wavelength range. The proposed sensor device exhibited high sensitivity, good uniformity, and linearity with an excellent endurance of 10,000 cycles. The ultrathin tactile sensor was made on a plastic substrate, providing high stability of its operation performance even on various substrates including leather and a fingertip [11].

Investigations into the body-sensory system and tactile perception of human skin significantly enhanced the operation performance of rubber-based medical

![Figure 5.](http://dx.doi.org/10.5772/intechopen.94451)

An illustrative diagram demonstrating different types of mechanical sensing methods.
sensors and synthetic electronic skins [44–46]. Chun et al. demonstrated sensing device emulating hairy skin for multimodal detection. The thermal spray coating of graphene nanoplatelets (GNPs) enabled to fabricate the array of sensors and electrodes onto a flexible substrate. The percolation network array structure of GNP (5 × 5 cm², 16 pixels) was successfully able to detect the spatially applied pressures as well as locally varied temperature distribution, evaluating the human skin behavior. The microhairs in electronic devices were able to offer a mapping of electrical signals enabled by contactless air currents to identify the direction, angle of incidence, and intensity of the applied wind [12].

3. Materials used in wearable sensors

Due to the boost in the area of flexible and stretchable electronic materials, various wearable sensor devices have been demonstrated [47]. In order to integrate the wearable sensor with the human body, the mechanical properties of the sensor must be delicate and elastic, and it must be placed on the surface of human skin. Ordinarily, Silicon is the basic material of semiconductor hardware, but its modulus is about 10,000 times higher than that of human skin. Given the huge mechanical inconsistency, the most intuitive approach is to develop electronic materials (Figure 6) that are inherently soft to achieve mechanical compatibility and thus implement unrecognizable biosensors. Several review articles on material synthesis, structural engineering, and platform design were published [47–52].

3.1 Carbon-based nanomaterials

The carbon-based nanomaterials (CNM) discussed in this Chapter are materials with honeycomb lattice structures such as carbon nanotubes (CNTs), graphene

![Figure 6. Typical soft electronic materials for wearable sensors. (A) Carbon-based materials. Adapted from Ref. [53]. (B) Inorganic structured materials. Adapted from Ref. [54]. (C) Polymer conductors and semiconductors. (D) Elastomers.](image-url)
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(containing graphene oxide (GO) and reduced graphene oxide (rGO)), etc [55]. CNMs contain superior properties such as good electrical conductivity, excellent mechanical properties, high chemical and thermal stability, low toxicity. These excellent properties of CNMs have drawn great attention in wearable electronics [56, 57].

Cohen et al. demonstrated a high elasticity strain gauge using the capacitive detection of carbon nanotubes-based parallel electrodes separated by dielectric elastomer as shown in Figure 7A [58]. The device relies on the Poisson effect, so that the uniaxial strain creates a scaled strain so that the two transmissive electrodes come closer together. Even in the 3000-cycle test with 3% strain, the sensor’s capacitance did not decrease.

Crumpled/wrinkled skin-like sensor using graphene for noninvasive and real-time pulsed sensing operation was demonstrated by Yang et al. (Figure 7B) [59]. The modification of PDMS (Polydimethyloxane) substrate stiffness achieves the optimal balance between acceptable linearity and high sensitivity, further realizing beat-to-beat radial pulse measurements for people of various ages and before and after motion.

A strain sensor device using a fish-scale-like graphene layer embedded on an elastic tape was accomplished by Liu et al. as shown in Figure 7C [60]. This configuration enabled graphene to form adjacent overlapping layers, realizing overlapping areas through reversible slip and consequently change contact resistance. Due to the fish-scale-like structure, this strain sensor was able to detect both stretching and bending deformation, as well as high performances including high sensitivity, low detection limit, wide range of deformation, excellent reliability and stability were achieved. This strain sensor can be manufactured by stretching/exhausting the composite film of rGO and elastic tape, so the process is simple, inexpensive, and has excellent energy saving and scalability.

By using dry spinning, Ryu et al. reported that they developed a strain sensor with an extremely elastic behavior based on highly oriented CNT fibers as shown in Figure 7D [61]. As The device was made of a flexible substrate, capable of measuring more than 900% strains with superior sensitivity and exhibited rapid response and good durability. Such sensors should be used extensively in applications involving large variants, including soft robotics. These devices can be adapted for normal strain gauge applications.

Figure 7. Wearable biosensors based on carbon nanomaterials. (A) Design of a Poisson Capacitor. Adapted from Ref. [58] (From left to right) Schematic of our device geometry. SEM data demonstrating percolation of the CNTs within the electrode; scale bar is 500 nm. Close-up image of the sensing region of the device. (B) Schematic illustration of the pulse sensor. Adapted from Ref. [59]. (C) Fish-scale-like graphene-based (FSG) strain sensors. (From left to right) Photograph. Top view and cross-section view of SEM images. Adapted from Ref. [60]. (D) Schematic showing the morphology of a CNT fiber under strain; scale bar is 0.75 cm. Adapted from Ref. [61].
3.2 Inorganic nanostructured materials

Conventional silicon-based semiconductor devices are essential elements for real-time data processing and data transmission, but these silicon-based semiconductor devices are mostly composed on rigid chips. To solve this problem, the electronic component can be bonded on a rigid chip through micro- or macroscopic structural changes of materials, then, a wearable device can be manufactured through this approach [62].

Kaltenbrunner et al. developed a sensing system that enables to electronics of virtually unbreakable and imperceptible behaviors with ultrathin materials [63]. A sensing device of 2 mm thick layer was very light, reducing electronic waste, and this device was able to be applied to curves and dynamic surfaces (i.e., plastic wrap) (Figure 8A). Organic TFTs using ultra-high-density oxide gate dielectrics several nanometers thick at room temperature enable sophisticated large-area electronic foils with unprecedented mechanical and environmental stability. It can be crumpled like paper, with a radius of less than 5mm, which is repeatedly bent, providing an elongation rate of up to 230% in a pre-modified elastomer.

Silver nanoparticles from ultra-thin silver powder can be applied to the electronics sector due to their high conductivity [54]. Typically, the diameter of Ag nanoparticles is of hundreds of nanometers, but the shape of those particles is uneven [64–67].

On the other hand, silver nanowires (Ag NWs) are widely investigated over a long time due to their versatile electrical, chemical, and biological properties. Peng et al. demonstrated a triboelectric nanogenerator (TENG)-based e-skin which is highly conformal and stretchable, enough to attach on human skin. They have used nanofiber for breathability, biodegradability, sensitivity and Ag NWs for antibacterial activity [68]. The developed devices have been designed for the detection of physiological characteristics and movement states of the whole body (Figure 8B). A 3D nano-porous structure was formed by combining PLGA Tribune layer and PVA substrate and nanofiber.

3.3 Polymer conductors and semiconductors

Polymer conductor and semiconductor are crucial materials for the fabrication of wearable sensors due to their low-cost, solution-processability and easy-chemical modification. Intrinsically flexible electronic materials are building blocks of

![Figure 8](image.png)

(A) Illustration of a thin large-area active-matrix sensor with 12 x 12 tactile pixels. Adapted from Ref. [63].
(B) Schematic illustration of the three-dimensional network structure of the all-nanofiber TENG-based e-skin. The images of the water contact angle and molecular structure of PLGA and PVA are inserted on the top left and lower left, respectively. The surface SEM image of the Ag NW electrode is inserted on the lower right (scale bar, 2 μm). Adapted from Ref. [68].
wearable sensors which enable scalable and low-cost manufacturing, high-density device integration and large strain tolerance [69, 70].

Kim et al. reported that highly stretchable sensors and transistors that consist of intrinsically stretchable composite semiconductors and conductors [71] as shown in Figure 9A. They consist of three main materials: (1) Stretchable semiconductor: P3HT nanofibrils (P3HT-NF)-filled PDMS, (2) Stretchable conductor: PDMS filled with AuNP-AgNW, (3) Stretchable gate dielectric: ions gel. (DoS) electronics are demonstrated (Figure 9B), which is deformable, conformal, customizable robust against the human motion. After drawing the electronic ink on desired surfaces, dried ink is strongly attached onto the surface that allows ultra-conformality [72]. Drawn-on-Skin (DoS) electronics were combined with simple fabrication avoiding from dedicated equipment. In addition, these devices can be stacked onto another electronic composite layer on diverse surfaces. Ink, pen, and stencil act as a tool kit for making a variety of DoS electronics that can be mechanically modified and customized to curved textured skins.

3.4 Elastomer

What is another important material in wearable sensor are elastomers which are polymers with viscoelasticity (i.e., both viscosity and elasticity). Elastomers have weak intermolecular forces, generally low Young’s modulus and high failure strain compared with other materials. Main strategy to construct a conductive elastomer is to combine elastomers and metallic nanomaterials for stretchability and conductivity. By optimizing the material design, elastomer-to-metallic nanomaterial composition ratio and fabrication processes of the metallic nanocomposites, stretchable conductors with exceptionally conductive and stretchable properties can be realized [73].

Maintaining electrical conductivity of the stretchable conductor during certain strain or tension is a critical parameter in the application of the wearable device. Usually, the electrical pathway in the composite materials should be formed in the composite. Various techniques, such as structural optimization of the nanomaterial, welding between the metallic nanomaterials (Figure 10A) [74], and additives [75], have been adopted In order to enhance the conductivity, (Figure 10B).

As the thickness decreases, the bending stiffness decreases at a rate of 3 times faster when the thickness of the elastomer is reduced to obtain a highly flexible wearable device. Elasticity can be obtained through various strategies for example fractal interconnect design, free deformation wavy configuration, bridge structure and serpentine structure [50, 76–84].

Figure 9.
(A) Schematic illustrations of a sensor (left) and a TFT (right), consisting of AuNP-AgNW conductors, P3HTNF/PDMS semiconductor composite, and ion gel dielectric vertically stacked on a PDMS substrate. Adapted from Ref. [71]. (B) Schematic of the DoS transistor based on the Ag-PEDOT:PSS ink as the conductor, P3HT-NF ink as the semiconductor, and ionic gel ink as the dielectric. Adapted from Ref. [72].
The representative elastomers for the stretchability of wearable sensors are poly(styrene-butadiene-styrene) (SBS), polyurethane, polydimethylsiloxane (PDMS) and hydrogel polymer materials. Those elastomers are usually used as substrates or a matrix while embedding nanoparticles, nanowires, nanosheets in wearable electronics. Liquid conductors such as gallium metal alloys are less reactive and non-toxic, thus, they are utilized in microfluidic channels of wearable sensors [52, 85]. Hydrogel and polymer have high biocompatibility but relatively low conductivity, limiting performance, and many hydrogels suffer from stiffness over time due to drying. Conventional biocompatible materials usually combine hydrogel and polymer with nanomaterials and were constructed as composite materials to enhance performance and stability. When using nanomaterials such as CNT, care should be taken by encapsulating inside the elastic system to prevent potential health problems [86, 87]. Advances of biocompatible materials was required to improve breathability and stability for pragmatic use [62].

Especially, hydrogel is a 3D structure of hydrophilic polymers, which has been widely applied as a biomaterial due to their biocompatibility with human skin surface. Conductive hydrogel can be synthesized by combining hydrogel polymer with nanostructured metal or conductive polymer (Figure 11A) [88]. The synthesis of hydrogel involves physical and chemical crosslinking at a molecular level. Two type of cross-linked hydrogel, physically or chemically cross-linked hydrogels can be considered. Physically cross-linked one usually has self-healing properties but poor mechanical properties (Figure 11B) [89]. Chemically cross-linked one has high mechanical properties that withstands physical deformation but no mechanical self-healing properties [90]. Several recent approaches of structure fabrication include a dual network and sliding cross-link, which adjusts the Young’s moduli from kilopascals to megapascals [91–93]. However, hydrogels suffer from dehydration and debonding. Encapsulation using elastomers on the hydrogels or the surface modification using supramolecules can be applied to avoid the dehydration and debonding [94].

Reliable signal acquisition from biophysical activity is paramount in the assessment of wearable sensors. Continuous physical movement of human body and dynamic skin surface condition facilitate detachment of wearable sensors during the signal acquisition. Thus, facile chemical and physical approaches have been adapted to achieve for the robust attachment of wearable sensor on arbitrary human skin surface under investigation. Yuk et al. investigated a simple yet effective strategy of inserting a cross-linked hydrophilic polymer (hydrogel skin) into various polymer

![Figure 10](image-url)
surfaces, including silicon rubber, polyurethane, PVC, nitrile rubber and natural rubber, to facilitate the robust attachment of hydrogel and device interfaces. Due to the unique combination of soluble initiators absorbed on the polymer surface and hydrogel pregel initiators dissolved in hydrogel solutions, hydrogel skin is placed on the surface and adapted to the complex and fine geometry of the polymer substrate [95]. Hydrogel skins provided tissue-like softness with excellent mechanical rigidity, low friction, anti-easing performance and ion conductivity.

Yuk et al. also reported fabrication of bio-compatible dry double-sided tape (DST). The bio-compatible DST consists of biopolymer and crosslinked poly(acrylic acid) [96]. The authors attached an elastic strain sensor to a beating porcine heart to evaluate thermal motion that can serve as a versatile platform for wearables and implantable devices. In addition, they demonstrated possible applications using ex vivo models and the combination of DST and biosensors. This DST offered advantages over conventional tissue adhesives and sealants, such as fast adhesive formation, strong adhesion performance, flexibility, storage, and ease of use.

4. A variety of transduction systems for Wearable biosensors

To obtain physiological information or signals from the human body using skin-mounted bio-sensors, they are mainly composed of stretchable or flexible materials. Generally, flexible substrates, electrodes, and sensing materials are three essential parts of skin-mounted biosensors. More importantly, appropriate device systems,
architectures, and sensing mechanisms should be combined with relevant electronic materials. In this Section, we mainly review widely used sensing mechanisms and architectures. [43, 97].

4.1 Piezoresistive type

Piezoresistive sensors operate as a mechanism of a pressure input into a resistance change output (Figure 5A). The active material is inserted between two electrodes in this resistive-type sensor. The active materials provide both sufficient charge transport ability for electrical current flow as well as good elasticity to offer various mechanical deformation during operation.

4.2 Piezocapacitive type

Piezocapacitive sensors can be obtained by a mechanism of a change in in the capacitance of a parallel plate capacitor as a function of the applied pressure stress (Figure 5B). Piezocapacitive sensors include three main components: electrode, substrate, and active material sandwiched by two electrodes. As a variation of the external pressure input, the capacitance varies, providing a detection of the target pressure sensing.

4.3 Piezoelectric type

Piezoelectricity defines as the phenomenon that occurs when positive and negative charges are localized when mechanical stress is applied, or vice versa (Figure 5C). The piezoelectric sensors are desirable for measuring the dynamic variation of the pressure or force. The output voltage produced by the sensor is impulsive and does not apply to static sensing.

4.4 Iontronic type

Supercapacitive iontronic pressure sensors convert the pressure input into the output of constant-capacity change. This type of pressure sensor enhances the compression effect by utilizing the formation of an electron double layer (EDL) at the dielectric layer and contact electrode. In other words, ionic gel with numerous positive and negative ions are spatially trapped between the two electrodes. The positive and negative ions are attracted to the negative and positive respectively, forming two EDLs as an increase of the applied voltage. The operating mechanism of this type of sensor depends on changes in the area between the electrode and the active material, as shown in Figure 5D. Increasing the contact area under certain pressure, positive or negative ions are induced, resulting in increased capacitance values [98].

4.5 Organic field-effect transistor type

Organic TFT-based sensors offer biosignals-sensing operation such as cell activity. In general, two major categories of organic TFTs are used for bio-sensing applications. Electrochemical doping and de-doping are the main reactions in an organic electrochemical transistor (OECT) to modulate ionic species to the active channel materials. Meanwhile, the capacitive field effect is the main reaction of electrolyte gate organic field effect transistor (EGOFET) at the interface of organic semiconductor and electrolyte [99].
Gualandi et al. reported a fully textile, wearable biosensor based on an OECT (Figure 12) using PEDOT: PSS conducting polymer. The fabricated OECT sensors can detect three biomolecules (ascorbic acid, adrenaline, and dopamine) by the reduction-oxidation reaction. Their performance is similar to normal OECTs. These results demonstrate that OECT can be established on a 3D-networked fiber substrate [100].

4.6 Photosensing type

Near-infrared (IR)-response organic light detector (OPD) has been investigated due to its potential applications of health monitoring, remote control, artificial vision, optical communication, and night vision. Especially, the short exposure of near-IR on human skin is not toxic and near-IR can propagate under tissue at ranges of 4 mm. Thus, near-IR is proper for skin-mountable health monitoring devices [101]. Furthermore, narrowband detection of near IR light between $\approx700$ and $1300$ nm is highly desirable for biomedical sensing. Park et al. demonstrated high-performance skin-mountable near-IR OPDs which are mechanically conformable for the application of health care electronics [101]. The OPD (thinner than $3\ \mu m$) exhibits stable operation under conditions of mechanical deformation ($10^3$ times bending). Thanks to its balanced properties of high responsivity and stable mechanical conformability, the IR sensor device showed superior sensitivity in the near-IR region when it is under operation in a skin-conformal photoplethysmogram sensor compared to that of an existing rigid substrate device of the glass.

4.7 Chemical sensing type

The biochemical signal of the human body significantly varies depending on the health condition of the subject. Biomarker concentrations range from complex patterns and other time scales, i.e., time-to-time fluctuations in metabolites, hormonal and inflammatory changes, from neuron synapses to millisecond spikes in ions and neurotransmitters.

Over the years, continuous wearable technology for non-invasive monitoring has been developed. Imani et al. developed wearable devices that could measure chemical and electrophysiological signals simultaneously in the single patch. The hybrid wearable, called Chem-Phys patch, consists of three-electrode ammeter lactate biosensors and two ECG electrodes printed on the screen, enabling simultaneous real-time measurements of lactate and ECG as shown in Figure 13 [102].

Nightingale et al. demonstrated a fully integrated wearable microfluid sensor, which not only provides accurate, precise, and powerful fluid sampling and control but also provides on-site chemical tests that use water droplets as microreactors [103].

Figure 12.
OECT working principle. Scheme of an OECT (A) operating in conditions of low (B) and high (C) conductivity of the channel. Adapted from Ref. [100].
5. Device fabrication and assembly strategies

As device-manufacturing technology is actively being developed, skin-mounted biosensors have attracted scientific and industrial attention to everyday applications such as e-skin, health testing, underwater sensing, and interaction between people and machines [104]. In this subsection, we review the novel fabrication strategies for wearable sensors.

Skin-mounted electronic devices should be established on flexible substrates with reasonable fabrication costs. In particular, the ability to realize flexible or wearable thin film-based sensors provides much freedom for target substrates. One of the most promising and powerful candidates to produce low-cost skin-mounted bio-sensors is ink-jet printing, and due to its ultra-low-cost, non-vibration, and environmentally friendly fairness, it is an appropriate strategy to implement commercial thin-film devices and systems [105]. Ink-jet printing originated from the graphic art industry for mass production of standard products including fabrics and papers. In addition, advanced printing machines and inks solutions can produce on large-area products with low-cost and high-printing-speeds on the order of 10 m s\(^{-1}\).

Holbery et al. demonstrated a demand (DOD) inkjet printing technique to fabricate touch sensors on polyethylene terephthalate (PET) substrates. The commercially available Poly(3,4-ethylenedioxythiophene): poly(styrenesulfonate) (PEDOT: PSS) solution and thermally curable methylsiloxane serves as transparent electrodes and dielectric, respectively. The resistance and transparency of PEDOT: PSS electrode gradually decreases from 20.8 to 6.9 k\(\Omega\) and from 85 to 75%, respectively [106].

Inkjet printing supplies pressure pulses to the fluid-filled chamber, depleting ink drops on demand and triggering pulses through heat evaporation, sound perturbation, or piezoelectric operation. However, inkjet printing using thermal steam, acoustic perturbation, or piezoelectric operation lacks inkjet droplet control function of the inkjet nozzle in a controlled manner, making it challenging to print high resolution [107]. In particular, in electrohydrodynamic (EHD) jet printing, electric fields are applied between deposition nozzles and substrate to induce moving ions of ink to accumulate on the liquid surface. Because of the Coulombic repulsion of ions at the edge of the ink, the hemispherical meniscus turns into a conical shape (Taylor cone). Thus, a smaller diameter of inkjet resolution than that of the nozzle is obtained during EHD jet printing Compared to normal inkjet printing and aerosol printing which has limited resolution (~ tens of micrometer), few hundred resolutions (nearly 700 nm) can be realized using EHD jet printing [108].

Lee et al. reported three different transfer-printing (TP) methods for nanowire (NW) based devices [109]. Fundamentally, NWs on donor substrate is likely to be
transferred onto acceptor substrates which have stronger adhesion force than that of donor substrate (Figure 14). (1) Single transfer printing (STP) enables fabricated NW devices on a Si wafer to be transferred onto a PDMS substrate through a single peel-off step. (2) Double transfer printing (DTP) required a two-times transfer process from NWs and electrodes to fabricate devices. (3) Multiple transfer printing (MTP) includes the transfer of multiple electrodes using thermal release tapes on both flexible and rigid substrates.

Inganäs et al. demonstrated the additive technique for producing all translucent and flexible polymer photodetectors with a wide area. PEDOT: PSS electrodes were printed on a flexible PET film substrate through roll-to-roll (RTR). The printed PEDOT: PSS electrodes were served as both cathode and anode by a coating of Polyethylenimine (PEI) on PEDOT: PSS. After the spin-coating of an active layer on top of PEDOT: PSS and PEDOT: PSS/PEI, the two multi films were laminated through a hot-pressing roller (120°C). The fabricated all-polymeric photodetector also demonstrated mechanical durability [110].

6. Future opportunities

As part of the era of digital health, widespread use and deployment of wearable sensors should overcome specific technical challenges. One such challenge is the

Figure 14.
Various transfer printing technique. (A) STP method on PDMS (Prefabricated NW devices → Deposition of liquid PDMS and curing → Peel off PDMS/NW devices → NW devices embedded inside PDMS). (B) DTP method (NWs on the growth substrate → HF etching to remove the native SiO₂ of NWs → Pressing down a tape to the NWs → Peel off the tape with NW mesh → Pressing down the tape/NW mesh to the prefabricated electrodes → 2nd Peel-off → NW device on the tape). (C) MTP method (1st column: pressing down a thermal release tape to the prefabricated electrodes → Peel off the thermal release tape with electrodes → Pressing down the thermal release tape / electrodes to a target substrate → The thermal release tape is thermally released at 90°C; 2nd column: NWs on the growth substrate → HF etching to remove the native SiO₂ of NWs → Pressing down a tape to the NWs → Peel off the tape with NW mesh → Assembling of the tape/NW and the transferred electrodes). Adapted from Ref. [109].
biological receptor in wearable chemical biosensors. Since the signal transducer material and technologies of wearable chemical biosensors have already been considerably advanced, a major obstacle that hinders the development of the wearable chemical biosensors field may be not a signal transducer material, but a biological material. A diversity of target materials is narrow in current biological receptors and needs to be improved in terms of material stability, selectivity, bonding power, and production cost.

Ideal wearable sensors are physically small and can store important personal health data; therefore, biosensors and personal health data may be lost. The development of more secure and encryption technologies is desired to keep personal privacy and security.

The personal calibration of the wearable sensor is also one of the main challenges. Everybody has different personal health conditions (e.g. diet, family medical history and genetics). Therefore, symptoms of early diagnosis may vary from person-to-person. It is necessary to develop hardware and software that can comprehensively interpret human health through the development of artificial intelligence, as well as calibration of personal health status. Although artificial intelligence's big data could be used to interpret an individual's health, the patient's disease should not be immediately evaluated through other people's precedents using wearable sensors. In addition, since individual's body shape and skin surface condition are all different, research that combines 3D printing technology to create a wearable sensor according to the individual's condition might be an interesting direction for further research.

7. Outlook and conclusions

Wearable sensors and portable point-of-care medical devices are getting intensive attention from academic and industry societies. However, intensive understanding and studies of biosensing mechanisms, transduction mechanisms from biosignal to an electrical signal, and proper device platforms for specified medical purposes are prior to the commercialization of wearable sensors. Although those technical developments have been made for the last decades, social understanding from society and medical approval and its prerequisite is at infancy. Accelerating personalization in one's lifestyle (currently due to Coronavirus Disease-19, COVID-19, and increasing interests in personal health care), point-of-care, and self-medical assessment will get attention more and more.

Recently, enormous development in soft electronic materials and advanced fabrication strategies have rendered to materialize wearable sensors. Wearable sensors can be applied in not only biosensing but also a lot of fields such as medical, industrial process, environmental monitoring, and military. The medical field is currently one of the most in-demand fields. By utilizing free movement of the sensors and their immediate recognition characteristics, it is possible to use drugs and perform rapid treatment for critically ill patients those who have issues in blood sugar, pregnancy hormones, cancer cells, cholesterol, lactic acid, and urea and etc. In addition, wearable sensors could be utilized in environmental monitoring field for the detection of environmental toxic substances in large areas rapidly and efficiently. The pollution in air, water and soil can be minimized for comfortable living environment. For example, the detection of environmental substances such as environmental hormones (dioxin), biological oxygen demand (BOD) of wastewater, heavy metals, and pesticides, can lead to an advanced life quality on human society. In the military, wearable sensors would allow for the detection of various biological sources. These can be used as a weapon that might drive mass destruction...
such as sarin and anthrax, which requires fast analysis time. In addition to that, miniaturized wearable sensor would also allow for a maximized range of motion for direct use.

In summary, it is still unobvious to best match the architectures of wearable sensors to which diagnostic tasks. Moreover, a wearable sensor that is functional in the lab may not be of use in the field or clinic for several reasons. Multidisciplinary research involving life science, engineering, and physics needs to be performed simultaneously to construct more reliable and affordable wearable biosensors.

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Conflict of interest

The authors declare no conflict of interest.

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