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REVIEW

Emerging wearable flexible sensors for sweat analysis

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Abstract
Sweat, as a biofluid with the potential for noninvasive collection, provides profound insights into human health conditions, because it contains various chemicals and information to be utilized for the monitoring of well-being, stress levels, exercise, and nutrition. Recently, wearable sweat sensors have been developed as a promising substitute to conventional laboratory sweat detection methods. Such sensors are promising to realize low-cost, real-time, in situ sweat measurements, and provide great opportunities for health status evaluation analysis based on personalized big data. This review first presents an overview of wearable sweat sensors from the perspective of basic components, including materials and structures for specific sensing applications and modalities. Current strategies and specific methods of the fabrication of wearable power management are also summarized. Finally, current challenges and future directions of wearable sweat sensors are discussed.

Keywords Flexible electronics · Wearable sensors · Sweat sensors · Electrochemical analysis · Noninvasive health monitoring · Power supply

Introduction

Methods of clinical invasive sampling, such as that of blood, lavage fluid, and tissue biopsy testing, are not only limited by relying on professional operators, but also are prone to cause physical pain and present a psychological burden to subjects. Although certain biofluids such as urine [1], saliva [2], tear [3], and interstitial fluid (ISF) [4] can be collected by painless techniques, their practical applications are substantially limited in many aspects. For instance, both urine and saliva collection are featured by inconvenience, hygiene, and privacy issues. Tear collection is hindered by the small collected volume and limited ocular space. In addition, invasive collection methods, such as the microneedle array for ISF collection, are inevitably associated with bacterial infection or inflammation, whereas noninvasive ISF collection methods are mainly performed by reverse iontophoresis or sonophoresis, which tend to cause discomfort and skin irritation to users [5]. In contrast, perspiration, a natural physiological phenomenon controlled by sympathetic nerves, plays an essential role in regulating both the thermal and chemical homeostasis of the milieu intérieur through the excretion of water and various chemical substances [6]. The chemical composition and physical information of sweat are of great value to reflect the human health status. Moreover, direct sweat collection from the skin surface is an easy-to-perform and straightforward method that avoids privacy concerns in physical implementation. These features make sweat have the potential to become a widely accessible sample type that can be monitored in a noninvasive manner.

In the past decade, increasing advances in engineering design, materials science, and fabrication technologies have enabled the rapid development of wearable sensors [7–9], including sweat sensors. Compared with conventional quantitative analysis methods of sweat for clinical purposes that require on-site sweat collection, expensive equipment, and trained professionals [10], wearable sweat sensors can be directly attached onto the skin surface for real-time sweat collection and analysis [11]. A continuous and seamless contact with the freshest sweat on skin allows sensors to monitor the concentration changes of chemical and physical information

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accurately and in real time, i.e., enable in situ sweat analysis. From the aspect of bioinformation density and abundance, traditional assays focus only on sweat composition over a small time period and as such have a relatively inefficient information characteristic that cannot prevail in the current digital era. On the contrary, long-term and real-time sweat monitoring through wearable sweat sensors offers considerable amounts of valuable health data, which is crucial for realizing personalized medicine that attracts great interest [12] and for building a large health database [10]. Furthermore, most wearable sweat sensors can be manufactured cost-effectively and operated conveniently by users with little experience [13]. With the convergence of sweat analysis and wearable technologies, wearable sweat sensors have been receiving tremendous attention by researchers, users, and industry players alike.

This review highlights the significant advances in wearable sweat sensors developed for in situ and real-time monitoring. The paper is organized as follows (see Fig. 1). The basic materials and mechanical structures are firstly introduced. The chemical sensors, including electrochemical, optical, and physical sensors, are then discussed. Subsequently, the fabrication methods for electrodes and microfluidic structures, sweat extraction and collection, and power supplies are briefly presented. Finally, we summarize the existing state-of-the-art approaches and challenges, and propose trends in the development of wearable sweat sensors.

Structural design and materials

The rapidly evolving fields of materials science and engineering design established the foundations for the development of wearable sweat sensors. The continuous collection and monitoring of fresh sweat require wearable sweat sensors to be seamlessly mounted onto the human skin. Thus, comfortability and adaptability are important indicators for a wearable sweat sensor. Although the fabrication of conventional rigid solid-state electronics with stable electrical performance has been well established, some non-negligible drawbacks of such rigid electronics have hindered their application in wearable sweat sensing. Firstly, the rigid materials tend to cause physical irritation when in direct contact with human skin, and they become unsafe when users are doing exercise. Moreover, the non-conformal attachment between rigid electronics and human skin interface makes it difficult to collect fresh sweat. Mimicking the mechanical properties of human skin provides solutions for addressing these challenges [14]. To make sweat sensors fit the skin more conformably, mechanical compliance can be improved via engineering appropriate materials and structures. This section introduces the means to enhance the attachment of sweat sensors to the human body from an engineering design and materials science perspective.

Structural designs

According to the principles of mechanics, some structural designs not only enable electronic devices made of inherently rigid materials to have a certain flexibility [15], but also to further enhance the flexibility of intrinsically soft devices compared to a flat structure [16]. For example, ultrathin and papercutting structures (e.g., kirigami [17] and origami [18]) can endow rigid materials with flexibility and high stretchability, respectively. The island–bridge structure is a great design combining flexible circuits with rigid components to meet the required stretch while maintaining the electrical properties. Additionally, the flexibility of intrinsically soft devices can be enhanced by weaving materials into textile structures [19] or wrinkling them [20].

Ultrathin

Compared with thick boards and pillars, thin films and wires exhibit higher flexibility. Almost any material in a sufficiently thin form can become flexible because bending strains decrease linearly with thickness [14]. Therefore, the ability to adapt to the small curvatures of human skin endows ultrathin electronic devices to stand out among wearable sweat sensors. At the same time, the ultrathin structure is a basis for the fabrication of other two-dimensional (2D) microstructures. Besides, the low weight and portable features of ultrathin devices enable an imperceptible wear experience for users [21]. For instance, an ultrathin skin-mounted humidity sensor system, whose total thickness is below 4 μm (including an encapsulation layer), with in situ frequency modulation signal processing capability was implemented to monitor the sweating of the human body by Zhang et al. [22] (Fig. 2a).

Textile

As the most common structure material of our daily wearable clothing, textile structures can be harnessed in sweat sensors due to their unique advantages. The multilayer and reticulated nature of textile sweat sensors can endure relatively large and long-term deformation. Moreover, the pores among fibers increase the air permeability of the sweat sensor to improve wearing comfort. Functional fibers and mature weaving technologies facilitate the fast, inexpensive, and accurate patterning of sweat sensors [23]. For instance, a silk fabric-derived carbon textile acting as a highly conductive, intrinsically nitrogen-doped, and structure-maintained electrode of a wearable sensor was demonstrated to detect six biomarkers in sweat by He et al. [19] (Fig. 2b).

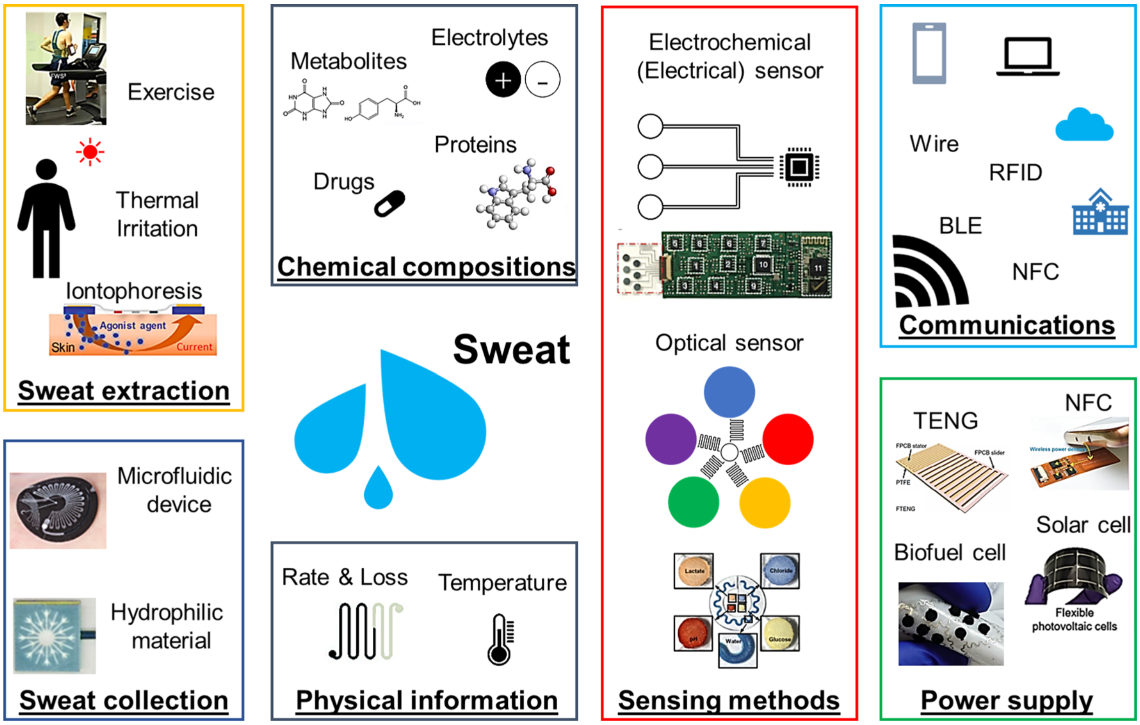

Fig. 1 Architecture of a sweat sensing system. Exercise: Adopted and reproduced from [126], Copyright 2020, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). Iontophoresis: Adopted and reproduced from [68], Copyright 2017, with permission from National Academy of Sciences, USA. Microfluidic device: Adopted and reproduced from [107], Copyright 2019, with permission from the authors, licensed under the terms of the Creative Commons Attribution 4.0 International License (CC BY). Hydrophilic material: Adopted and reproduced from [45], Copyright 2020, with permission from IEEE. Electrochemical (electrical) sensor: Adopted and reproduced from [67], Copyright 2016, with permission from Springer Nature. Optical sensor: Adopted and reproduced from [101], Copyright 2016, with permission from AAAS. TENG: Adopted and reproduced from [126], Copyright 2020, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). NFC: Adopted and reproduced from [87], Copyright 2019, with permission from Wiley–VCH. Biofuel cell: Adopted and reproduced from [129], Copyright 2021, with permission from the authors, licensed under the terms of the Creative Commons Attribution 4.0 International License (CC BY). Solar cell: Adopted and reproduced from [124], Copyright 2019, with permission from American Chemical Society

Wrinkle

Wrinkles are common naturally occurring three-dimensional (3D) stretchable structures. For example, animal skin often has tiny wrinkles to accommodate the stretching and contraction of muscles. Wrinkles usually store a certain amount of pre-strain in a limited space to absorb the energy during stretching. Fabrication methods of flexible devices with wrinkles usually include tensile pre-strain [20], micromolding [24], graphic photopolymerization [25], etc. Wrinkles not only can boost the stretchability and shape adaptability of flexible sweat sensors, but also provide a large surface area for electrochemical reactions involving sweat. For example, Toi et al. [26] fabricated a wrinkled, stretchable, nanohybrid fiber with gold nanowrinkles partially covered with reduced graphene oxide as an electrode for detecting glucose in sweat (Fig. 2c).

Island–bridge

The island–bridge design is one of the most widely studied structures in stretchable and flexible electronics. Its mechanism mainly depends on the different mechanical properties and fixation of the “island” and “bridge” structures to distinguish the deformation state of the two structures. In this structure, the strain of stretch is mainly concentrated on the “bridge” structure, while the shape of the “island” relatively remains unchanged to ensure the electrical stability of the electronic components on it. The shape design and geometric parameters of the “bridge” play a crucial role in the mechanical properties of the “island–bridge” structure [16]. These curves can be classified into coplanar geometries (e.g., serpentines, self-similarity, and arcs) and non-coplanar geometries (e.g., 3D arcs, non-coplanar serpentine, and helices). The structures can be fabricated by

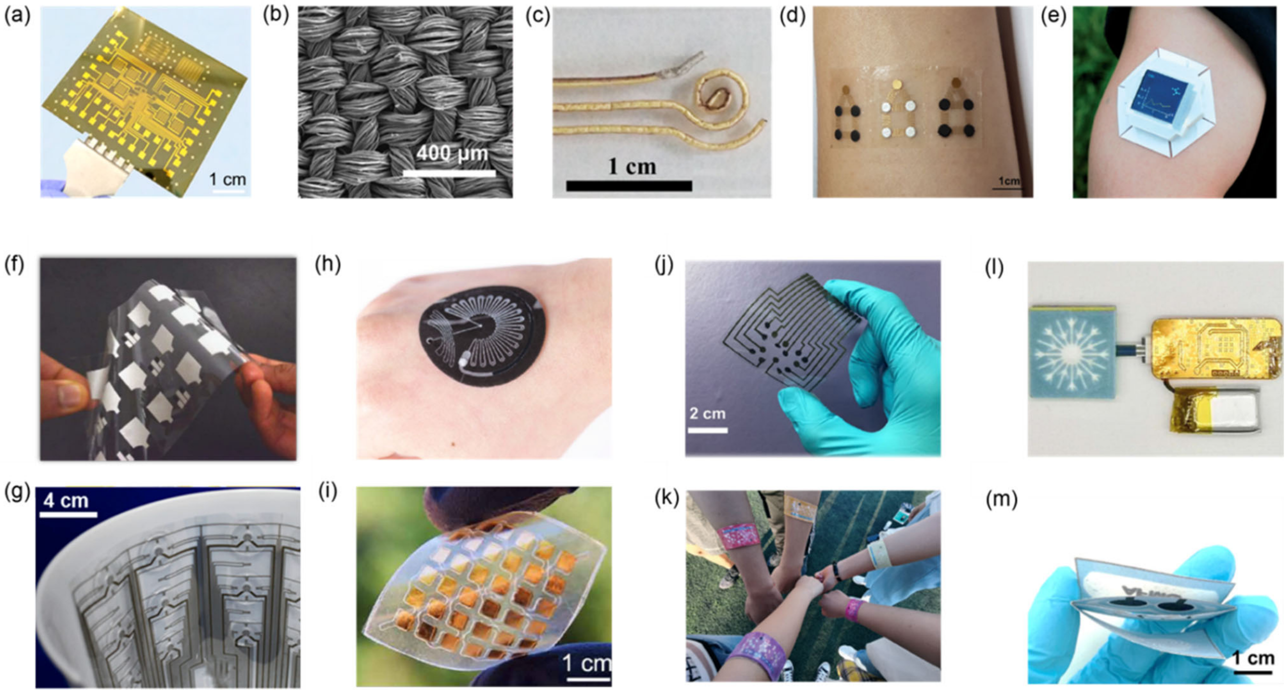

Fig. 2 Various structures and materials of sweat sensors: **a** a sweat sensor system on ultrathin plastic foil. Reproduced from [22], Copyright 2018, with permission from American Chemical Society. **b** An SEM photograph of the textile structure of carbonized silk fabric. Reproduced from [19], Copyright 2019, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). **c** A stretchable nanohybrid fiber-based sweat sensor with wrinkled structures. Reproduced from [26], Copyright 2019, with permission from American Chemical Society. **d** An island–bridge sweat sensor fabricated by thin- and thick-film technology. Reproduced from [27], Copyright 2019, with permission from Wiley–VCH. **e** An autonomous wearable system with kirigami structure for conformal integration onto skin. Reproduced from [29], Copyright 2021, with permission from The Royal Society of Chemistry. **f** A wearable chemical–electrophysiological hybrid biosensing system based on polyvinyl chloride plastic. Reproduced from [36], Copyright 2016, with permission from the authors, licensed under the terms of the Creative Commons Attribution 4.0 International License (CC BY). **g** A sweat flow sensor whose substrate material is PET film. Reproduced from [34], Copyright 2019, with permission from ACS. **h** PDMS acting as the substrate of a waterproof device for sweat collection. Reproduced from [107], Copyright 2019, with permission from the authors, licensed under the terms of the Creative Commons Attribution 4.0 International License (CC BY). **i** Inherent vertical conductivity of the anisotropic conductive film facilitates out-of-plane signal interconnection of the sweat sensor. Reproduced from [41], Copyright 2020, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). **j** A flexible sweat analysis patch based on a silk fabric-derived carbon textile. Reproduced from [19], Copyright 2019, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). **k** A thread/fabric-based band as a flexible and wearable microfluidic device for sweat sensing and monitoring. Reproduced from [42], Copyright 2021, with permission from The Royal Society of Chemistry. **l** An integrated paper-based microfluidic device for real-time sweat potassium monitoring. Reproduced from [45], Copyright 2021, with permission from IEEE. **m** A highly integrated sensing paper for wearable electrochemical sweat analysis. Reproduced from [46], Copyright 2021, with permission from Elsevier

micromachining and laser engraving. Mohan et al. [27] introduced a sweat sensor with an island–bridge structure, where the sensor remained stable in its electrical properties under tension (Fig. 2d).

Papercutting

Papercutting (e.g., kirigami and origami) is the latest structural design type in stretchable electronics [28], which incorporates papercutting art with electronics to release strain energy in the pre-designed position and transform a 2D structure into a 3D structure. The delicate papercutting structures make electronics stretchable and compressible to adapt to the skin morphology while having a certain esthetic value. In an exemplary case, Hojaiji et al. [29] presented a sweat sensor based on a papercutting structure, which not only improved the conformal adhesion of the sensor to the skin, but also isolated different electrodes for the separate monitoring of individual components (Fig. 2e).

Porous foam

As a broadly applied 3D structure in flexible pressure sensors [30, 31], porous foam has also been used as a substrate for sweat sensors due to its porous microfluidic structure. Huang et al. [32] prepared a sponge-based sweat sensor that can absorb sweat from the human skin by exploiting the microporous structures in the sponge. In this system, a colorimetric measurement mode can also be implemented by introducing indicator compounds deep into the sponge to track specific components in sweat. Ding et al. [33] reported a sponge-based microfluidic sampling method to measure the ion concentration in sweat by potentiometric methods. The sponge substrate in this design not only acts as a microfluidic device, but also protects the electrodes on it from mechanical damage.

Materials

The substrate materials, as the interface between the device and the human skin, determine both the users' wearing experience and the device performance. This subsection discusses various sweat sensor substrate materials and their application examples in typical devices. Their advantages and shortcomings are described from the perspective of sweat sensor applications.

Plastic polymer

Flexible plastics, such as polyethylene terephthalate (PET) [34], polyimide (PI) [35], and polyester (PE) [36], are used extensively as substrates and encapsulation materials for flexible electronics. Some mature manufacturing techniques that can be applied on plastic material-based substrates, such as flexible printed circuit boards (FPCBs), inkjet printing, and roll-to-roll (R2R) screen printing, support the expanse of plastic materials in flexible electronics. Imani et al. [36] reported a chemical and physical hybrid signal acquisition patch that was fabricated by screen printing methods on a thin, highly flexible PE board. This device can conform well to the complex 3D morphology of human skin while providing low-noise chemical and electrophysiological signals (Fig. 2f). Xu et al. [37] proposed a flow sensor based on a flexible PET substrate, which can be potentially adopted in sweat flow sensing. (Fig. 2g). Although plastic materials are bendable, their inherent non-stretchable properties present obstacles to their application in sweat sensors.

Rubber polymer

Rubber, such as polydimethylsiloxane (PDMS) [38] and Ecoflex [39], is inherently stretchable and elastic materials, making the mechanical properties of rubber-based sweat sensors approach those of human skin. Therefore, rubber is much more compliant to skin stretching than other materials, making rubber-based sweat sensors highly suitable for application on the human skin in exercise situations. Notably, the most promising application of rubber materials for sweat sensing is the soft microfluidic sweat collection devices (to be described in detail in Sect. 5.2). Reeder et al. [40] presented a PDMS-based sweat collection device with sensing and feedback stimulation to remind the users of potential dehydration caused by sweating (Fig. 2h). Zhao et al. [41] designed a freestanding electrochemical sensing system with an electrode substrate of PDMS for monitoring sweat metabolites in individuals in resting and high-intensity exercise environments (Fig. 2i). However, similar to plastic, rubber is not breathable and may cause discomfort as well as skin irritation to the user if worn for long periods of time.

Fabrics and silks

Fabrics and silks are natural materials with favorable biocompatibility and almost no irritation to human skin. Functional fabrics/silks based on the long history of these natural materials have shown promising applications in sweat sensing [19] (Fig. 2j). Thanks to their water absorption properties, fabric/silk can be used as low-cost substrate materials for microfluidic sweat-related devices. Moreover, the existing commercial spinning technology facilitates the patterned manufacturing and mass production of fabrics. For example, after chromogenic reaction treatment, thread-embroidered patterns can serve as a detection zone for sweat, which is transferred from the skin to the detection zone through hydrophilic threads. Such fabric-based sweat sensors are capable of accurately analyzing local sweat loss, pH, or the concentration of chlorine and glucose in sweat [42] (Fig. 2k).

Paper

Paper has been widely applied in commercialized rapid chemical testing due to its low cost, degradability and renewable characteristics [43, 44]. Similar to the properties of fabric, the capillary effect of paper promotes sweat flow in paper-based devices, thus contributing to sweat collection. A cellulose paper pad acting as a simple and low-cost microfluidic component of a sweat sensor was described by Liang et al. [45] (Fig. 2l). A sweat analysis patch based on all-paper substrate was introduced by Li et al. [46] to detect the concentration of glucose and lactate in sweat (Fig. 2m). However, paper is fragile and not wear-resistant, which probably makes it unsuitable for long-term sweat monitoring.

Sweat sensing mechanisms

Analyzing the rich chemical composition and physical information in sweat can provide attractive insights into human health conditions in various application scenarios. In this section, we classify the sweat sensing applications into chemical and physical sensing. The main sweat sensing applications are typically chemically related devices. In hybrid sweat sensing platforms, physical sensing is usually performed as a complementary feature.

Chemical sensing

A variety of studies have intensively explored the relationship between chemical component levels and human health states. For example, sweat chloride is accepted as the golden standard for the diagnosis of cystic fibrosis in newborns [47, 48]. Furthermore, diabetes can be diagnosed by measuring the concentration of glucose in sweat [49]. During exercise, sodium and chloride levels in sweat can reflect the transepidermal water loss of the human body [50, 51]. Drug metabolites, such as caffeine or acetaminophen in sweat, have also been exploited to monitor the metabolism of drugs in the body [52, 53]. From the perspective of nutrition monitoring, the physiological levels of vitamin C in sweat can be utilized to assess the intake of fruit juices. The concentration of cortisol, also known as the "stress" hormone, in sweat has been extensively investigated to continuously monitor the mental state of subjects [54, 55]. Electrochemical and optical chemical sensing modalities have been developed to detect the concentrations of these chemical compositions in sweat. This subsection mainly reviews certain emerging technologies and their corresponding applications in chemical sensing.

Electrochemical sensing

Benefiting from the convenience of conformal physical integration on the human body and data transmission to smartwatches or smartphones in the current digital age, wearable electronics have attracted substantial interest from users and researchers alike. Nevertheless, most wearable electronics focus mainly on measuring physical information, including strain [56], pressure [12], and electrophysiology signals [57], and neglect the real-time monitoring of the chemical composition and concentration of biofluids, which would otherwise offer tremendous opportunities to promote the depth of wellness analysis [58]. Wearable electronic devices for the detection of sweat chemistry represent an excellent alternative for real-time and continuous monitoring. Among these electronic devices, electrochemical sweat sensors have the distinct advantages of high sensitivity, low response time, and the options of long-term and real-time recording of sweat data [59]. Their output signals can be fed back to the users either directly through circuits or by wireless communication. Various electrochemical sensing mechanisms, such as potentiometry [60, 61], chronoamperometry [46, 62], voltammetry [63, 64], and electrochemical impedance spectroscopy [65, 66], are substantially leveraged toward specific application scenarios where they all have their unique advantages.

Potentiometric electrochemical methods have been extensively exploited to detect dominant ions, such as Na^+, K^+, Ca^{2+}, Cl^-, and H^+ [67–71], whose concentrations are mainly distributed in the μM to mM range [59]. The target ion level in sweat can be calculated according to the Nernst equation [72] by utilizing the potential measured between the sensing and the reference electrodes (two electrodes). The detection of target-specific ions demands highly selective and sensitive ion-selective membranes (ISMs) to reduce the influence of other interfering ions on the potential measurement [60]. For example, Alizadeh et al. [73] merged Na^+ and K^+ ion-selective electrodes (ISEs) with a microfluidic module on a PET substrate to simultaneously monitor the concentrations of Na^+ and K^+. When adding other interfering ions on these ISEs, the device shows a slight change in the potential, which is negligible compared with that of target ions. Targets with low concentration or uncharged targets cannot be measured intuitively by the potentiometric method. However, the level of charged products of enzymatic reactions can permit the indirect detection of neutral biomarker levels by means of a potentiometric readout. For example, urea in sweat is an uncharged metabolite of amino acid metabolism. You et al. [74] fabricated a urea sensor containing an additional enzymatic layer, where urease converts urea to carbon dioxide and ammonia (NH_4^+). The increased NH_4^+ ion level can be measured by NH_4^+ ISEs based on the potentiometric method and indirectly reflect the urea level.

Unlike potentiometric methods that detect chemical compositions by measuring the electrode potential, amperometric and voltammetric methods both work by measuring the current flowing between the electrodes. The mechanism of amperometry as an electrochemical method is mainly to detect the response current generated by the redox reaction through the working electrode and the counter electrode after inputting constant step voltage between them. Conventional three-electrode systems are widely adopted in amperometric sensors and include a functionalized working electrode with a target enzyme for an electrochemical reaction, the counter electrode for the current source, and the reference electrode as standard. In order to make the electrical signal of the electrochemical reaction easier to measure, some corresponding oxidases and reductases are commonly applied to catalyze enzymatic redox reactions among electrodes [75, 76]. Due to the specificity of enzymatic reactions, amperometry is generally employed in the selective detection of glucose and metabolites in sweat, such as lactate, uric acid, and ethanol. For example, Anastasova et al. [69] fabricated a multisensing patch for continuous sweat lactate and Na^+ level monitoring. In particular, the lactate level in sweat can be measured through the chronoamperometry method with the aid of lactate oxidase and an internal selective membrane (a copolymer of sulfonated polyesther ether sulfone–polyether sulfone) for lactate on the electrode. Ethanol in sweat can be also qualified by chronoamperometry. Kim et al. described an alcohol oxidase enzymatic electrode along with a printed Prussian Blue (PB) electrode transducer acting as the detector of concentration of ethanol in sweat [77].

As opposed to chronoamperometry, the current curve of voltammetry contains information on the concentration of various analytes at the same time. The target concentration can be extracted by applying a varying potential excitation and analyzing current peaks between working and counter electrodes. Several waveforms of potential excitations in voltammetry have been proposed for application in the detection of different analytes, such as drugs and heavy ions in sweat. Firstly, cyclic voltammetry (CV) is widely used for first experiments performed in electroanalytical studies (i.e., the preliminary electrochemical characterization of sensors) to explore the electron transfer kinetics and redox processes [59]. The first demonstration of voltammetry in sweat sensing was a functional electrode system based on temporary transfer on-skin tattoos reported by Windmiller et al. [78], which can detect ascorbic acid on skin by harnessing CV. Similar to CV, linear sweep voltammetry plays an important role in the detection of electroactive molecule levels. For example, Jia et al. [79] reported an electrochemical tattoo biosensor for the real-time monitoring of lactate, whose operating potential was selected by linear sweep voltammetry. Pulse-like voltammetric techniques exhibit the potential to increase the ratio between the faradaic and non-faradaic currents and reduce interference. Square wave anodic stripping voltammetry (SWASV) has its distinct advantage of detecting traces of heavy metals. Gao et al. [80] elaborated a wearable sensing platform based on the SWASV technology to detect the concentration of heavy metal ions in human sweat. The device adopts the pre-concentration/deposition step to accumulate heavy ions from sweat, followed by a stripping step to detect their concentration. Differential pulse voltammetry (DPV) has high sensitivity and selectivity, but also needs a relatively long time for analysis. To solve this challenge, the selection of the pulse amplitude and potential scan rate is usually performed by a trade-off among sensitivity, resolution, and speed. Among the common voltammetry techniques, DPV is often adopted for the quantification of target drugs, as it allows for mitigating the contribution of non-faradaic background, thus achieving high signal-to-background ratio measurements. Lin et al. [81] designed a sweat sensor aimed at measuring electroactive drug levels in sweat for pharmacokinetic monitoring. Three model drugs, dipyridamole, acetaminophen, and caffeine, served as target molecules to demonstrate the operation of the platform.

Electrochemical impedance spectroscopy (EIS) is used to reflect the resistive feature of sensor surface by analyzing the relationship between the recorded current and the input sinusoidal voltage. Generally, binders play the key roles as functional electrodes of EIS. The function of binders on the sensor surface is to selectively capture target molecules, which affects the impedance feature of sensor surface according to the concentration of target molecules. From the perspective of sweat sensing, EIS is of practical value for the detection of cortisol in existing sweat sensors. For instance, cortisol level monitoring has been achieved by using electrochemical impedance spectroscopy to measure impedance changes associated with the binding of cortisol to antibodies at the interface of MoS_2 nanosheets [65]. In addition to antibodies, aptamers can act as binders to capture cortisol. A sweat sensor based on a highly specific single-stranded DNA (ssDNA) aptamer used for the affinity capture of cortisol hormone dynamically eluted in sweat was illustrated by Ganguly et al. [66]. The size of aptamer is much smaller compared to that of the antibody, which allows for more capture probes to be installed on a sensor with a given effective surface area, thereby reducing the device cost.

Among the applications of biochemical sensing, glucose measurement occupies a large market share of biosensors and has received the most attention in the commercial market due to the increased prevalence of diabetes caused by obesity and other problems [82]. Moreover, the rapidly increasing demand for noninvasive, real-time, long-term glucose monitoring solutions provides unprecedented opportunities for the development of glucose level monitoring technologies employing sweat. Among the amperometric electrochemical techniques, three generations of glucose enzymatic reactions have been developed for glucose measurement, which are classified according to the type of relay between enzyme and sensor [82]. The concepts of all of these three generations can also be applied in sweat glucose sensing. Electrochemical reactions in the conventional (so-called first-generation) glucose amperometry sweat sensor consume the dissolved oxygen in sweat, and produce hydrogen peroxide. The concentration of product (hydrogen peroxide, H_2O_2) can subsequently reflect the glucose level in sweat. However, the first-generation amperometric detection of glucose commonly requires a relatively high potential for H_2O_2 measurement, which is therefore susceptible to potential electroactive interference. To resolve this difficulty, scholars have extensively explored two different solutions. Firstly, the modification electrode with permselective membranes can achieve selectivity against electroactive interferences. In the platform reported by Cheng et al. [83], a platinum (Pt) nanoparticle-modified electrode with a permselective membrane (poly-m-phenylenediamine) was utilized to selectively detect H_2O_2, which could be leveraged for analyzing glucose concentration. Nonetheless, oxygen fluctuations in sweat also influence the first glucose measurement. The alternative approach, known as the second-generation amperometric detection of glucose, can potentially solve the two problems mentioned above. Artificial mediators, such as tetrathiafulvalene and PB, are adopted in second-generation sweat glucose sensors to shuttle electrons from the redox center of enzyme to the surface of electrode. This achieves target detection at lower potentials and eliminates the effect of oxygen concentration fluctuation in sweat [79]. In one example, an amperometric biosensor for glucose level in sweat monitoring was designed by Martín et al. [84]. This device has immobilized oxidase enzymes on a PB-modified amperometric transducer platform. However, the second-generation glucose sensors suffer from interference from ions and relatively poor operational stability. The mechanism of third-generation sweat glucose sensor is that electrons can be transported between the enzyme active sites and electrode directly. The two advantages of eliminating leachable artificial mediators and operating in a potential window close to the enzyme's REDOX potential attribute this type of sensors a promising prospect [85]. Several reports have relied on this approach to detect glucose concentration [63], but this principle has yet to be applied to wearable sweat platforms.

A fundamental problem of electrochemical sweat sensing lies in the interference of irrelevant signals. Thus, the reduction or even elimination of any interference from unrelated signals establishes the basis for accurate sweat sensing. Temperature and humidity, which can affect enzyme structure and catalytic activities, are the most common interfering effects in electrochemical sweat sensors [86]. Many sweat sensors have integrated temperature sensors to compensate for this temperature effect [33, 87]. Diverse unrelated ions or electroactive species can also potentially affect sensor response. To address these interferences, corresponding methods are being adopted in these electrochemical modalities. Various ISEs based on the combination of plasticized polymeric membranes and ion-to-electron transducers have been developed in the potentiometric method. Specific enzymes, relays, and functionalized electrodes are widely adapted in chronoamperometry and voltammetry. Lastly, selective binder molecules are fixed on the sensor surface in electrochemical impedance spectroscopy to specifically capture the target molecule [88–90].

Signal processing and transmission are used to bridge raw data from sweat sensors with user-friendly output devices. Along the signal path, on-site signal processing is beneficial to reduce the loss of sensing information, filter noise, improve the transmission efficiency, and reduce the calculation load of the cloud. For users, on-site data processing can reduce the dependence of sweat sensing on other electronic products (smartphones), thus providing an opportunity to present sweat data more conveniently and without delay. In order to ensure the connection stability of electrical signals and the computational ability of processing circuits, commercial silicon-based chips and FPCBs technologies are exploited that incorporate the critical signal conditioning, processing, and wireless transmission functionalities by using off-the-shelf integrated circuit components. Wireless data transmission technologies, such as Bluetooth Low Energy (BLE) [15, 91] and radio frequency identification (RFID) [73, 92], act as information gateways between sweat sensors and output devices. For example, Kim et al. [77] presented a skin-worn alcohol sensor coupled with a flexible electronics board. This flexible processing board controls the iontophoresis/amperometry operation and transmits data wirelessly in real time via Bluetooth communication. In the digital era, smartphones can be connected to record and display sweat monitoring results after the completion of analysis [93, 94]. Moreover, liquid crystal display screens can be used to directly display monitoring results [37, 95]. With the aid of online cloud servers, big health-related sweat data can be shared with personal doctors for further analysis. Moreover, by leveraging these data and machine learning or doctor's advice, personalized medicine and health care can become more accurate, predictive, and comprehensive.

The integration of multiplexed in situ sweat sensing is a hot topic in electrochemical sensing research, which allows the simultaneous monitoring of serval chemical ingredients and physical information of sweat, requiring the application of multiple electrochemical modes, the physical integration of electronic components, accurate data decoupling, and the compensation of signal interference. In a representative example, Gao et al. [67] reported fully integrated wearable sensor arrays for multiplexed in situ perspiration analysis. In this system, potentiometric sensors with ISEs are exploited to measure Na^+ and K^+ levels, and amperometric sensors based on glucose oxidase and lactate oxidase are adopted to detect the concentration of glucose and lactate. A linear temperature resistive response sensor is used for thermal monitoring. Commercially available conventional integrated circuit components (more than 10 chips) are applied on FPCBs to serve as data processing and transmission parts of the platform. By integrating the in situ sensing, on-site processing, and data transmission modules, the platform can achieve the goal of continuous, multiplexed sensing of ions and metabolites, which is crucial to obtain a more comprehensive knowledge of the wearer's well-being (Figs. 3a–3g).

Colorimetry

This diagnostic principle, which relies on color changes of chemical reactions between reagents and target compositions, is another prominent approach utilized in sweat analysis owing to its minimal or even zero power consumption, easy signal readout, and low-cost construction [93]. Compared with electrochemical sweat sensors whose reaction sites are electrodes, colorimetric reactions usually take place in microfluidic chambers [96, 97] or on the surface region with colorimetric reagents [98, 99] for sweat absorption. For example, after chromogenic reaction treatment,

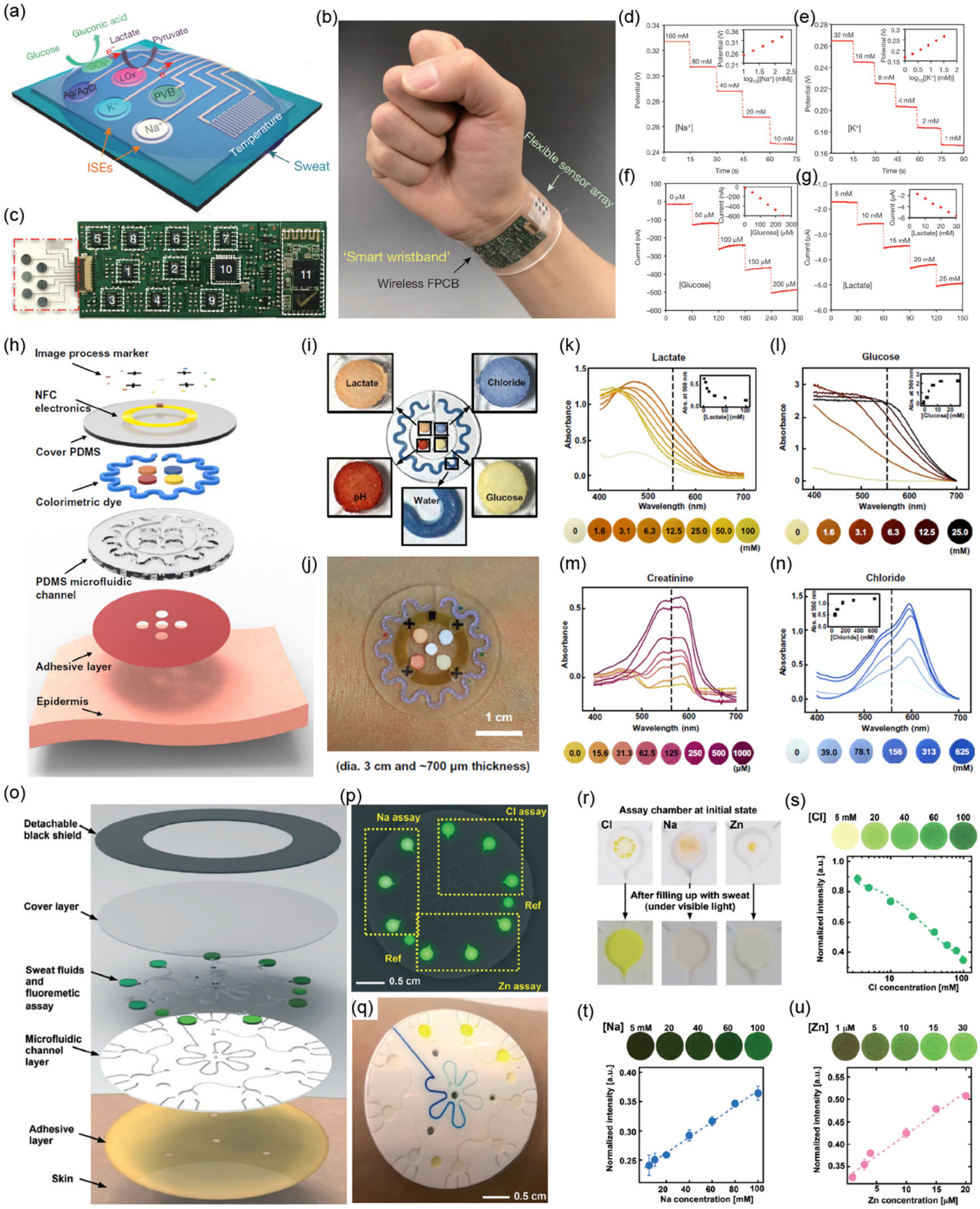

Fig. 3 Various sensing modalities of sweat sensors. **a**–**g** Fully integrated wearable sensor arrays (FISA) based on the electrochemical method for multiplexed in situ perspiration analysis. Reproduced from [67], Copyright 2016, with permission from Springer Nature. **a** Schematic of the sensor array of FISA; **b** photograph of FISA on a subject's wrist; **c** photograph of a flattened FISA; **d** corresponding electrochemical signals of Na^+; **e** corresponding electrochemical signals of K^+; **f** corresponding electrochemical signals of glucose; **g** corresponding electrochemical signals of lactate. **h**–**n** A soft, wearable microfluidic device for the capture, storage, and colorimetric sensing of sweat. Reproduced from [101], Copyright 2016, with permission from AAAS. **h** Schematic illustration of the colorimetric sweat sensor; **i** colorimetric detection reservoirs; **j** optical image of the colorimetric sweat sensor mounted on the forearm; **k** corresponding colorimetric signals of lactate; **l** corresponding colorimetric signals of glucose; **m** corresponding colorimetric signals of creatinine; **n** corresponding colorimetric signals of Cl^-. **o**–**u** A fluorometric skin-interfaced microfluidic device. Reproduced from [104], Copyright 2018, with permission from The Royal Society of Chemistry. **o** Schematic exploded view of the microfluidic platform; **p** image illustrating the fluorescence signals associated with chemical probes; **q** photograph of a subject wearing the microfluidic device during testing under visible light; **r** image of the microreservoirs for the assays before (upper) and after (lower) filling with sweat collected under visible light illumination; **s** corresponding fluorometric signals of Cl^-; **t** corresponding fluorometric signals of Na^+; **u** corresponding fluorometric signals of Zn^{2+}

some hydrophilic materials such as paper or thread can serve as the detection zones of sweat. These materials and possible simple designs dramatically reduce the cost of disposable colorimetric sweat sensors and improve the efficiency of mass production. For instance, He et al. [100] proposed a paper-based colorimetric glucose sensor design, and dropped colorimetric reagents onto the filter paper substrate directly. At a preset temperature, a folded polyurethane-textile-based microfluidic device could gradually open to guide the sweat to paper-based glucose sensor, triggering enzyme-catalyzed colorimetric reactions. The challenges associated with evaporation and contamination through exposure to the atmosphere, however, have hindered the practical utility of this colorimetric sweat detection method.

Microfluidic epidermal devices represent a promising alternative to prevent sweat from evaporation and contamination while simultaneously enabling continuous and separate monitoring. Embedded chemical analyses that respond in a colorimetric fashion to markers, such as chloride and hydronium ions, glucose, and lactate, were proposed by Koh et al. [101]. After flowing into the microfluidic channels of the device, the sweat is divided into multiple microreservoirs to have chromogenic enzymatic reactions with different reagents. The concentration of targets can be recorded by analyzing corresponding color changes. In addition, the water-reactive chromogenic reagent in the serpentine channel allows the extent of sweat filling to be measured, which can be translated into overall sweat rate and volume (Figs. 3h–3n).

Considering the variation in the color perception ability of people, the colorimetric sensing method judged by the naked eye can only be defined as the semiquantitative tracking of physiological status. Capturing photographs of colorimetric assays and quantitatively analyzing color composition by smartphones solves this problem to some extent [102]. For instance, Choi et al. [103] designed a colorimetric sweat sensor in which the color change can be quantitatively analyzed by dividing it into three original colors with the aid of a smartphone.

Fluorometry

The relatively narrow concentration detection range of biomarkers is a major limitation of colorimetric methods in sweat sensing applications [104]. Unlike colorimetric methods, fluorometric assays are more broadly applied in the diagnosis and analysis of biosensors due to their high sensitivity in the detection of trace analytes in sweat. As a noteworthy example, Kim et al. [90] fabricated a fluorometric sweat sensor for detecting glucose and ascorbic acid by glucose oxidase and ascorbic acid oxidase enzymes, respectively. The oxidation reactions for both substrates generate hydrogen peroxide, and any excess horseradish peroxidase activity leads to the reduction of a fluorometric probe to form resorufin as the basis of fluorescence signals. Under normal circumstances, the level of zinc ions in sweat is far less than that of sodium and chloride ions. To the best of our knowledge, the most common method for the measurement of zinc is the SWASV electrochemical method, and no colorimetric sweat sensor has been shown to be capable of measuring zinc ions in sweat. However, the fluorometric method is able to overcome this gap. Sekine et al. [104] proposed a versatile advanced fluorescence-based imaging modality in body-worn sweat microfluidics platforms. To demonstrate the application value of this modality, they fabricated a skin-interfaced microfluidic device, which can measure the concentrations of chloride, sodium, and even zinc in sweat through fluorometry, and the accuracy of results matches that of conventional laboratory techniques (Figs. 3o–3u). Nevertheless, the requirement of fluorescent accessories still limits the convenience of its use.

Physical sensing

Apart from a range of chemical ingredients, sweat also contains physical information to evaluate the personal health status. Compared with chemical sensing, physical sensing has received less attention in sweat sensing; however, its importance in reflecting human health and calibrating chemical sensing modules cannot be ignored. The relatively important physical information focuses on sweat loss and rate. Localized sweat rate and loss are intensely associated with water loss of the human skin and body [105]. Meanwhile, some other physical information, such as pressure and temperature, plays auxiliary roles in physiological analysis.

Sweat loss and rate

The most crucial and intensively studied physical parameters of perspiration are sweat loss and sweat rate, which can not only act as indicators of the hydration state of the human body and conditions for the risk assessment of possible physiological failures under extreme conditions [106], but also reflect the wellness of users both physiologically and psychologically. Various sensing modalities, like colorimetric, thermal, and electrical sensing, have been proposed to endow sensors for a real-time detection of sweat loss and rate. In colorimetric sensing, dyes are commonly used as markers to reflect the sweat loss around localized zones [107]. For example, Reeder et al. [36] proposed an epidermal microfluidic device for sweat collection, which contains food dye with red and blue water-soluble particles having different dissolution rates. This dye can generate a volume-dependent color gradient as the device fills with sweat. To verify the effectiveness and accuracy of the device, researchers suc-

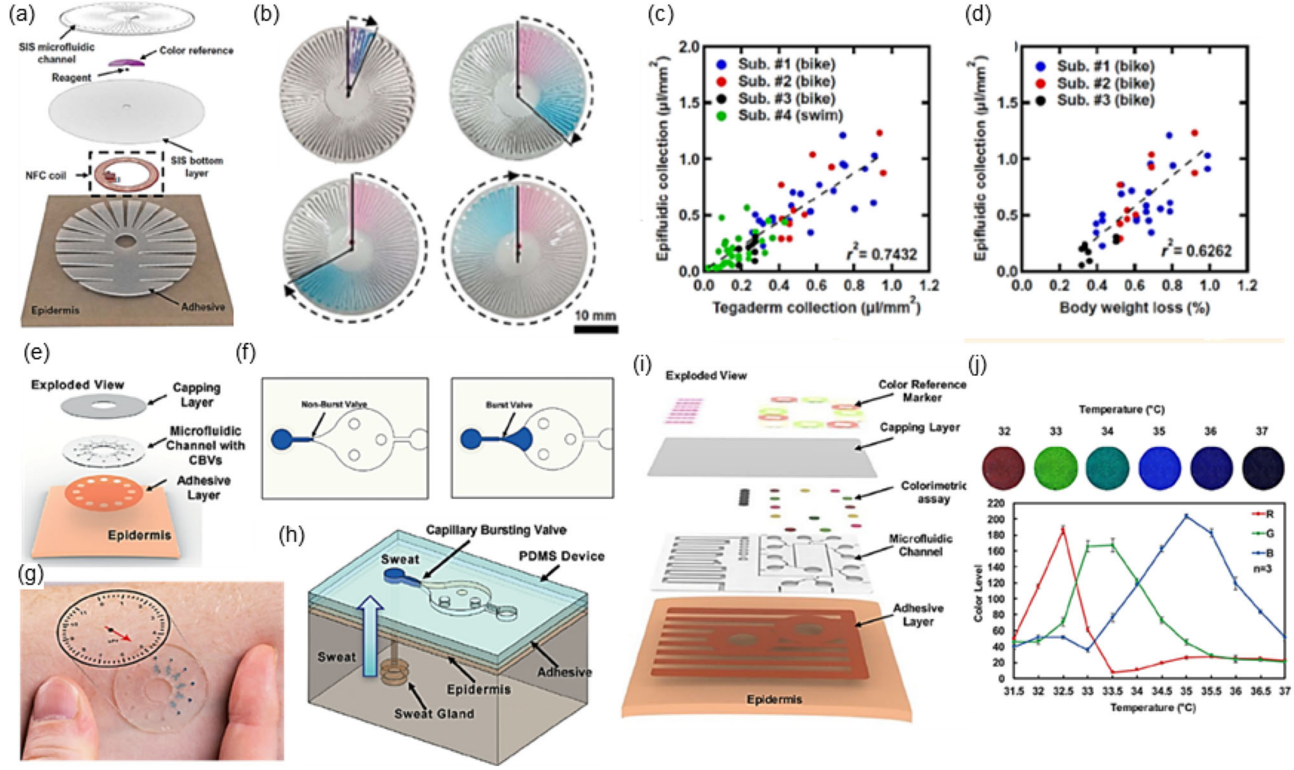

Fig. 4 Several sweat sensing platforms for detecting physical signals. **a**–**d** An epidermal colorimetric microfluidic device for sweat collection and loss rate monitoring. Reproduced from [40], Copyright 2019, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). **a** Exploded schematic illustration of the key layers of the epidermal sensor; **b** a dye composed of blue and red water-soluble particles that dissolve at different rates enables a flow-driven change in color; **c** a strong correlation exists between the sweat loss collected by the device and Tegaderm collection; **d** a strong correlation exists between the sweat loss collected by the device and the body loss rate. **e**–**h** A microfluidic system for measuring secretory fluidic pressures generated at the surface of the skin. Reproduced from [110], Copyright 2017, with permission from The Royal Society of Chemistry. **e** Schematic illustration of the sweat sensor to measure fluidic pressures; **f** capillary bursting valve that has not yet burst and a valve that has burst; **g** optical image of the fluidic sweat sensor mounted on the skin; **h** mechanism of the fluidic sweat sensor. **i**, **j** A multifunctional microfluidic system for the accurate colorimetric analysis of sweat biomarkers and temperature. Reproduced from [103], Copyright 2019, with permission from American Chemical Society. **i** Exploded view illustration of the device and its interface with the skin; **j** optical images of the color development of a thermochromic liquid crystal temperature sensor as a function to temperature (top) and color level for each color (bottom)

cessfully compared the performance of the device with that of clinical sweat absorption pads and body weight changes, with excellent consistency (Figs. 4a–4d). The sweat rate can also be indicated through the relationship between medium velocity and heat dissipation. For instance, Kwon et al. [94] reported the sweat rate using a cumulative loss monitoring platform, which consists of a power-efficient thermal actuator and a collection of precision thermistors to measure the flow rate through the calibration of flow rate and temperature. The mechanism of electrical detection is transforming sweat loss and rate into electrical signals, such as resistance [108] and capacitance [109]. Choi et al. [109] designed a capacitive-type sensor, whose key components are two conducting parallel plates, plastic insulating layers, and a central microfluidic channel. Sweat in the channels acts as part of a dielectric layer, affecting the capacitance between two electrodes.

Sweat pressure and temperature

The magnitude of sweat pressure may provide insights into the health state, exercise intensity, mental stress factors, and other information of interest [110]. A crucial function of sweat pressure in sweat sensors is to drive sweat throughout devices based on microfluidic channels. Certain dedicated microfluidic structures, such as a capillary bursting valve with a unique designed bursting pressure, can be used to detect the secretory fluidic pressures generated by eccrine sweat glands on the skin surface [110] (Figs. 4e–4h).

Sweat temperature has an intense relationship with that of the skin, which can be measured through electrical [67] and colorimetric [103] methods. As mentioned in Sect. 4.1.1, sweat temperature is an important parameter to compensate for chemical sensing in electrochemical sweat sensors, because it has a significant effect on the rate of enzymatic reaction. As a result, most enzymatic sweat sensing platforms have been integrated with temperature sensors [36, 67]. Choi et al. [103] fabricated a multifunctional microfluidic system for the accurate colorimetric analysis of sweat biomarkers and temperature. To measure sweat temperature, researchers embedded a thermochromic liquid crystal in a separate layer of polyester, which provides a colorimetric method for determining the temperature of sweat through analyzing the level of three original colors (Figs. 4i and 4j).

Fabrication

Taking the requirements, costs, and manufacturing challenges of various sensing mechanisms into consideration, a variety of fabrication methods have been proposed and are continuously evolving to promote the low-cost, functional, and efficient mass production of sweat sensors. In this part, several fabrication methods of the key components of sweat sensors are discussed.

Electrode fabrication

As one of the most widely accepted and mature electronic fabrication techniques, microfabrication, including deposition, photolithography, etching, etc., serves as a critical process in patterning electrodes of sweat sensors. As an example, Gao et al. [67] fabricated a flexible Ag/AgCl electrode array by means of microfabrication, including patterning, photolithography, etching, and chlorination steps (Fig. 5a). Although microfabrication technologies have high precision, the expensive microfabrication facilities and complicated processes involved are inevitable constraints to the commercialization of sweat sensors. In contrast, inkjet printing [111], screen printing [112], stamping [113], and 3D printing [114] are additive manufacturing methods with a high utilization rate of raw materials to reduce production costs. For instance, He et al. [111] demonstrated an ion-selective electrode using inkjet-printed graphene, which shows great potential for electrode manufacturing in sweat sensors (Fig. 5b). R2R rotary screen printing is another promising method for the high-throughput and cost-effective fabrication of flexible electronics. Nyein et al. [115] developed a high-throughput microfluidic sweat sensing patch, whose sensing layer on a PET substrate is fabricated by R2R rotary screen printing. This sensor hosts silver-based electrodes with active areas modified by a chemically inert graphite-based ink to support electrochemical sensing (Fig. 5c). Owing to the low cost and precise patterning function, direct laser writing has been established for graphene-based electrode fabrication [13]. Laser engraving also allows for rapid microfluidic patterning on flexible plastic substrates at small scales. For instance, an entirely laser-engraved sensor for simultaneous sweat sampling and measurement was designed by Yang et al. [13]. This device integrates chemical sensors, vital sign monitoring sensors, and microfluidic swear channels fabricated by different modes of laser processing. Using this device, the continuous monitoring of temperature, respiration rate, and low concentrations of uric acid and tyrosine (analytes associated with diseases such as gout and metabolic disorders) were successfully demonstrated (Fig. 5d). Unlike sheet electrodes, fibrous electrodes are more suitable for integration into textile-based sweat sensing platforms. Xu et al. [116] proposed a highly stretchable fiber-based sweat sensor. Therein, a dry spinning process is used in fabricating the fiber electrodes of the sensors. After pre-stretching the Au/styrene–ethylene/butylene–styrene fiber, plate Au is grown on the pre-stretchable fiber to form a highly stretchable Au fiber electrode. Then, ISMs are used to fill the cracked spaces of the wrinkled gold film, resulting in the formation of a strong attachment with the fiber electrodes (Fig. 5e).

Microfluidic module

Recent studies have demonstrated the availability of epidermal microfluidic devices for the direct collection of sweat from the human skin surface [104, 107]. In sweat sensors with microfluidic systems, sweat enters microfluidic channels and separates from the skin surface, preventing chemicals from constantly seeping into sweat from the skin. Moreover, minimizing sweat evaporation is another advantage of microfluidic structures, which enhances the accuracy of sweat measurement. Microfluidic channels can also be designed to direct old sweat away from and allow the flow of new sweat into the sensing area, which ensures data readings as close to real time as possible, rather than a rolling average of analyte concentration [59]. Various manufacturing technologies, such as 3D printing [117, 118], microfabrication [119], and laser engraving [115], have been adopted in the fabrication of microfluidic structure-based sweat sensors. Soft lithography is widely employed in the fabrication of sweat sensor microchannels. Koh et al. [96] used the soft lithography technology to fabricate a sensing platform with microfluidic channels. In this process, firstly, PDMS is cast and cured on lithographically prepared molds to yield solid elastomers with reversed patterns. Then, separate pieces of PDMS are applied to fabricate sealed microfluidic channels and containment reservoirs (Fig. 5f).

Power supply

Wired connections or onboard batteries for powering wearable sweat sensors and corresponding data processing cir-

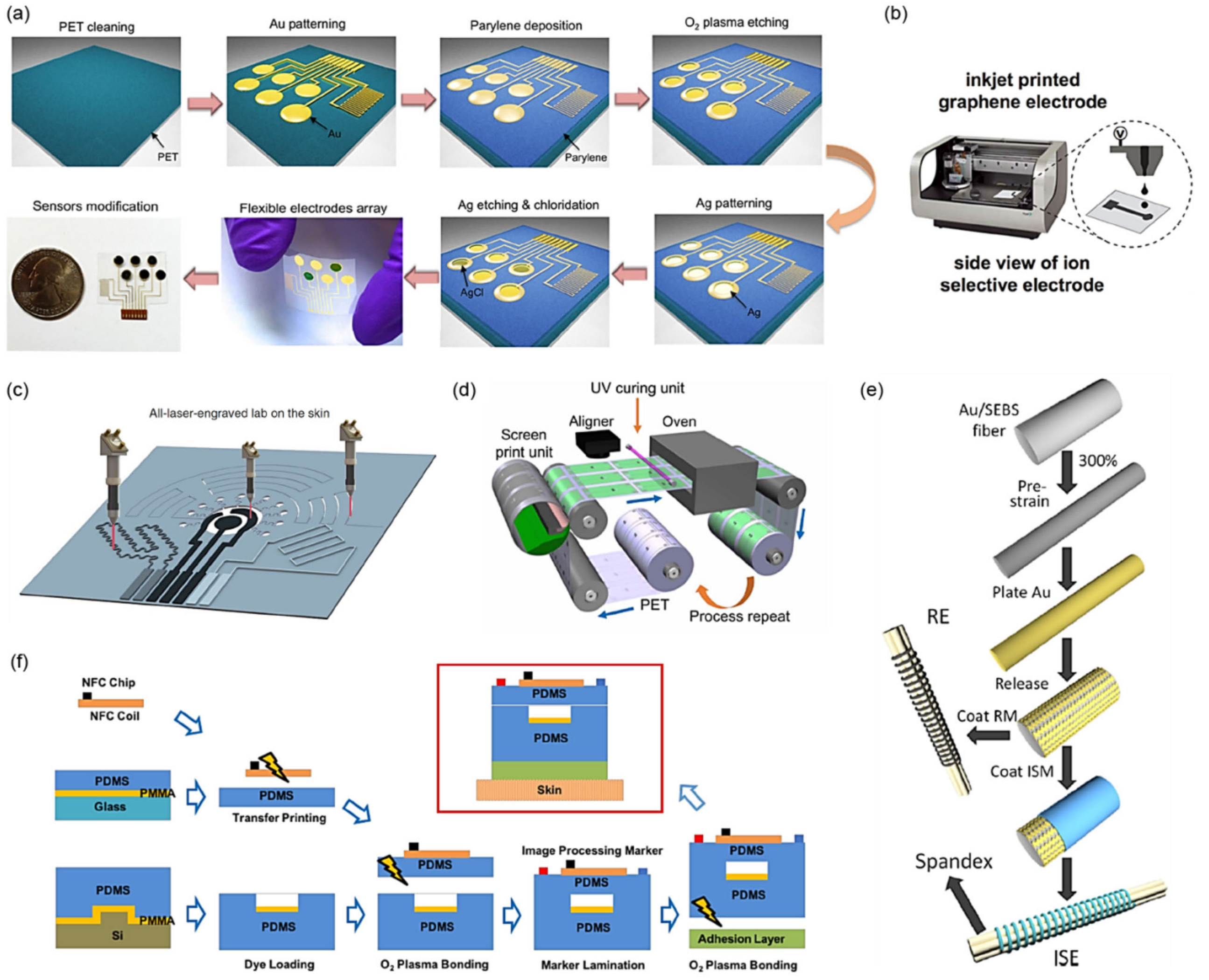

Fig. 5 Fabrication processes of sweat sensors: **a** microfabrication process of electrodes. Reproduced from [67], Copyright 2016, with permission from Springer Nature. **b** Fabrication of electrodes by inkjet printing. Reproduced from [111], Copyright 2017, with permission from American Chemical Society. **c** Laser engraving process of electrodes and microfluidic channels. Reproduced from [13], Copyright 2020, with permission from Springer Nature. **d** R2R screen printing method of electrodes and microfluidic channel fabrication. Reproduced from [115], Copyright 2019, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). **e** An example of stretchable fiber-based electrode. Reproduced from [116], Copyright 2020, with permission from American Chemical Society. **f** Soft lithography steps of microfluidic channels. Reproduced from [101], Copyright 2016, with permission from AAAS

cuits would largely confine the flexibility, simplification, and miniaturization of such devices. At the same time, the device unavailability during recharging would disrupt the continuity of the long-term monitoring process. Currently, advances in wireless power supplies, like near-field communication (NFC) or self-powered methods (solar cells and wearable power supply cells that rely on human activities), play an essential role to provide solutions to power the data reading, processing, transmission, and even display modules of sweat sensing platforms [120–122].

Wireless power supply

Wireless power sources, such as ultrasonic powering and NFC, have been utilized in many wearable devices as emerging power supply methods. The ultrasonic power supply often requires a specialized transceiver module, which limits its use in daily life. As for NFC, it usually contains a miniaturized NFC chip and an NFC antenna, which is a short-distance radio technology based on RFID technology. Nowadays, benefiting from the extensive NFC module equipment on

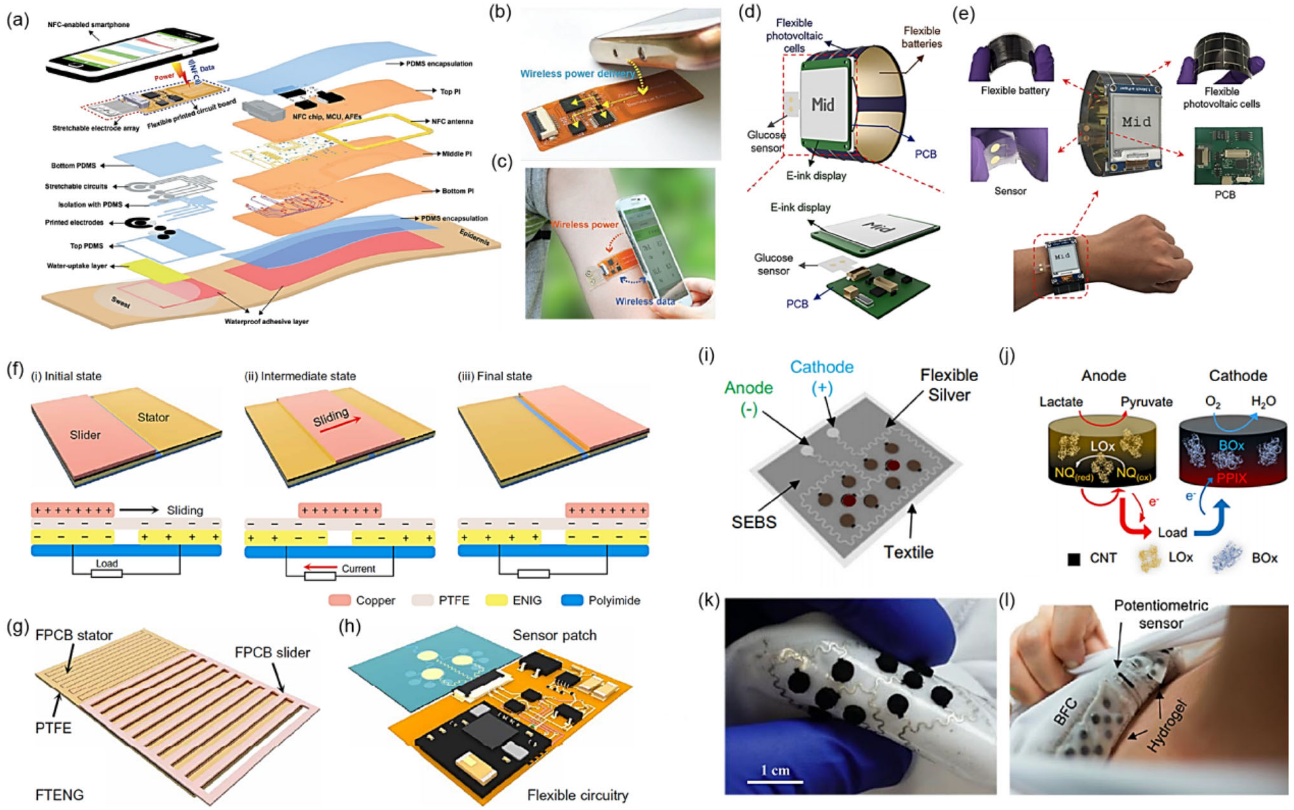

Fig. 6 Power supplies for sweat sensors. **a**–**c** An NFC power supply-based sweat sensor. Reproduced from [87], Copyright 2019, with permission from Wiley–VCH. **a** Wireless power/data transmission and the exploded view of the device when adhered to the epidermis; **b** schematic illustration of the power transmission from an NFC-enabled smartphone to the device; **c** photograph of the device bonded to a subject's arm, with a smartphone for wireless power and data transmission. **d**, **e** A solar cell power supply-based sweat smartwatch. Reproduced from [124], Copyright 2019, with permission from American Chemical Society. **d** Schematic illustrations of the self-powered smartwatch; **e** images of the smartwatch on a subject's wrist and separate components. **f**–**h** A TENG power supply-based sweat sensor. Reproduced from [126], Copyright 2020, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). **f** Schematic illustration of the working mechanism and charge distribution of a flexible TENG; **g** schematic diagram of the flexible TENG with a grating slider and an interdigital stator; **h** schematic diagram of the TENG-based flexible sweat sensor. **i**–**l** BFC power supply part of a multimodular bioenergy microgrid system. Reproduced from [129], Copyright 2021, with permission from the authors, licensed under the terms of the Creative Commons Attribution 4.0 International License (CC BY). **i** Schematic image of a textile-based BFC module; **j** charge generation mechanism of the BFC from lactate and oxygen in sweats; **k** image of the BFC module under 180° outward bending. **l** BFC modules and potentiometric sensor inside the shirt for direct sweat contact

smartphones, wireless power supply and data transmission between smartphones and sweat sensors through NFC modules offer an attractive prospect for eliminating battery restrictions. For example, Xu et al. [87] fabricated a battery-free, wireless epidermal electrochemical system by adopting NFC and printing techniques in the device. The wireless energy supply is modulated to a stable voltage output (about 2.75 V), which can be used to power the microcontroller unit (MCU) and the analog front ends for electrochemical sensing via the power management of the NFC chip. Meanwhile, smartphones integrated with NFC modules can power the system wirelessly, send commands, and obtain the detection results for further data analysis (Figs. 6a–6c).

Self-powered methods

Self-powered sweat sensors operate without the need for external power supply equipment, which greatly enhances the convenience of wearing sweat sensors while embodying the basic concepts of green energy and environmental conservation.

Solar cells

Owing to its sustainability and pollution-free nature, solar power holds great promise as a primary renewable energy source of future human societies [123]. Wearing a solar cell in direct sunshine can effectively provide the necessary power to the sweat sensor. For example, Zhao et al. [124] integrated flexible photovoltaic cells and flexible batteries onto a wrist watch to provide power for a sweat sensor and electronic ink display unit. Notably, the operations of NFC and solar cells are mainly dependent on uncontrollable external sources, such as sunlight or wireless power transmitters, which restricts their applications in cloudy weather and remote power supply scenarios (Figs. 6d and 6e).

Triboelectric nanogenerator (TENG)

The TENG is a kind of device that uses Maxwell's displacement current as the driving source to efficiently convert mechanical energy into electrical energy and signals. In random and low-frequency microenergy collection, TENG has higher energy conversion efficiency than an electromagnetic generator [125]. Since the human body is in constant motion for most of the time, wearable TENGs on the user can potentially supply sufficient energy for sweat sensors. For example, Song et al. [126] proposed a battery-free, fully self-powered wearable system that consists of a highly efficient wearable freestanding mode TENG (FTENG), a low-power wireless circuit, and a microfluidic sweat sensor patch on a single FPCB platform to dynamically monitor key sweat biomarkers. In this device, capacitors serve as the modulators and storage devices of the power generated by FTENG, and a corresponding efficient power management strategy was also proposed (Figs. 6f–6h).

Biofluid cell (BFC)

The BFC is an energy conversion device that mainly uses enzymatic reactions to convert chemical energy stored in organic compositions of biofluid into electrical energy [127]. Consisting of an anode, a cathode, and an electrolyte solution that carries charge between the two electrodes in a biofluid, the BFC can be integrated with sweat sensors to form a complete circuit system. Organic compounds of high concentration, such as lactate [102] and glucose [128] in human sweat, can serve as ideal and sustainable bioenergy sources for powering future sweat sensors. Yin et al. [129] developed the concept of a wearable smart microgrid system that consists a biofuel cell module, a triboelectric generator module for energy harvesting, and a supercapacitor module of energy storage. The BFC module in this system harvests energy from human sweat through lactate-related enzymatic electrochemical reaction, providing a continuous power supply for the whole wearable smart microgrid (Figs. 6i–6l).

Sweat extraction and collection

The volume of sweat secreted by sedentary individuals is very limited (about 20 nL per gland per min and 3 μL of sweat are generated per minute per cm^2 on the forehead or the arm) [59], which cannot provide a sufficient amount ($\geq$ 10 μL) for sweat analysis. This key challenge greatly restrains sweat sensors from obtaining enough fresh sweat. Various solutions, such as iontophoresis, heat irritation, gloves, and sweat absorb pads, have been employed in sweat extraction and collection to fulfill the first requirement of sweat sensing.

Iontophoresis is a widely adopted process to stimulate local sweat secretion at a selected skin site by using a continuous direct current to drive ions or charged chemical drugs into the skin. In one example, Emaminejad et al. [68] developed an electrochemically enhanced iontophoresis interface that can extract a sufficient volume of sweat for robust analysis without causing discomfort to patients. The result indicated that the device could consistently achieve secretory rates in excess of 100 nL/(min·cm^2) and extract sufficient amounts of sweat for reliable analysis without causing skin damage or discomfort in the subjects (Figs. 7a and 7b). However, improper iontophoresis parameters, such as current and drug dosage, can easily result in a feeling of chemical, thermal, and electrical burning on the skin of subjects. In addition, sweating rates decrease after repeated current applications [75]. These challenges still need to be addressed for a wider implementation of iontophoresis.

Further methods of sweat collection have also been proposed. Leveraging the design of microfluidic structures and hydrophilic fillers can accelerate the process of sweat collection. For instance, Nyein et al. [108] presented a wearable device for the rapid uptake of nL min^{-1} cm^{-2} rates of thermoregulatory sweat at rest, enabling a near real-time sweat rate and composition analysis at resting state. Compared with devices without hydrophilic filler, the integration of hydrophilic filler in this design enables the rapid collection and transport of fluid into the channel (Fig. 7c). The fingertips, palm, and back of the hand have the highest sweat gland densities, thus presenting attractive sites for accessing natural sweat. The inhibition of sweat evaporation in these sites is also an effective way for sweat collection. For example, Bariya et al. [75] presented wearable sweat sensors in airtight gloves for the rapid accumulation of natural thermoregulatory sweat without active sweat stimulation. The main function of the glove-based platform is to create an evaporation barrier (Fig. 7d). As the most natural methods of sweat extraction, thermal irritation, including a passive warm environment and active exercises, is widely employed to generate sweat samples for analysis. High room temperature can irritate the human body that responds by the secretion of sweat to maintain a relatively stable body temperature [49]. When people do exercise, like swimming, boxing, cycling, or

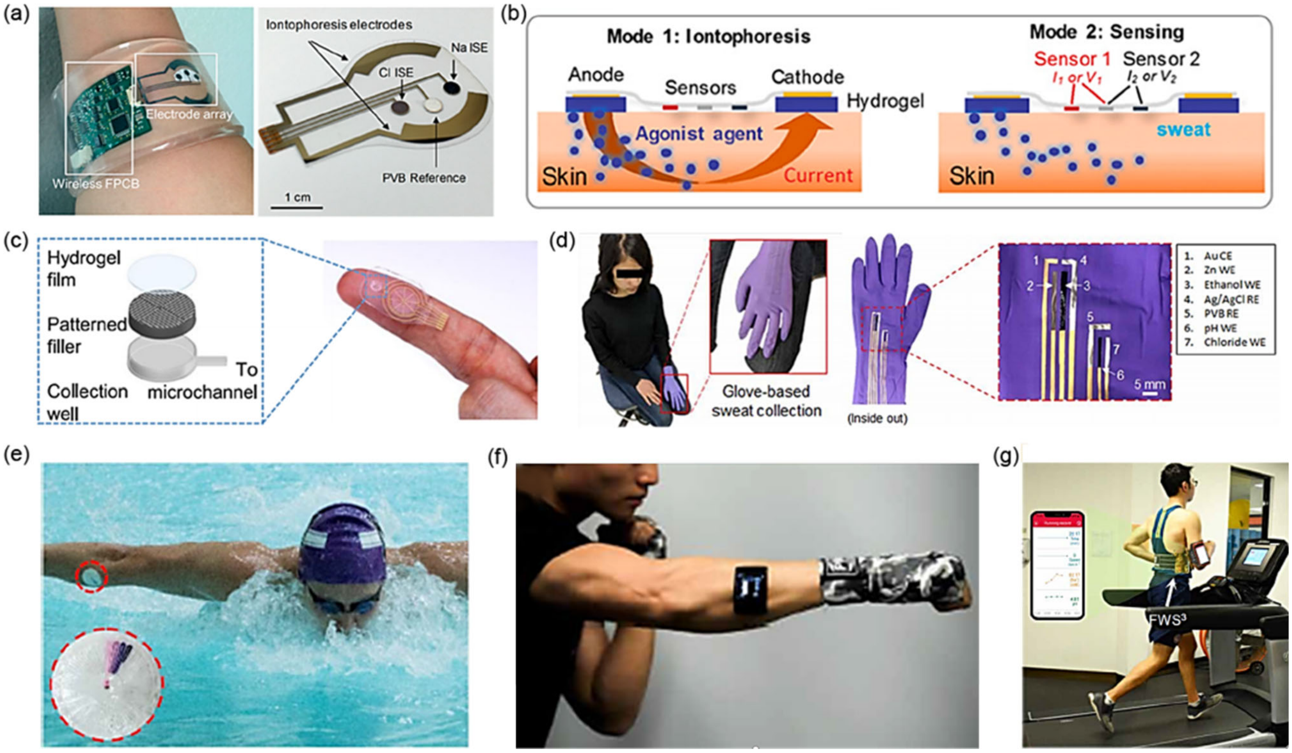

Fig. 7 Various sweat extraction and collection methods: **a** a sweat band with iontophoresis electrodes. Reproduced from [68], Copyright 2017, with permission from National Academy of Sciences, USA. **b** Mechanism of iontophoresis. Reproduced from [68], Copyright 2017, with permission from National Academy of Sciences, USA. **c** Hydrophilic fillers for rapid sweat uptake into the sensing channel. Reproduced from [108], Copyright 2021, with permission from the authors, licensed under the terms of the Creative Commons Attribution 4.0 International License (CC BY). **d** Photograph of a subject wearing a gloved-based sweat sensor. Gold electrodes are evaporated on the inner glove surface and functionalized with sensing layers to target chemical compositions. Reproduced from [75], Copyright 2020, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). **e** Sweat sensing during swimming. Reproduced from [40], Copyright 2019, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). **f** Sweat sensing during boxing. Reproduced from [41], Copyright 2020, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC). **g** Sweat sensing during running. Reproduced from [126], Copyright 2020, with permission from the authors, licensed under a Creative Commons Attribution NonCommercial License 4.0 (CC BY-NC)

running, the body's sweat glands also secrete large amounts of sweat in order to maintain thermal homeostasis, which provides a great opportunity to monitor body water loss and analyze sweat chemical compositions (Figs. 7e–7g).

Conclusions and outlook

This review highlighted the recent advances in wearable sweat sensors in terms of devices and applications. We firstly introduced basic structural designs and materials applied in sweat sensors. Next, various electrochemical and colorimetric sensing mechanisms were compared and discussed for the in-depth analysis of the rich chemical and physical information found in human sweat. In addition, several well-established fabrication technologies of electrodes and microfluidic channels were summarized. Ancillary issues, such as power supply and methods of sweat extraction and collection, were also discussed.

Although numerous proof-of-concept demonstrations have been presented in the relevant literature, the challenges detailed below should be addressed to realize the true potential of wearable sweat sensing technologies [130, 131].

1. A significant challenge is variation in the sweat contents of individuals and body regions due to environmental and physiological differences [132]. As aforementioned, various sweat extraction methods and different attachment regions of the human body have been proposed to collect enough sweat for analysis. Nevertheless, one problem is that the chemical composition of sweat varies depending on where it is collected and how it is extracted [5, 113]. Differences in age and gender also affect the sweat composition. Establishing an accurate and personalized

database of sweat composition with dynamic fluctuation ranges enables the further development and applications of wearable sensors. Addressing this challenge requires methods like gender- and age-based long-term monitoring, so as to collect enough sweat data for database mining.
2. The existing golden standard of clinical scenarios is the blood test. A better understanding of the mechanism of sweat secretion and relationships between analyte concentrations in blood and sweat is needed to enhance the reliability and validity of sweat-based results [5, 68]. Therefore, massive wearable sweat sensor performance and blood test relationship studies are necessary, which can potentially facilitate the clinical acceptance of data gathered by wearable sweat sensors.
3. The chemical composition level of sweat has a strong relationship with the physical parameters, such as sweat loss and sweat rate [5, 48]. Using a sweat sensing platform to monitor both the chemical and the physical signals simultaneously can compensate for the effects of external temperature and help to more accurately analyze sweat composition levels by referring to sweat loss and rates.
4. The chemical composition of sweat is extremely diverse [133], while some trace level target analytes, such as proteins, cytokines, and antigens [134], require the device to have a high sensitivity. Several sensing modalities in the biosensing field, such as immune sensing, aptamer sensing, and fluorescence sensing technologies [66, 90, 135], can potentially detect these trace substances, thereby extracting further valuable information from sweat analysis.
5. Wireless data communication and power management need to be further explored and established for practical applications with higher efficiency. The sweat sampling frequency needs to be controlled depending on the user's status, such as exercise with high sweating or little sweating while sleeping. Although wireless data communications have been demonstrated by conventional wireless fidelity (Wi-Fi), NFC, or RFID technologies, more energy-efficient wireless communication methods require the ambulatory wireless sweat sensing technology. Energy-efficient modules and consumer-oriented power regulating algorithms can be integrated into the devices for smart power management.
6. Calibration issues, which are also of concern in sweat sensors, have a great impact on the convenience of use. Usually, most of the sweat sensors with fixed sensitivity require single-point calibration in a standard concentration solution before use, while the sweat sensors with unstable sensitivity (device differences, sensitivity fluctuation over long time periods) require multipoint calibration to improve the reliability of monitoring data. Although various calibration-free strategies have been proposed [136], calibration accuracy remains one of the major concerns of sweat sensors.

The above challenges and corresponding potential solutions provide great opportunities for the constant evolution and wide adoption of sweat sensing technologies. Interdisciplinary engineering efforts are needed to design several elements of wearable sweat sensors. Thus, a close cooperation among clinical doctors, scientists and engineers is crucial. The ideal sweat sensing system should be of high clinical acceptance, stable, and low cost, which could thus play an essential role in the monitoring of daily health and athletic activities, as well as the prevention, diagnosis, treatment, and prognosis of diseases.

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Declarations

Conflict of interest The authors declare that there is no conflict of interest.

Ethical approval This article does not contain any studies with human or animal subjects performed by any of the authors.

References

1. Yu Y, Suh MJ, Sikorski P et al (2014) Urine sample preparation in 96-well filter plates for quantitative clinical proteomics. Anal Chem 86(11):5470–5477. https://doi.org/10.1021/ac5008317
2. Torrente-Rodríguez RM, Lukas H, Tu J et al (2020) SARS-CoV-2 RapidPlex: a graphene-based multiplexed telemedicine platform for rapid and low-cost COVID-19 diagnosis and monitoring. Matter 3(6):1981–1998. https://doi.org/10.1016/j.matt.2020.09.027
3. Farandos NM, Yetisen AK, Monteiro MJ et al (2015) Contact lens sensors in ocular diagnostics. Adv Healthcare Mater 4(6):792–810. https://doi.org/10.1002/adhm.201400504
4. Kim J, Sempionatto JR, Imani S et al (2018) Simultaneous monitoring of sweat and interstitial fluid using a single wearable biosensor platform. Adv Sci 5(10):1800880. https://doi.org/10.1002/advs.201800880
5. Kim J, Campbell AS, de Ávila BEF et al (2019) Wearable biosensors for healthcare monitoring. Nat Biotechnol 37(4):389–406. https://doi.org/10.1038/s41587-019-0045-y
6. Jessen C (2001) Temperature regulation in humans and other mammals. Springer, Berlin
7. Xu K, Lu Y, Takei K (2021) Flexible hybrid sensor systems with feedback functions. Adv Funct Mater 31(39):2007436. https://doi.org/10.1002/adfm.202007436

8. Lu Y, Fujita Y, Honda S et al (2021) Wireless and flexible skin moisture and temperature sensor sheets toward the study of thermoregulator center. Adv Healthcare Mater 10(17):2100103. https://doi.org/10.1002/adhm.202100103
9. Yang G, Deng J, Pang G et al (2018) An IoT-enabled stroke rehabilitation system based on smart wearable armband and machine learning. IEEE J Transl Eng Health Med 6:1–10. https://doi.org/10.1109/JTEHM.2018.2822681
10. Xu K, Lu Y, Takei K (2019) Multifunctional skin-inspired flexible sensor systems for wearable electronics. Adv Mater Technol 4(3):1800628. https://doi.org/10.1002/admt.201800628
11. Heng W, Pang G, Xu F et al (2019) Flexible insole sensors with stably connected electrodes for gait phase detection. Sensors 19(23):5197. https://doi.org/10.3390/s19235197
12. Yang G, Pang G, Pang Z et al (2019) Non-invasive flexible and stretchable wearable sensors with nano-based enhancement for chronic disease care. IEEE Rev Biomed Eng 12:34–71. https://doi.org/10.1109/RBME.2018.2887301
13. Yang Y, Song Y, Bo X et al (2020) A laser-engraved wearable sensor for sensitive detection of uric acid and tyrosine in sweat. Nat Biotechnol 38(2):217–224. https://doi.org/10.1038/s41587-019-0321-x
14. Rogers JA, Someya T, Huang Y (2010) Materials and mechanics for stretchable electronics. Science 327(5973):1603–1607. https://doi.org/10.1126/science.1182383
15. Wang G, Zhang S, Dong S et al (2019) Stretchable optical sensing patch system integrated heart rate, pulse oxygen saturation, and sweat pH detection. IEEE Trans Biomed Eng 66(4):1000–1005. https://doi.org/10.1109/TBME.2018.2866151
16. Wang C, Wang C, Huang Z et al (2018) Materials and structures toward soft electronics. Adv Mater 30(50):1801368. https://doi.org/10.1002/adma.201801368
17. Li BM, Kim I, Zhou Y et al (2019) Kirigami-inspired textile electronics: K.I.T.E. Adv Mater Technol 4(11):1900511. https://doi.org/10.1002/admt.201900511
18. Ning X, Wang X, Zhang Y et al (2018) Assembly of advanced materials into 3D functional structures by methods inspired by origami and kirigami: a review. Adv Mater Interf 5(13):1800284. https://doi.org/10.1002/admi.201800284
19. He W, Wang C, Wang H et al (2019) Integrated textile sensor patch for real-time and multiplex sweat analysis. Sci Adv 5(11):eaax0649. https://doi.org/10.1126/sciadv.aax0649
20. Xu F, Zhu Y (2012) Highly conductive and stretchable silver nanowire conductors. Adv Mater 24(37):5117–5122. https://doi.org/10.1002/adma.201201886
21. Kaltenbrunner M, Sekitani T, Reeder J et al (2013) An ultra-lightweight design for imperceptible plastic electronics. Nature 499(7459):458–463. https://doi.org/10.1038/nature12314
22. Zhang H, Xiang L, Yang Y et al (2018) High-performance carbon nanotube complementary electronics and integrated sensor systems on ultrathin plastic foil. ACS Nano 12(3):2773–2779. https://doi.org/10.1021/acsnano.7b09145
23. Wang L, Wang L, Zhang Y et al (2018) Weaving sensing fibers into electrochemical fabric for real-time health monitoring. Adv Funct Mater 28(42):1804456. https://doi.org/10.1002/adfm.201804456
24. Chan EP, Smith EJ, Hayward RC et al (2008) Surface wrinkles for smart adhesion. Adv Mater 20(4):711–716. https://doi.org/10.1002/adma.200701530
25. Kim K, Kim SU, Choi S et al (2020) High-definition optophysical image construction using mosaics of pixelated wrinkles. Adv Sci 7(24):2002134. https://doi.org/10.1002/advs.202002134
26. Toi PT, Trung TQ, Dang TML et al (2019) Highly electrocatalytic, durable, and stretchable nanohybrid fiber for on-body sweat glucose detection. ACS Appl Mater Interf 11(11):10707–10717. https://doi.org/10.1021/acsami.8b20583
27. Mohan AMV, Kim N, Gu Y et al (2017) Merging of thin- and thick-film fabrication technologies: toward soft stretchable "island–bridge" devices. Adv Mater Technol 2(4):1600284. https://doi.org/10.1002/admt.201600284
28. Song Z, Ma T, Tang R et al (2014) Origami lithium-ion batteries Nat Commun 5(1):1–6. https://doi.org/10.1038/ncomms4140
29. Hojaiji H, Zhao Y, Gong MC et al (2020) An autonomous wearable system for diurnal sweat biomarker data acquisition. Lab Chip 20(24):4582–4591. https://doi.org/10.1039/D0LC00820F
30. Heng W, Yang G, Pang G et al (2021) Fluid-driven soft CoboSkin for safer human–robot collaboration: fabrication and adaptation. Adv Intell Syst 3(3):2000038. https://doi.org/10.1002/aisy.202000038
31. Pang G, Yang G, Heng W et al (2021) CoboSkin: soft robot skin with variable stiffness for safer human–robot collaboration. IEEE Trans Ind Electron 68(4):3303–3314. https://doi.org/10.1109/TIE.2020.2978728
32. Huang X, Liu Y, Chen K et al (2014) Stretchable, wireless sensors and functional substrates for epidermal characterization of sweat. Small 10(15):3083–3090. https://doi.org/10.1002/smll.201400483
33. Ding R, Lisak G (2019) Sponge-based microfluidic sampling for potentiometric ion sensing. Anal Chim Acta 1091:103–111. https://doi.org/10.1016/j.aca.2019.09.024
34. Xu K, Lu Y, Yamaguchi T et al (2019) Highly precise multifunctional thermal management-based flexible sensing sheets. ACS Nano 13(12):14348–14356. https://doi.org/10.1021/acsnano.9b07805
35. Lu Y, Xu K, Yang MQ et al (2021) Highly stable Pd/HNb$_3$O$_8$-based flexible humidity sensor for perdurable wireless wearable applications. Nanoscale Horiz 6(3):260–270. https://doi.org/10.1039/D0NH00594K
36. Imani S, Bandodkar AJ, Mohan AMV et al (2016) A wearable chemical–electrophysiological hybrid biosensing system for real-time health and fitness monitoring. Nat Commun 7(1):1–7. https://doi.org/10.1038/ncomms11650
37. Nakata S, Shiomi M, Fujita Y et al (2018) A wearable pH sensor with high sensitivity based on a flexible charge-coupled device. Nat Electron 1(11):596–603. https://doi.org/10.1038/s41928-018-0162-5
38. Xu K, Fujita Y, Lu Y et al (2021) A wearable body condition sensor system with wireless feedback alarm functions. Adv Mater 33(18):2008701. https://doi.org/10.1002/adma.202008701
39. Yang H, Xu K, Xu C et al (2019) Femtosecond laser fabricated elastomeric superhydrophobic surface with stretching-enhanced water repellency. Nanoscale Res Lett 14(1):1–10. https://doi.org/10.1186/s11671-019-3140-6
40. Reeder JT, Choi J, Xue Y et al (2019) Waterproof, electronics-enabled, epidermal microfluidic devices for sweat collection, biomarker analysis, and thermography in aquatic settings. Sci Adv 5(1):eaau6356. https://doi.org/10.1126/sciadv.aau6356
41. Zhao Y, Wang B, Hojaiji H et al (2020) A wearable freestanding electrochemical sensing system. Sci Adv 6(12):eaaz0007. https://doi.org/10.1126/sciadv.aaz0007
42. Zhao Z, Li Q, Chen L et al (2021) A thread/fabric-based band as a flexible and wearable microfluidic device for sweat sensing and monitoring. Lab Chip 21(5):916–932. https://doi.org/10.1039/D0LC01075H
43. Xu K, Zhou R, Takei K et al (2019) Toward flexible surface-enhanced Raman scattering (SERS) sensors for point-of-care diagnostics. Adv Sci 6(16):1900925. https://doi.org/10.1002/advs.201900925
44. Li H, Cheng F, Robledo-Lara JA et al (2020) Fabrication of paper-based devices for in vitro tissue modeling. Bio-Des Manuf 3:252–265. https://doi.org/10.1007/s42242-020-00077-5

45. Liang B, Cao Q, Mao X et al (2021) An integrated paper-based microfluidic device for real-time sweat potassium monitoring. IEEE Sens J 21(8):9642–9648. https://doi.org/10.1109/JSEN.2020.3009327
46. Li M, Wang L, Liu R et al (2021) A highly integrated sensing paper for wearable electrochemical sweat analysis. Biosens Bioelectron 174:112828. https://doi.org/10.1016/j.bios.2020.112828
47. Sato K, Kang WH, Saga K et al (1989) Biology of sweat glands and their disorders. I. Normal sweat gland function. J Am Acad Dermatol 20:537–563. https://doi.org/10.1016/S0190-9622(89)70063-3
48. Yang Y, Gao W (2019) Wearable and flexible electronics for continuous molecular monitoring. Chem Soc Rev 48(6):1465–1491. https://doi.org/10.1039/C7CS00730B
49. Lee H, Choi TK, Lee YB et al (2016) A graphene-based electrochemical device with thermoresponsive microneedles for diabetes monitoring and therapy. Nat Nanotechnol 11(6):566–572. https://doi.org/10.1038/nnano.2016.38
50. Zhang J, Xu J, Lim J et al (2021) Wearable glucose monitoring and implantable drug delivery systems for diabetes management. Adv Healthcare Mater 10(17):2100194. https://doi.org/10.1002/adhm.202100194
51. Kim SB, Lee K, Raj MS et al (2018) Soft, skin-interfaced microfluidic systems with wireless, battery-free electronics for digital, real-time tracking of sweat loss and electrolyte composition. Small 14(45):1802876. https://doi.org/10.1002/smll.201802876
52. Sempionatto JR, Lin M, Yin L et al (2021) An epidermal patch for the simultaneous monitoring of haemodynamic and metabolic biomarkers. Nat Biomed Eng 5:737–748. https://doi.org/10.1038/s41551-021-00685-1
53. Kidwell DA, Holland JC, Athanaselis S (1998) Testing for drugs of abuse in saliva and sweat. J Chromatogr B Biomed Sci Appl 713(1):111–135. https://doi.org/10.1016/S0378-4347(97)00572-0
54. Torrente-Rodríguez RM, Tu J, Yang Y et al (2020) Investigation of cortisol dynamics in human sweat using a graphene-based wireless mHealth system. Matter 2(4):921–937. https://doi.org/10.1016/j.matt.2020.01.021
55. Madhu S, Anthuuvan AJ, Ramasamy S et al (2020) ZnO nanorod integrated flexible carbon fibers for sweat cortisol detection. ACS Appl Electron Mater 2(2):499–509. https://doi.org/10.1021/acsaelm.9b00730
56. Amjadi M, Kyung KU, Park I et al (2016) Stretchable, skin-mountable, and wearable strain sensors and their potential applications: a review. Adv Funct Mater 26(11):1678–1698. https://doi.org/10.1002/adfm.201504755
57. Zhou W, Yao S, Wang H et al (2020) Gas-permeable, ultrathin, stretchable epidermal electronics with porous electrodes. ACS Nano 14(5):5798–5805. https://doi.org/10.1021/acsnano.0c00906
58. Yu Y, Nyein HYY, Gao W et al (2020) Flexible electrochemical bioelectronics: the rise of in situ bioanalysis. Adv Mater 32(15):1902083. https://doi.org/10.1002/adma.201902083
59. Bariya M, Nyein HYY, Javey A (2018) Wearable sweat sensors Nat Electron 1(3):160–171. https://doi.org/10.1038/s41928-018-0043-y
60. Parrilla M, Cuartero M, Crespo GA (2019) Wearable potentiometric ion sensors. TrAC Trends Anal Chem 110:303–320. https://doi.org/10.1016/j.trac.2018.11.024
61. Zhai Q, Yap LW, Wang R et al (2020) Vertically aligned gold nanowires as stretchable and wearable epidermal ion-selective electrode for noninvasive multiplexed sweat analysis. Anal Chem 92(6):4647–4655. https://doi.org/10.1021/acs.analchem.0c00274
62. Oh SY, Hong SY, Jeong YR et al (2018) Skin-attachable, stretchable electrochemical sweat sensor for glucose and pH detection. ACS Appl Mater Interf 10(16):13729–13740. https://doi.org/10.1021/acsami.8b03342
63. Bai YF, Xu TB, Luong JHT et al (2014) Direct electron transfer of glucose oxidase-boron doped diamond interface: a new solution for a classical problem. Anal Chem 86(10):4910–4918. https://doi.org/10.1021/ac501143e
64. Hui X, Sharifuzzaman M, Sharma S et al (2020) High-performance flexible electrochemical heavy metal sensor based on layer-by-layer assembly of $Ti_3C_2T_x$ /MWNTs nanocomposites for noninvasive detection of copper and zinc ions in human biofluids. ACS Appl Mater Interf 12(43):48928–48937. https://doi.org/10.1021/acsami.0c12239
65. Kinnamon D, Ghanta R, Lin KC et al (2017) Portable biosensor for monitoring cortisol in low-volume perspired human sweat. Sci Rep 7(1):13312. https://doi.org/10.1038/s41598-017-13684-7
66. Ganguly A, Lin KC, Muthukumar S et al (2021) Autonomous, real-time monitoring electrochemical aptasensor for circadian tracking of cortisol hormone in sub-microliter volumes of passively eluted human sweat. ACS Sens 6(1):63–72. https://doi.org/10.1021/acssensors.0c01754
67. Gao W, Emaminejad S, Nyein HYY et al (2016) Fully integrated wearable sensor arrays for multiplexed in situ perspiration analysis. Nature 529(7587):509–514. https://doi.org/10.1038/nature16521
68. Emaminejad S, Gao W, Wu E et al (2017) Autonomous sweat extraction and analysis applied to cystic fibrosis and glucose monitoring using a fully integrated wearable platform. Proc Natl Acad Sci 114(18):4625–4630. https://doi.org/10.1073/pnas.1701740114
69. Anastasova S, Crewther B, Bembnowicz P et al (2017) A wearable multisensing patch for continuous sweat monitoring. Biosens Bioelectron 93:139–145. https://doi.org/10.1016/j.bios.2016.09.038
70. Guinovart T, Bandodkar AJ, Windmiller JR et al (2013) A potentiometric tattoo sensor for monitoring ammonium in sweat. Analyst 138(22):7031–7038. https://doi.org/10.1039/C3AN01672B
71. Nyein HYY, Gao W, Shahpar Z et al (2016) A wearable electrochemical platform for noninvasive simultaneous monitoring of Ca^{2+} and pH. ACS Nano 10(7):7216–7224. https://doi.org/10.1021/acsnano.6b04005
72. Amatore C, Szunerits S, Thouin L (2000) Mapping concentration profiles within the diffusion layer of an electrode Part II. Potentiometric measurements with an ultramicroelectrode. Electrochem Commun 2(4):248–253. https://doi.org/10.1016/S1388-2481(00)00016-3
73. Alizadeh A, Burns A, Lenigk R et al (2018) A wearable patch for continuous monitoring of sweat electrolytes during exertion. Lab Chip 18(17):2632–2641. https://doi.org/10.1039/C8LC00510A
74. Yu Y, Nassar J, Xu C et al (2020) Biofuel-powered soft electronic skin with multiplexed and wireless sensing for human-machine interfaces. Sci Robot 5(41):eaaz7946. https://doi.org/10.1126/scirobotics.aaz7946
75. Bariya M, Li L, Ghattamaneni R et al (2020) Glove-based sensors for multimodal monitoring of natural sweat. Sci Adv 6(35):eabb8308. https://doi.org/10.1126/sciadv.abb8308
76. Xu Y, Zhao G, Zhu L et al (2020) Pencil–paper on-skin electronics. Proc Natl Acad Sci 117(31):18292–18301. https://doi.org/10.1073/pnas.2008422117
77. Kim J, Jeerapan I, Imani S et al (2016) Noninvasive alcohol monitoring using a wearable tattoo-based iontophoretic-biosensing system. ACS Sens 1(8):1011–1019. https://doi.org/10.1021/acssensors.6b00356
78. Windmiller JR, Bandodkar AJ, Valdés-Ramírez G et al (2012) Electrochemical sensing based on printable temporary transfer tattoos. Chem Commun 48(54):6794–6796. https://doi.org/10.1039/c2cc32839a

79. Jia W, Bandodkar AJ, Valdés-Ramírez G et al (2013) Electrochemical tattoo biosensors for real-time noninvasive lactate monitoring in human perspiration. Anal Chem 85(14):6553–6560. https://doi.org/10.1021/ac401573r
80. Gao W, Nyein HYY, Shahpar Z et al (2016) Wearable microsensor array for multiplexed heavy metal monitoring of body fluids. ACS Sens 1(17):866–874. https://doi.org/10.1021/acssensors.6b00287
81. Lin S, Wang B, Yu W et al (2020) Design framework and sensing system for noninvasive wearable electroactive drug monitoring. ACS Sens 5(1):265–273. https://doi.org/10.1021/acssensors.9b02233
82. Wang J (2008) Electrochemical glucose biosensors. Chem Rev 108(2):814–825. https://doi.org/10.1021/cr068123a
83. Cheng X, Wang B, Zhao Y et al (2020) A mediator-free electroenzymatic sensing methodology to mitigate ionic and electroactive interferents' effects for reliable wearable metabolite and nutrient monitoring. Adv Funct Mater 30(10):1908507. https://doi.org/10.1002/adfm.201908507
84. Martín A, Kim J, Kurniawan JF et al (2017) Epidermal microfluidic electrochemical detection system: enhanced sweat sampling and metabolite detection. ACS Sens 2(12):1860–1868. https://doi.org/10.1021/acssensors.7b00729
85. Teymourian H, Barfidokht A, Wang J (2020) Electrochemical glucose sensors in diabetes management: an updated review (2010–2020). Chem Soc Rev 49:7671–7709. https://doi.org/10.1039/D0CS00304B
86. Tai LC, Ahn CH, Nyein HYY et al (2020) Nicotine monitoring with a wearable sweat band. ACS Sens 5(6):1831–1837. https://doi.org/10.1021/acssensors.0c00791
87. Xu G, Cheng C, Liu Z et al (2019) Battery-free and wireless epidermal electrochemical system with all-printed stretchable electrode array for multiplexed in situ sweat analysis. Adv Mater Technol 4(7):1800658. https://doi.org/10.1002/admt.201800658
88. Bandodkar AJ, Hung VWS, Jia W et al (2013) Tattoo-based potentiometric ion-selective sensors for epidermal pH monitoring. Analyst 138(1):123–128. https://doi.org/10.1039/C2AN36422K
89. Zhao Y, Zhai Q, Dong D et al (2019) Highly stretchable and strain-insensitive fiber-based wearable electrochemical biosensor to monitor glucose in the sweat. Anal Chem 91(10):6569–6576. https://doi.org/10.1021/acs.analchem.9b00152
90. Kim S, Lee B, Reeder JT et al (2020) Soft, skin-interfaced microfluidic systems with integrated immunoassays, fluorometric sensors, and impedance measurement capabilities. Proc Natl Acad Sci 117(45):27906–27915. https://doi.org/10.1073/pnas.2012700117
91. Nyein HYY, Tai LC, Ngo QP et al (2018) A wearable microfluidic sensing patch for dynamic sweat secretion analysis. ACS Sens 3(5):944–952. https://doi.org/10.1021/acssensors.7b00961
92. Rose DP, Ratterman ME, Griffin DK et al (2015) Adhesive RFID sensor patch for monitoring of sweat electrolytes. IEEE Trans Biomed Eng 62(6):1457–1465. https://doi.org/10.1109/TBME.2014.2369991
93. Xiao G, He J, Chen X et al (2019) A wearable, cotton thread/paper-based microfluidic device coupled with smartphone for sweat glucose sensing. Cellulose 26(7):4553–4562. https://doi.org/10.1007/s10570-019-02396-y
94. Kwon K, Kim JU, Deng Y et al (2021) An on-skin platform for wireless monitoring of flow rate, cumulative loss and temperature of sweat in real time. Nat Electron 4(4):302–312. https://doi.org/10.1038/s41928-021-00556-2
95. Lin S, Yu W, Wang B et al (2020) Noninvasive wearable electroactive pharmaceutical monitoring for personalized therapeutics. Proc Natl Acad Sci 117(32):19017–19025. https://doi.org/10.1073/pnas.2009979117
96. Ghaffari R, Choi J, Raj MS et al (2020) Soft wearable systems for colorimetric and electrochemical analysis of biofluids. Adv Funct Mater 30(37):1907269. https://doi.org/10.1002/adfm.201907269
97. Kim SB, Zhang Y, Won SM et al (2018) Super-absorbent polymer valves and colorimetric chemistries for time-sequenced discrete sampling and chloride analysis of sweat via skin-mounted soft microfluidics. Small 14(12):1703334. https://doi.org/10.1002/smll.201703334
98. Promphet N, Rattanawaleedirojn P, Siralertmukul K et al (2019) Non-invasive textile based colorimetric sensor for the simultaneous detection of sweat pH and lactate. Talanta 192:424–430. https://doi.org/10.1016/j.talanta.2018.09.086
99. Vaquer A, Barón E, de la Rica R (2021) Wearable analytical platform with enzyme-modulated dynamic range for the simultaneous colorimetric detection of sweat volume and sweat biomarkers. ACS Sens 6(1):130–136. https://doi.org/10.1021/acssensors.0c01980
100. He J, Xiao G, Chen X et al (2019) A thermoresponsive microfluidic system integrating a shape memory polymer-modified textile and a paper-based colorimetric sensor for the detection of glucose in human sweat. RSC Adv 9(41):23957–23963. https://doi.org/10.1039/C9RA02831E
101. Koh A, Kang D, Xue Y et al (2016) A soft, wearable microfluidic device for the capture, storage, and colorimetric sensing of sweat. Sci Transl Med 8(366):366ra165. https://doi.org/10.1126/scitranslmed.aaf2593
102. Bandodkar AJ, Gutruf P, Choi J et al (2019) Battery-free, skin-interfaced microfluidic/electronic systems for simultaneous electrochemical, colorimetric, and volumetric analysis of sweat. Sci Adv 5(1):eaav3294. https://doi.org/10.1126/sciadv.aav3294
103. Choi J, Bandodkar AJ, Reeder JT et al (2019) Soft, skin-integrated multifunctional microfluidic systems for accurate colorimetric analysis of sweat biomarkers and temperature. ACS Sens 4(2):379–388. https://doi.org/10.1021/acssensors.8b01218
104. Sekine Y, Kim SB, Zhang Y et al (2018) A fluorometric skin-interfaced microfluidic device and smartphone imaging module for in situ quantitative analysis of sweat chemistry. Lab Chip 18(15):2178–2186. https://doi.org/10.1039/C8LC00530C
105. Morris NB, Cramer MN, Hodder SG et al (2013) A comparison between the technical absorbent and ventilated capsule methods for measuring local sweat rate. J Appl Physiol 114(6):816–823. https://doi.org/10.1152/japplphysiol.01088.2012
106. Parrilla M, Guinovart T, Ferré J et al (2019) A wearable paper-based sweat sensor for human perspiration monitoring. Adv Healthcare Mater 8(16):1900342. https://doi.org/10.1002/adhm.201900342
107. Reeder JT, Xue Y, Franklin D et al (2019) Resettable skin interfaced microfluidic sweat collection devices with chemesthetic hydration feedback. Nat Commun 10(1):1–12. https://doi.org/10.1038/s41467-019-13431-8
108. Nyein HYY, Bariya M, Tran B et al (2021) A wearable patch for continuous analysis of thermoregulatory sweat at rest. Nat Commun 12(1):1–13. https://doi.org/10.1038/s41467-021-22109-z
109. Choi DH, Gonzales M, Kitchen GB et al (2020) A capacitive sweat rate sensor for continuous and real-time monitoring of sweat loss. ACS Sens 5(12):3821–3826. https://doi.org/10.1021/acssensors.0c01219
110. Choi J, Xue Y, Xia W et al (2017) Soft, skin-mounted microfluidic systems for measuring secretory fluidic pressures generated at the surface of the skin by eccrine sweat glands. Lab Chip 17(15):2572–2580. https://doi.org/10.1039/C7LC00525C
111. He Q, Das SR, Garland NT et al (2017) Enabling inkjet printed graphene for ion selective electrodes with postprint thermal annealing. ACS Appl Mater Interf 9(14):12719–12727. https://doi.org/10.1021/acsami.7b00092

112. Zoerner A, Oertel S, Jank MPM et al (2018) Human sweat analysis using a portable device based on a screen-printed electrolyte sensor. Electroanalysis 30(4):665–671. https://doi.org/10.1002/elan.201700672
113. Abrar M, Dong Y, Lee P et al (2016) Bendable electro-chemical lactate sensor with printed silver nano ink. Sci Rep 6(1):1–9. https://doi.org/10.1038/srep30565
114. Dong Y, Min X, Kim WS (2018) A 3D printed integrated electrochemical sensor system. IEEE Sens J 18(7):2959–2966. https://doi.org/10.1109/JSEN.2018.2801459
115. Nyein HYY, Bariya M, Kivimäki L et al (2019) Regional and correlative sweat analysis using high-throughput microfluidic sensing patches toward decoding sweat. Sci Adv 5(8):eaaw9906. https://doi.org/10.1126/sciadv.aaw9906
116. Xu J, Zhang Z, Gan S et al (2020) Highly stretchable fiber-based potentiometric ion sensors for multichannel real-time analysis of human sweat. ACS Sens 5(9):2834–2842. https://doi.org/10.1021/acssensors.0c00960
117. Su R, Wen J, Su Q et al (2020) 3D printed self-supporting elastomeric structures for multifunctional microfluidics. Sci Adv 6(41):eabc9846. https://doi.org/10.1126/sciadv.abc9846
118. Mehta V, Rath SN (2021) 3D printed microfluidic devices: a review focused on four fundamental manufacturing approaches and implications on the field of healthcare. Bio-Des Manuf 4:311–343. https://doi.org/10.1007/s42242-020-00112-5
119. Francis J, Stamper I, Heikenfeld J et al (2018) Digital nanoliter to milliliter flow rate sensor with in vivo demonstration for continuous sweat rate measurement. Lab Chip 19(1):178–185. https://doi.org/10.1039/C8LC00968F
120. Ouyang H, Jiang D, Fan Y et al (2021) Self-powered technology for next-generation biosensor. Sci Bull 66(17):1709–1712. https://doi.org/10.1016/j.scib.2021.04.035
121. Zou Y, Bo L, Li Z (2021) Recent progress in human body energy harvesting for smart bioelectronic system. Fundam Res 1(3):364–382. https://doi.org/10.1016/j.fmre.2021.05.002
122. Tan P, Zou Y, Fan Y et al (2020) Self-powered wearable electronics. Wearable Technol 1:e5. https://doi.org/10.1017/wtc.2020.3
123. Gu X, Zhou Y, Gu K et al (2017) Roll-to-roll printed large-area all-polymer solar cells with 5% efficiency based on a low crystallinity conjugated polymer blend. Adv Energy Mater 7(14):1602742. https://doi.org/10.1002/aenm.201602742
124. Zhao J, Lin Y, Wu J et al (2019) A fully integrated and self-powered smartwatch for continuous sweat glucose monitoring. ACS Sens 4(7):1925–1933. https://doi.org/10.1021/acssensors.9b00891
125. Luo J, Gao W, Wang ZL (2021) The triboelectric nanogenerator as an innovative technology toward intelligent sports. Adv Mater 33(17):2004178. https://doi.org/10.1002/adma.202004178
126. Song Y, Min J, Yu Y et al (2020) Wireless battery-free wearable sweat sensor powered by human motion. Sci Adv 6(40):eaay9842. https://doi.org/10.1126/sciadv.aay9842
127. Yin L, Moon JM, Sempionatto JR et al (2021) A passive perspiration biofuel cell: high energy return on investment. Joule 5(7):1888–1904. https://doi.org/10.1016/j.joule.2021.06.004
128. Yeknami AF, Wang X, Jeerapan I et al (2018) A 0.3-V CMOS biofuel-cell-powered wireless glucose/lactate biosensing system. IEEE J Solid-State Circ 53(11):3126–3139. https://doi.org/10.1109/JSSC.2018.2869569
129. Yin L, Kim KN, Lv J et al (2021) A self-sustainable wearable multi-modular E-textile bioenergy microgrid system. Nat Commun 12(1):1–12. https://doi.org/10.1038/s41467-021-21701-7
130. Jing Y, Wang A, Li J et al (2021) Preparation of conductive and transparent dipeptide hydrogels for wearable biosensor. Bio-Des Manuf. https://doi.org/10.1007/s42242-021-00143-6
131. Chen H, Zhang Y, Zhang L et al (2021) Applications of bioinspired approaches and challenges in medical devices. Bio-Des Manuf 4:146–148. https://doi.org/10.1007/s42242-020-00103-6
132. Heikenfeld J, Jajack A, Feldman B et al (2019) Accessing analytes in biofluids for peripheral biochemical monitoring. Nat Biotechnol 37(4):407–419. https://doi.org/10.1038/s41587-019-0040-3
133. Huang X, Li J, Liu Y et al (2021) Epidermal self-powered sweat sensors for glucose and lactate monitoring. Bio-Des Manuf. https://doi.org/10.1007/s42242-021-00156-1
134. Bandodkar AJ, Jeang WJ, Ghaffari R et al (2019) Wearable sensors for biochemical sweat analysis. Annu Rev Anal Chem 12:1–22. https://doi.org/10.1146/annurev-anchem-061318-114910
135. Dunn MR, Jimenez RM, Chaput JC (2017) Analysis of aptamer discovery and technology. Nat Rev Chem 1(10):0076. https://doi.org/10.1038/s41570-017-0076
136. Parrilla M, Ferré J, Guinovart T et al (2016) Wearable potentiometric sensors based on commercial carbon fibres for monitoring sodium in sweat. Electroanalysis 28(6):1267–1275. https://doi.org/10.1002/elan.201600070