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Wearable mechanical and electrochemical sensors for real-time health monitoring

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Wearable sensors provide a good solution for real-time monitoring of human health, and great progress has been made in miniaturization, flexibility, low power consumption and intelligence in recent years. Here, we introduce the principles of wearable sensors and their applications in disease surveillance. Physiological signals mainly include physical signals and biochemical signals. Among various sensors used to monitor physiological signals, we have introduced the basic working principles of mechanical sensors and electrochemical sensors. We summarize the examples of the clever integration of sensors with daily wearable products, and introduce cases of disease monitoring applied to the respiratory system, cardiovascular system, nervous system, musculoskeletal system and metabolic system. In view of the current situation of wearable sensors in terms of materials, structure, technology and energy, we discuss challenges and solutions of wearable mechanical and electrochemical sensors, and look forward to the application prospects of wearable sensors.

With the advancement of materials science, electronics, and micro-nano-processing technologies, the development of wearable sensors has been focused on miniaturization, flexibility, low energy consumption, and intelligent capabilities. The real-time monitoring of human physiological signals has emerged as a crucial application of wearable sensors in personalized medicine, Internet of Things (IoT) for health, and sports, and has garnered considerable attention from both academia and industry.

Existing wearable sensors can monitor physical signals, such as heart rate, electrocardiogram (ECG), blood pressure, pulse, respiration, and posture, in real time. They can also accurately measure biochemical and metabolic substances in various bodily fluids, including sweat, tears, saliva, and inter-tissue fluids[1]. Post-operative rehabilitation, fall prevention, motor status feedback, and early diagnosis of cardiac and metabolic diseases have also been demonstrated as potential applications of wearable sensors[2,3]. Studies have attempted to enhance user/patient compliance and sensor stability by exploring innovative materials with exceptional properties—such as flexibility, stretchability, self-healing, and self-adhesion—for constructing sensor core units. Furthermore, the implementation of self-powered technology[4] in wearable sensors is a novel approach to mitigating the persistent challenge of continuous energy supply and realizing battery-free wearables. This innovation can catalyze the evolution and transformation of wearable sensors.

Despite the various advancements, wearable sensors with single signal acquisition are not adequate to meet current demands. Multi-channel wearable sensing systems that seamlessly integrate physical and biochemical signal monitoring are promising futuristic solutions. To this end, multi-signal transmission necessitates intelligent processing and analysis. These aspects are indispensable for comprehensive user/patient health status measurement and the analysis of large-scale medical data. Furthermore, advanced processing is crucial to achieving optimal sensor performance and facilitating widespread industrial applications. Collaborative efforts among multidisciplinary domain experts are crucial to progressively advance these facets. In this article, we present an overview of the principles, advancements, and future developments in wearable sensors. Additionally, we offer prospective solutions for the encountered challenges.

Principle of wearable mechanical signal sensors

Among the myriad physiological signals in the human body, mechanical signals are the foremost physical signals in sensing monitoring, encompassing blood pressure, pulse, plantar pressure, etc. Mechanical sensors convert force-induced mechanical deformation into electrical signals,

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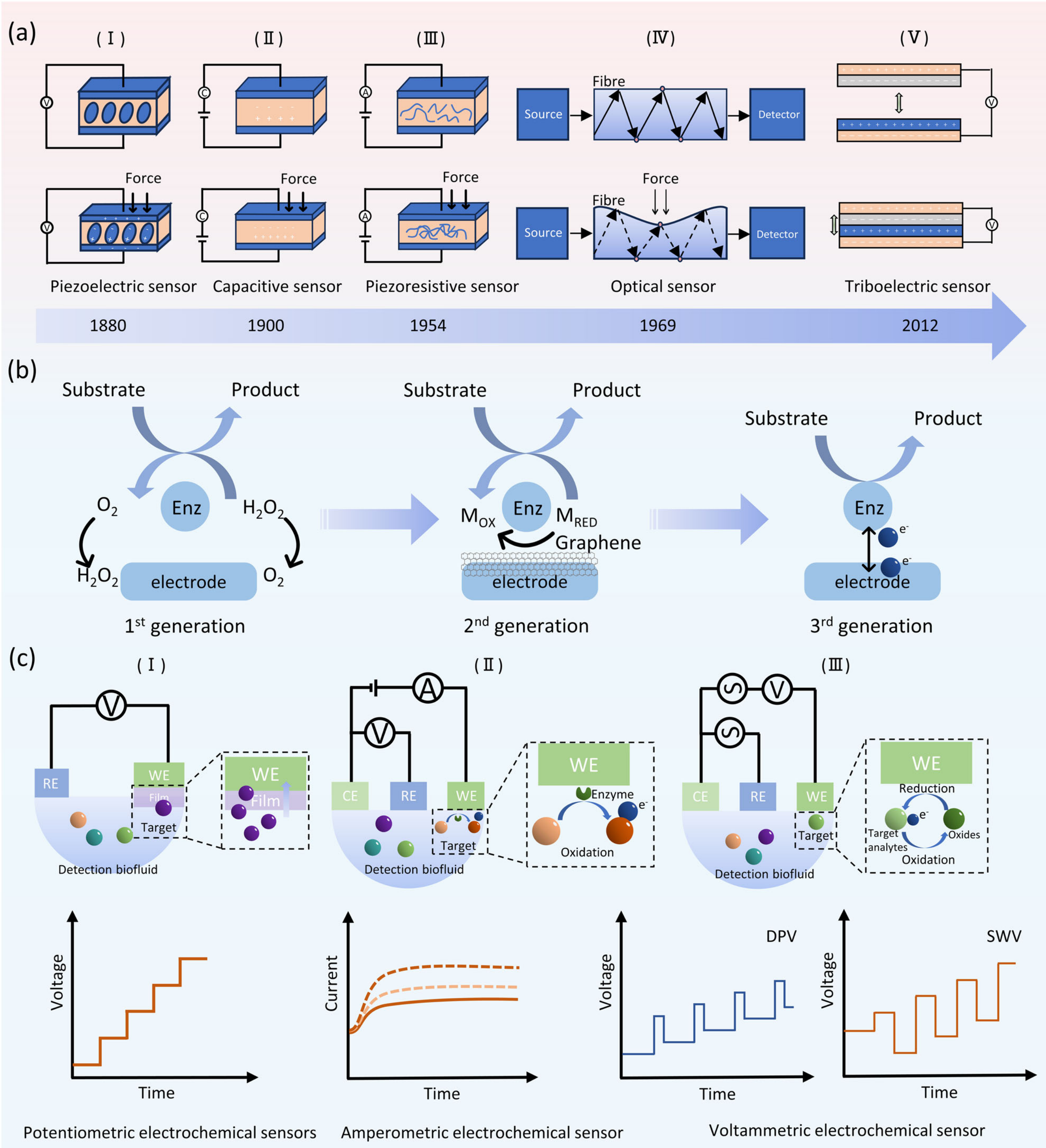

Fig. 1 | Principle of wearable sensors. a Principle of wearable mechanical signal sensors: (I) Piezoelectric sensor[5], (II) Capacitive sensor[46], (III) Piezoresistive sensor[47], (IV) Optical sensor[48], (V) Triboelectric sensor[7]. **b** Development of enzyme sensor. **c** Different types of wearable electrochemical sensors: (I) Electrochemical potentiometric sensor, (II) Electrochemical amperometric sensor, (III) Electrochemical voltammetric sensor.

primarily employing piezoelectric sensors, triboelectric sensors, capacitive sensors, piezoresistive sensors, and photoelectric sensors (Fig. 1a).

Piezoelectric sensors and triboelectric sensors represent two categories of self-powered sensors, capable of directly converting mechanical signal into electrical signal. The piezoelectric effect, discovered by Pierre Curie in 1880, involves the polarization of a piezoelectric material under external stress, generating a potential difference[5]. Simultaneously, positive and negative charges emerge on its opposing surfaces, with charge density proportional to the external mechanical force. Piezoelectric sensors, developed based on this effect, boast advantages of simple fabrication, miniaturization, and high sensitivity. Due to these advantages, piezoelectric sensors are widely used in the watchmaking industry and resultantly scalability of devices based on piezoelectricity. They are predominantly suitable for dynamic pressure conditions and find widespread use in monitoring human movement. Notably, flexible piezoelectric sensors are primarily fabricated using polyvinylidene fluoride (PVDF)[6]. Triboelectric sensors, first reported in 2012[7], have received widespread attention and leverage the coupling effect of triboelectric electrification and electrostatic induction to transform mechanical energy into electrical energy/electrical signals. These sensors exhibit excellent mechanical performance at low operation frequency, rendering them suitable for capturing signals and energy associated with human motion. Their performance hinges on the choice of materials and structures, offering a diverse range of material options. Commonly used electron acceptor materials include polytetrafluoroethylene (PTFE), polydimethylsiloxane (PDMS), fluorinated ethylene propylene (FEP), and Kapton, while aluminum, copper, and nylon serve as prevalent electron donor materials in this field[8]. Triboelectric sensors designed for wearable applications can incorporate relevant structures to ensure accuracy and sensitivity. Structural packaging addresses environmental humidity impacts on triboelectric sensors, mitigates surface charge loss, and reduces output power. Additionally, hybrid sensors, combining piezoelectric and triboelectric elements, have emerged to enrich sensor information[9].

Capacitive sensors and piezoresistive sensors, characterized by a straightforward working principle and a facile manufacturing process, exhibit considerable potential for a broad spectrum of applications[10]. A capacitive sensor comprises two parallel plate electrodes separated by a dielectric interlayer. The formula governing capacitive sensors is as follows:

$$C = \varepsilon * A/d$$

where ε denotes the dielectric constant between the two plates, A represents the area covered by the two plates, and d signifies the distance between them. When external pressure is applied to the capacitive sensor, the distance between the two plates diminishes, leading to an increase in capacitance. The performance of capacitive sensors hinges on the quality of the electrode and dielectric layer. To enhance sensitivity, flexible materials can be chosen, and the dielectric layer and electrode can be endowed with surface microstructures[10], generating a smaller initial capacitance and resulting in substantial capacitance changes. With the same high industrial transfer potential, accelerometers are commonly made by the capacitive sensors in the automotive industry. Piezoresistive sensors register alterations in externally applied pressure by tracking changes in the resistance value of the piezoresistive material. Their performance is primarily contingent on the quality of the piezoresistive material and electrode. Current research on piezoresistive sensors predominantly concentrates on the design of substrates, electrodes, and structures[11,12]. Opting for flexible materials is a common strategy for achieving flexibility in piezoresistive sensors, and the surface microstructure design of piezoresistive materials aids in further elevating their sensitivity. In monitoring physiological signals such as pulse, respiration, limb movements, etc., piezoresistive sensors display superior linearity, low hysteresis, and swift responses during low-strain motion. Conversely, capacitive sensors offer heightened sensitivity for monitoring high-strain motion[13].

The optical sensors are obviously different from the aforementioned four sensors, which do not undergo direct alterations in their electrical characteristics due to external forces. Optical sensors comprise a light source, optical fiber, and a detector. The performance of optical sensors is chiefly contingent on the optical fiber. When subjected to external forces, the deformation of the optical fiber induces changes in the optical path within the fiber, leading to spectral alterations in the reflected light wavelength accordingly[14]. Hence, wearable optical sensors can discern wavelength changes in light resulting from minor changes on the surface of human skin. This capability extends to detecting factors such as heart rate[15] and respiratory rate[16]. Notably, optical sensors remain unaffected by electromagnetic noise. However, owing to structural factors, they exhibit a larger volume. Additionally, the accuracy and sensitivity of the sensor are influenced when the deformation ability of the optical fiber is impacted by temperature fluctuations.

Construction of wearable electrochemical sensors

Monitoring biochemical indicators at the molecular level becomes imperative. For patients with chronic diseases, such as diabetes patients, monitoring blood glucose can provide guidance for lifestyle intervention, optimize blood glucose management then, reduce the occurrence of hypoglycemia, and improve life quality. Wearable electrochemical sensors, capable of eliciting electrical signal changes commensurate with the concentration of the target substance in the tested liquid. Compared to the high-sensitivity lab equipment, wearable electrochemical sensors that are advantageous in term of size/cost/wearable/continuous health monitoring, finding increasing utility in quantifying biochemical metabolites in the human body.

The common electrochemical amperometric sensor, often an enzyme sensor, has undergone three generations of development (Fig. 1b)[17]. The first generation indirectly monitors electron transfer on the electrode surface by observing hydrogen peroxide in enzymatic reactions. However, it is susceptible to fluctuations in oxygen concentration. To address this, the second generation substitutes a synthetic medium for oxygen as the electron acceptor, though it compromises stability over time. The third-generation enzyme sensor pursues direct electron transfer between enzyme and electrode to achieve mediator-free sensing, with higher independence and stability. According to the detection method of electrochemical signals, electrochemical sensors can be divided into electrochemical potentiometric sensors, electrochemical amperometric sensors, and electrochemical voltammetric sensors (Fig. 1c). Electrochemical potentiometric sensors typically comprise a working electrode and a reference electrode, and the typical target analytes are ions in electrolytes. Most potentiometric sensors rely on ion-selective electrodes, with a typical structure including an electron-conductive electrode substrate, an ion-electron exchange layer, and an ion-selective membrane. Potential-based wearable sensors exhibit characteristics of low cost, simplicity of operation, reliability, and continuous measurement. Their detection range spans from several hundred μM to tens of mM[17]. Both electrochemical amperometric and electrochemical voltammetric sensors adopt a three-electrode system, incorporating a working electrode, counter electrode, and reference electrode. The working electrode is used to react electrochemically with the test substance and can be measured in a large potential range. The counter electrode and the working electrode form a loop to ensure that the electrochemical reaction occurs on the working electrode. The reference electrode has a constant value and provides a stable potential reference for accurately controlling and measuring the potential of the working electrode. The distinguishing factor lies in the potential applied to the working electrode, the electrochemical amperometric sensor employs a stable potential, while the electrochemical voltammetric sensor employs a non-constant potential. Lactic acid and glucose are typical target analytes for electrochemical amperometric sensor, target-specific enzyme (lactate oxidase, glucose oxidase) was immobilized on the working electrode to catalyze the oxidation of the target at a constant potential. For protein detection, electroactive label is needed for target sensing such as enzymes. Cause protein cannot directly generate electron transfer on the surface of electrochemical voltametric sensor[18]. With a stable potential applied to the working electrode (vs the constant potential of the reference electrode), the tested liquid undergoes oxidation reaction on the working electrode, causing the oxide to lose electrons and undergo a charge change. The current density of an idealized Electrochemical Amperometric sensor linearly relates to the target substance, with the analyte concentration range spanning from a few μM to tens of mM[17]. Sensitivity depends on electrode size, with nanomaterials such as gold nanonets, gold fibers, MXenes, etc., utilized to increase sensor electroactive surface area (ESA) for performance improvement without sensor enlarging (same footprint but larger ESA) that also meant to address the challenge of working with small sample size, such as tears and interstitial fluids (IFS), and minimize device invasiveness. Electrochemical voltammetric sensors typically employ square wave voltammetry (SWV) and differential pulse voltammetry (DPV). Depending on the potential change pattern, the working electrode surface undergoes reduction when the potential is lower than the oxidation-reduction potential, and oxidation occurs when the potential is higher. DPV and SWV minimize background charge current and realize highly sensitive electrochemical target analysis[17,19], which are nowadays preferred voltammetric methods. However, the DPV method requires a longer scanning cycle, impacting detection continuity. Moreover, as the working cycle increases, the DPV electrode may experience analyte absorption and biofouling and cause diminishing sensing accuracy[17]. While electrochemical sensors are versatile for various analytes and support continuous monitoring, due to power supply[20], face limitation in wearability than self-powered sensor[21].

Application cases of wearable sensors

Based on the principles governing wearable sensors and their practical applications, researchers have endeavored to fashion sensors with diverse structures and forms. From masks, watches, and gloves to contact lenses and tooth protectors, nearly all daily essentials can be seamlessly integrated with wearable sensors (Fig. 2a). This integration has expanded the scope of monitored targets from fundamental physiological parameters like breathing, posture, pulse, and blood pressure to encompass virtually all biochemical components in body fluids today[1]. Existing wearable sensors are primarily designed for monitoring diseases affecting the respiratory system, cardiovascular system, nervous system, musculoskeletal system, and endocrine system (Fig. 2b).

Respiration, as a fundamental and continuous life activity, serves as a reflection of changes in the body's health status. Respiratory diseases are typically assessed by gauging the strength of respiratory airflow and exhaled analytes[22]. Current respiratory monitoring primarily accounts for changes in airflow through the mouth and nose or fluctuations in the chest and abdominal cavity. Strain sensors integrated into masks can directly and precisely capture the airflow signals generated by human respiration. The relational indicators include inspiratory capacity (IC), forced vital capacity (FVC), forced expiratory volume in the first 1 s (FEV1), which is used to evaluate lung function[9,23,24]. In addition to mechanical signal, respiration also produces heat, water, and some molecular gases[25]. Some of the molecular gases exhaled are associated with diseases. For example, nitrogen oxides (NOx) are a gas marker of respiratory tract inflammatory diseases[26], acetate is related to diabetes[27], and ammonia relates to hepatitis[28]. Besides, the alcohol is recognized as an indicator of fatty liver and plays a vital role in the exhaled gas identifying of drunk drivers[29]. Given the subdued airflow during breathing, respiratory monitoring sensors necessitate high sensitivity. Additionally, the sensitivity of monitoring respiratory biochemical markers is challenged by factors like air pollution and humid exhaled gas.

The cardiovascular system, a pivotal circulatory component in the human body, relies on the heart as its circulatory engine. Blood pressure and pulse serve as crucial indicators for measuring heart function. There are numerous commercial instances of watches used for monitoring blood pressure or pulse, typically employing Photoplethysmography (PPG) methods[30]. Compared to the PPG measurement method, using a pressure sensor for direct blood pressure and pulse measurement, particularly on the wrist with a thinner skin surface, proves more direct. However, dynamic blood pressure monitoring poses a challenge. Rogers et al.[31] integrated Electrocardiography (ECG) and Microwave Photoplethysmography (MWPPG) technologies on electronic skin to achieve real-time monitoring of dynamic blood pressure through synchronous sensing. Assisted by data science, wearable sensors for the cardiovascular system can not only achieve real-time monitoring but also predict diseases such as atrial fibrillation[32].

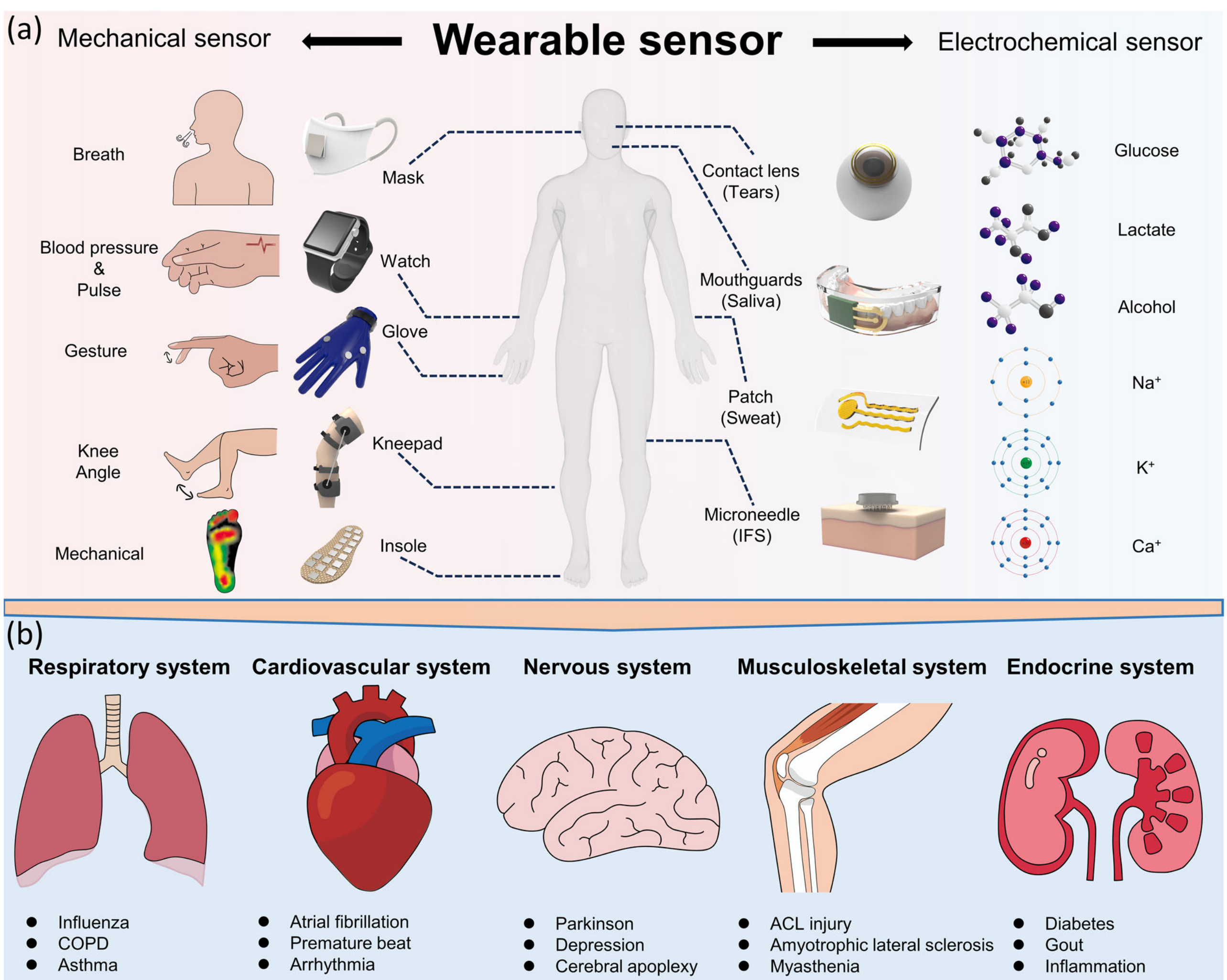

Fig. 2 | Application of wearable sensors for human health detection. **a** Application of wearable sensors for human physiological signals detection. **b** Application of wearable sensors in disease monitoring, diagnosis, and recovery.

The musculoskeletal system, integral to the human body's motor system, complements the nervous system in jointly influencing motor function. Emphasis is typically placed on the mechanical force and posture signals it generates. Gloves integrated with sensor arrays can recognize various gestures based on changes in the wearer's hand posture, enhancing the user's operating experience[33]. Simultaneously, precise perception of subtle gestures and durability against multiple bends are achieved through stretchable substrate materials. For safeguarding the often-injured anterior cruciate ligament (ACL) in the knee joint, patients wear protective gear. Integrated sensors in such protective gear face challenges from external noise interference while sensing posture signals. To address this, Xue et al.[34] proposed a magnetic-driven piezoelectric cantilever generator (MPCG) array, utilizing a Kapton thin-film encapsulated cantilever structure to reduce external mechanical interference. Gait monitoring, reflecting the movement status of the lower limbs, is facilitated by an array of hybrid sensors embedded in the insole, effectively monitoring changes in gait and collecting mechanical energy generated by human movement for self-powered operation[21]. The use of polytetrafluoroethylene (PTFE) and Kapton as packaging layers ensures the durability and stability of the sensor. A polyvinylidene fluoride (PVDF) film converts pulse vibration signals into effective electrical signals. Additionally, it can predict the occurrence of diseases leading to gait changes, such as neuromuscular weakness and Parkinson's disease.

Monitoring the endocrine system necessitates attention to key biochemical indicators, including blood sugar, lactate, cortisol, and others, crucial for predicting and longitudinally monitoring chronic metabolic diseases[35–37]. Historically, diabetes monitoring involved fingertip blood sampling, a method hampered by low patient acceptance and a risk of sample contamination[38]. Interstitial fluids, positioned around skin cells and supplying nutrients through capillary endothelium diffusion, emerged as an optimal source for accurate and swift glucose concentration measurement. Despite widespread studies on reverse ion electroosmosis (RI) for glucose extraction from interstitial fluids, concerns regarding skin irritation and potential cross-contamination with sweat persisted[39]. In response, microneedle arrays were used to improve accuracy albeit with minor trauma[40].

Efforts to achieve non-invasive and sustained biochemical monitoring have propelled research in fluid diagnosis[41]. Fluids commonly used for health monitoring include sweat, saliva, tears, etc. that contain biochemical markers are closely related to diseases. Sweat, abundant in metabolites, electrolytes, trace elements, and macromolecules, serves as a readily accessible biological fluid for chemical sensing applications. Sweat analysis facilitates non-invasive monitoring of physiological health, enabling disease diagnosis and effective management. Notably, diabetes patients exhibit higher glucose concentrations in sweat compared to healthy individuals, making sweat analysis a viable method for monitoring glucose levels. Saliva, another non-invasive body fluid rich in biomarkers. Researchers integrated electrochemical sensors onto teeth guards for direct biochemical component detection in saliva[42]. To eliminate interference, a layer of cellulose acetate (CA) film was applied to the sensor's surface. The CA was expected to suppress of ascorbic acid (AA) and uric acid (UA) which cause electrochemically contaminated in the saliva due to the electrostatic repulsion and size effect of the acetate group. However, this tooth guard sensor is susceptible to food consumption, impacting accuracy and stability, and is unsuitable for prolonged wear. Tears, a challenging body fluid to obtain, saw the integration of electrochemical sensors into contact lenses to alleviate acquisition difficulties and contamination risks[43]. These lenses can concurrently monitor glucose concentration and treat diabetes retinopathy. Constructed from a biocompatible polymer, these lenses comprise ultra-thin, flexible circuits, and micro control chips, offering a non-invasive solution with the added benefit of diabetes retinopathy treatment. However, there is a slight delay compared to immediate blood glucose readings.

Outlook

In recent years, considerable strides have been made in the flexibility, integration, and non-invasive monitoring capabilities of wearable sensors, leading to numerous exploratory cases in early disease diagnosis[2]. However, these sensors confront several challenges related to materials, structure, technology, and energy. Currently, to meet the comfort requirements of wearable sensors, research has focused on ultra-soft and ultra-thin materials such as PDMS, eco-flex, graphene, MXene, etc. However, these materials still exhibit poor breathability, especially in the context of body fluid monitoring. Electrochemical sensors, crucial for this application, need to closely adhere to the skin, necessitating the development of breathable, flexible, and stretchable materials suitable for wearable applications[2]. Simultaneously, self-adhesive materials can mitigate the need for excessive fixation, reducing tightness caused by sensor attachment. Nevertheless, the synthesis of current materials remains complex and costly, hindering large-scale application[3]. Fig. 3 shows the challenges that wearable sensors face in materials, manufacturing, and energy in the future.

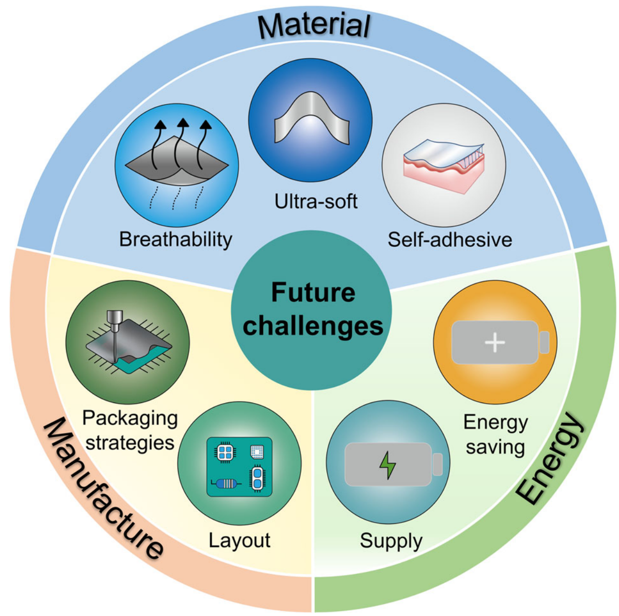

Fig. 3 | Wearable sensors with future challenges in material, manufacture, and energy.

In the integration of wearable sensors, a strategic layout of various functional parts and the adoption of appropriate packaging strategies are imperative. The tight interconnection between different parts and variations in manufacturing processes pose challenges. For instance, the sensor part of wearable chemical sensors must come into contact with biological fluids, while other electronic components need sealing to prevent contact with liquids[44]. Even triboelectric sensors are affected by environmental humidity, directly impacting their surface charge dissipation rate[8]. Although packaging is currently achieved using Kapton tape, PDMS, and eco-flex, these methods still face issues with stability and durability. Future developments should aim for improved packaging methods.

Existing passive or self-powered technologies have addressed energy supply concerns and contributed to the reduction in the size of wearable sensors. Future strategies should focus on enhancing energy supply and reducing energy costs. Composite structures, like piezoelectric composite triboelectricity, can increase surface charge and device output power[9,21]. Material improvements, such as adjusting surface functional groups or morphology, pre-charging surfaces with static charges, and using inorganic fillers to modify dielectric or charge capture properties, can further enhance performance. Triboelectricity's most advanced surface charge density can reach ~8.8 mC/m^2, with average power reaching the mW scale[8]. There have been generous cases of using TENG to support wearable sensors[23,45]. Lastly, ongoing optimization of efficiency, circuit standardization, and circuit miniaturization are essential for achieving low power consumption.

In conclusion, wearable sensors not only precisely quantify various physiological indicators but also offer a smaller and more portable alternative to fixed medical instruments. This characteristic meets user needs for prolonged wear and continuous monitoring without sacrificing sensitivity. With the advancements in multi-signal path composites and micro/nano-processing technology, wearable sensors have expanded their detection range and sensing accuracy, emerging as promising instruments for human health monitoring. Future advancements require interdisciplinary collaboration to enhance material performance, optimize structure and appearance, downsize devices, and design low-power circuits. Ensuring resistance to environmental noise interference during daily activities and maintaining long-term stability are imperative. The development of low-cost industrial-scale manufacturing processes will reduce production costs, facilitating broader industrial applications. The adoption of advanced information processing technology and the establishment of automated decision-making systems will aid users/patients in swiftly identifying abnormal conditions.

Nowadays, physiological and chemical signals can be monitored by wearable sensors, such as electrocardiogram, heart rate, blood oxygen, respiration, blood sugar, lactate, etc. The importance of signals is influenced their wide commercial applications, such as most smart watches and smart bands currently being able to monitor heart rate, which is highly correlated with vital indicators. The satisfaction of users with product use is another factor that affects its commercial promotion. Currently, commercial wearable sensor devices do not have the characteristics of flexibility and breathability. In the future, flexible and breathable wearable sensor product solutions will have a wide range of commercial applications. The performance of products can also affect user purchasing decisions, which requires wearable sensors to have higher efficiency, accuracy, stability, and durability in various environmental scenarios. For the application of clinical medicine, it is necessary to optimize the correlation between detection markers and monitoring indicators, and improve the reliability of sensors. Further large-cohort validation of wearable sensor performance will be conducted to demonstrate its clinical usability. Furthermore, the absence of a unified monitoring standard for wearable sensors underscores the need for future improvements to measure their attainment of medical standards. Through interdisciplinary integration and collaborative development, wearable sensors will find wider and deeper applications in personalized healthcare, IoT health, sports, and other fields, emerging as indispensable tools for human health monitoring.

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Z.Li, Z.Liu, and Y.W. contributed to the conceptualization of the manuscript. Z.X., Z.Liu, and Y.G. wrote the initial manuscript draft and produced Figures. All authors discussed the manuscript and contributed to the preparation of the manuscript.

Competing interests
The authors declare no competing interests.

Additional information
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