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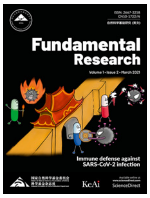

Review

Recent progress in human body energy harvesting for smart bioelectronic system

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ABSTRACT

From every heartbeat to every footstep, human beings dissipate energy all the time. Researchers are trying to harvest energy from the human body and convert it into electricity, which can be supplied to electronic medical devices closely related to human health. Such an energy recycling form is currently a research hotspot in the fields of energy harvesting and bioelectronics. This review firstly summarizes the distribution and characteristics of three primary energy sources contained in the human body, including thermal energy, chemical energy, and mechanical energy. Afterwards, the applicable energy harvesting technologies and corresponding working mechanisms for different energy sources are introduced. Some typical demos and practical applications of each type of human body energy harvesting technology are also presented. Specifically, the advantages and critical issues of different energy harvesting technologies are summarized, and corresponding promising solutions are also provided. Besides, the interaction strategies between various energy harvesting devices and the human body are summarized from the aspects of wearable and implantable applications. Finally, the concept of a self-powered closed-loop bioelectronic system (SCBS) is put forward for the first time, which organically combines portable electronic devices, implantable electronic medical devices, energy harvesting devices, and the human body. The prospect of symbiosis between the SCBS and the human body is provided. The demands and future development trends of the SCBS are also discussed.

1. Introduction

Energy is the cornerstone of the development of human civilization. The contradiction between the ever-increasing demand for energy and the declining existing energy resources is a serious problem facing the world today. Furthermore, environmental pollution caused by the overuse of fossil energy is also increasing. Therefore, it is urgent to find and develop new energy sources which are sustainable and eco-friendly.

The discovery and utilization of new energy sources including water energy, wind energy, solar energy, ocean energy and biological energy, have greatly promoted human society's development. In addition to the above sustainable new energy sources derived from the natural environment, energy from the human body has recently proved to be a potential clean energy for sustainable use. The human body relies on food intake to obtain energy, which is mainly used to maintain the body temperature and the operation of body organs except some useless energy which is dissipated into the environment. If human energy could be harnessed properly, the benefits would be immeasurable in terms of the current global population base.

Although scientists have devoted efforts for decades to exploring the possibilities of human body energy, current research on human body energy harvesting is still relatively rudimentary [1–3]. One of the critical issues is that the harvested human body energy must not affect the human body's normal life activities, which is the premise of all research on human body energy harvesting. Therefore, although the human body has huge energy dissipation every day, the proportion of energy that can be actually utilized is small. In addition, the conversion efficiency of the existing energy harvesting technologies is still relatively low, so the actual conversion power can only reach the order of microwatts to milliwatts.

Although such an output level is far from enough to meet people's daily electricity demand, the energy sources from the human body still have their potential application scenarios. In the era of the rise of high-efficiency and low-power electronic components, various wearable and

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portable electronics and implantable electronic medical devices have gradually integrated into people's lives [4,5]. The energy source from the human body provides new possibilities for people to get rid of periodic battery replacement, cumbersome daily charging, and even surgical replacement of implanted electronic medical devices such as pacemaker batteries [6–9]. The energy from the human body is safe, reliable, eco-friendly, and not restricted by space and environmental conditions. As long as life is still alive, it can provide a continuous stream of energy for various bioelectronic devices. In the near future, it may be possible to realize the symbiosis and mutual benefit between human and bioelectronic devices, which will provide unlimited possibilities for prolonging human lifespan and exploiting the human potential.

This review has made a comprehensive summary and analysis of recent progress in human body energy harvesting. Firstly, the source and distribution of human body energy are summarized. The energy from the human body can be divided into thermal energy, chemical energy, and mechanical energy. Afterward, relevant energy harvesting technologies for different forms of human body energy are detailly discussed from the aspects of working mechanisms, advantages, critical issues, and possible solutions. Some representative research works of each energy harvesting technology are also introduced from demos to practical applications. In addition, the general interaction strategies for various energy harvesting devices and the human body are summarized from the aspects of wearable and implantable applications. Finally, a self-powered closed-loop bioelectronic system (SCBS) is proposed here for the first time, which integrates energy harvesting unit, sensing unit, feedback unit, and micro control unit with the human body. The possible routes of symbiosis between SCBS and the human body are prospected. The demands and future development trends of SCBS are further discussed in terms of materials, structures, function, and integration.

2. Source and distribution of human body energy

The human body is a natural energy conversion factory. Through the intake of food, the carbohydrate, fat, protein, and other nutrients in the food will be absorbed. Some of the nutrients will be converted into glycogen, lipids, amino acids, and other energy substances stored in the human body, while the other part will be converted into adenosine triphosphate (ATP), the minimum energy substances unit that the human body can directly use through various metabolic pathways. The total amount of ATP in the human body is approximately 0.2 mol, which is equivalent to the energy of an AA battery [10]. Ann adult usually consumes ATP energy (∼ 100–150 mol) equivalent to his body weight in one day to maintain normal physiological functions and major life activities [10]. These energies will be consumed and released by the human body by means of different forms of energy flow. Specifically, we mainly summarize three forms of energy flow in the human body as thermal energy, chemical energy, and mechanical energy (middle right side of Fig. 1). From every breath and heartbeat to every movement, energy will be released all the time. These energy flows are the primary basis of the human body as a potential energy source.

In terms of thermal energy flow, the human body consumes a large amount of energy every day to maintain a stable body temperature. Most of the thermal energy is released to the ambient in the form of heat exchange between the body and ambient, while other energy is dissipated through breathing or evaporation of sweat on the skin. In terms of chemical energy flow, after digestion and absorption, food will be converted into glucose and delivered to various parts of the body in the form of blood glucose for further use and energy generation. In addition, after strenuous exercise, the human body will produce excessive lactate in muscle, some of which will be slowly consumed and decomposed in muscle, while the other part will be excreted with water and electrolytes in the form of sweat. In terms of mechanical energy flow, the movements of limbs including foot lifting, stepping, arm raising, tapping, knocking, etc., respiratory movement, heartbeat, and even the contraction and relaxation of blood vessels, are accompanied by the consumption and release of the energy. Mechanical energy mainly depends on the contraction and relaxation of muscles in corresponding parts of the human body to do external work for energy flow transmission.

Some researchers have theoretically estimated the power of different energy flows during the transmission process for further evaluation of their potential as human energy sources [10] (left side of Fig. 1). It is worth noting that the actual human body energy that can be utilized to collect and convert into electricity must be far less than the total energy consumed by the energy flow of each part of the human body to avoid possible negative effects on the human body. This is the fundamental premise that all human body energy harvesting technologies discussed below must comply with. We have also summarized the related emerging energy harvesting technologies according to different energy sources of the human body (far right side of Fig. 1), which are mainly introduced in the following sections. Thermoelectric generator (TEG) and pyroelectric generator (PEG) are applicable for harvesting thermal energy. Biofuel cell (BFC) and hydrovoltaic effect generator (HEG) are applicable for harvesting chemical energy. Piezoelectric nanogenerator (PENG) and triboelectric nanogenerator (TENG) are applicable for harvesting mechanical energy.

3. Recent progress of human body energy harvesting technology

This section successively introduces the recent research progress of energy harvesting technology related to three forms of human energy flow including thermal energy, chemical energy, and mechanical energy. Specifically, for each energy harvesting technology, we elaborate the working mechanism and introduce representative research works from demos to practical applications. In addition, the advantages, critical issues and promising solutions for different energy harvesting technologies are also summarized in this section.

3.1. *Thermal energy harvesting of the human body*

At present, the harvesting of thermal energy from the human body mainly depends on the thermoelectric effect and the pyroelectric effect, which respectively correspond to two types of energy harvester as thermoelectric generator (TEG) and pyroelectric generator (PEG). Although the two types of thermal energy harvester both can collect the heat from the human body and convert it into electricity, they work in different ways. TEGs depend on the spatial temperature difference for energy conversion, while PEGs depend on the temporal temperature difference. Therefore, these two types of thermal energy harvesters have their applicable situations and specific forms when harvesting thermal energy from the human body. We respectively introduce TEG and PEG below from the aspects of working principles and typical works.

3.1.1. *Thermoelectric generator*

3.1.1.1. Principle of TEG. Thermoelectric generator is a type of thermal energy harvester based on the thermoelectric effect, which can directly convert thermal energy into electrical energy [11, 12]. The thermoelectric effect mentioned here refers to the first thermoelectric effect, also known as the Seebeck effect. The Seebeck effect is mainly caused by the diffusion of carriers from the hot end to the cold end. Both metal conductors and semiconductors are able to produce the Seebeck effect, while the Seebeck effect of metals is much smaller than that of semiconductors since the carrier concentration and the position of the Fermi energy level of metals basically do not change with temperature [13].

P-type semiconductor is taken as an example for description. The holes will diffuse from the high-temperature end to the low-temperature end due to the high concentration of holes at the hot end. Space charges will thus be formed at both ends of the p-type semiconductor in an open circuit (negative charges accumulated at the hot end and positive charges accumulated at the cold end), which leads to an electric field appearing inside the semiconductor. When the electric field's drift counteracts the diffusion action and a stable state has been reached, an

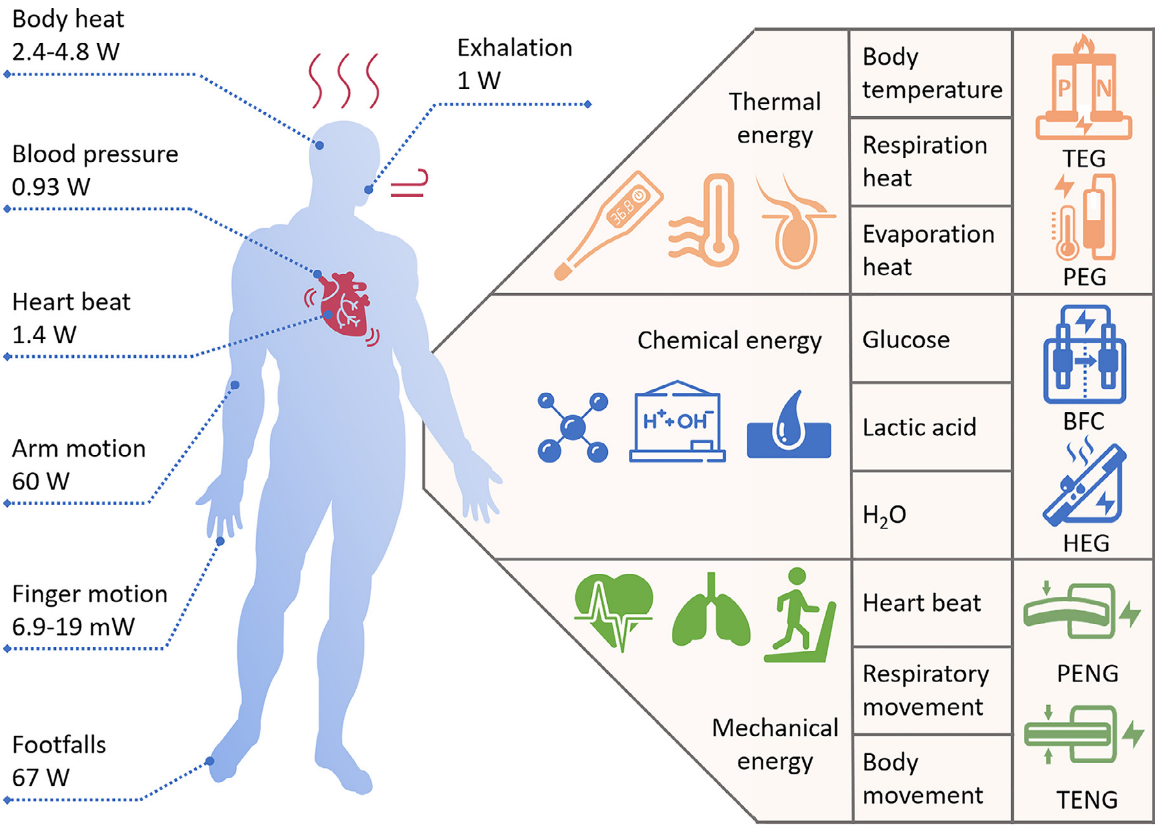

Fig. 1. Source and distribution of human body energy and applicable energy harvesting technologies.

electromotive force caused by the temperature gradient appears at two ends of the semiconductor, which is called thermoelectromotive force.

TEG is a direct-current power generation device made by sets of semiconductor thermocouples connected in series or in parallel. The structure and working principle of a TEG are demonstrated in Fig. 2 (a). Each thermocouple consists of an n-type semiconductor and a p-type semiconductor in series. The connected end of the two semiconductors is in contact with the heat source, and the non-junction ends are connected with the heat sink through wires. Due to the temperature difference between the hot end and the cold end, there are positive charges accumulation at the cold end of the p-type semiconductor and negative charges accumulation at the cold end of the n-type semiconductor, thus forming a potential difference between the cold ends of two semiconductors [11,14]. If the two semiconductors are connected to an external circuit through wires, there will be a current flowing through the external circuit. In order to obtain a high power output, many pairs of thermocouples are usually connected in series or in parallel to form a thermopile [15, 16].

3.1.1.2. Demos of TEG.

Kim Sun Jin et al. reported a thin, lightweight, flexible, and wearable TEG based on glass fabric and self-sustaining structure [17] (Fig. 2b), the power density of the device can reach 3.8 mW cm^{-2} and 28 mW g^{-1} at a temperature difference of 50K. Although such output performance is good for flexible TEGs, it is still difficult for the human body to reach a temperature difference of 50K, unless the ambient temperature is at least minus ten degrees.

Kim Min-Ki et al. demonstrated a fabric TEG that can be integrated with clothing [18]. Two types of thermoelectric materials are embedded into the polymer fabric by dispenser printing to fabricate thermocouples. When the ambient temperature is 5 °C, the TEG composed of 12 sets of thermocouples on the wearer's chest can produce an output power of 146.8 nW.

Ren et al. designed a wearable TEG with stretchability, self-healability, recyclability, and reconfigurability [19] (Fig. 2c), which is fabricated with modular thermoelectric chips, dynamic covalent polyimine, and liquid-metal utilizing a "soft motherboard-rigid plugin modules" architecture. In addition, a radiative cooling metamaterial film is integrated onto the cold side of the TEG to improve the performance of the device under sunlight. Under a temperature difference of 95 K, the device achieved a record open-circuit voltage up to 1 V/cm^2 among flexible TEGs.

3.1.2. Pyroelectric generator

3.1.2.1. Principle of PEG.

Pyroelectric generator (PEG) is another type of thermal energy harvester, which is based on the pyroelectric effect [20]. For a crystal with spontaneous polarization property, when the crystal is heated or cooled, the intensity of spontaneous polarization changes due to the change of temperature, which leads to the generation of surface polarization charges in a certain direction of the crystal [21]. This phenomenon is called the pyroelectric effect. The crystals which can produce pyroelectric effect are called pyroelectrics. Pyroelectrics generally have first-order and second-order pyroelectric effects.

The first-order pyroelectric effect describes the charges generated in the absence of strain, which usually exists in ferroelectric materials such as lead zirconate titanate ceramic (PZT) and barium titanate ceramic (BTO). The corresponding working mechanism is shown in Fig. 2 (d), which is based on the random oscillation of the thermal-induced electric dipole near the aligning axes. The oscillation angle will increase as the temperature rises. At room temperature (RT), the electric dipoles will oscillate randomly on the respective aligning axes to a certain extent. At a constant temperature, the total average intensity of the spontaneous polarization of the electric dipole is constant and no flow of electrons exists. When the temperature increases, the electric dipoles oscillate more violently around the axes, and the total average spontaneous polarization decreases with the increase of oscillation angle. As a result, the

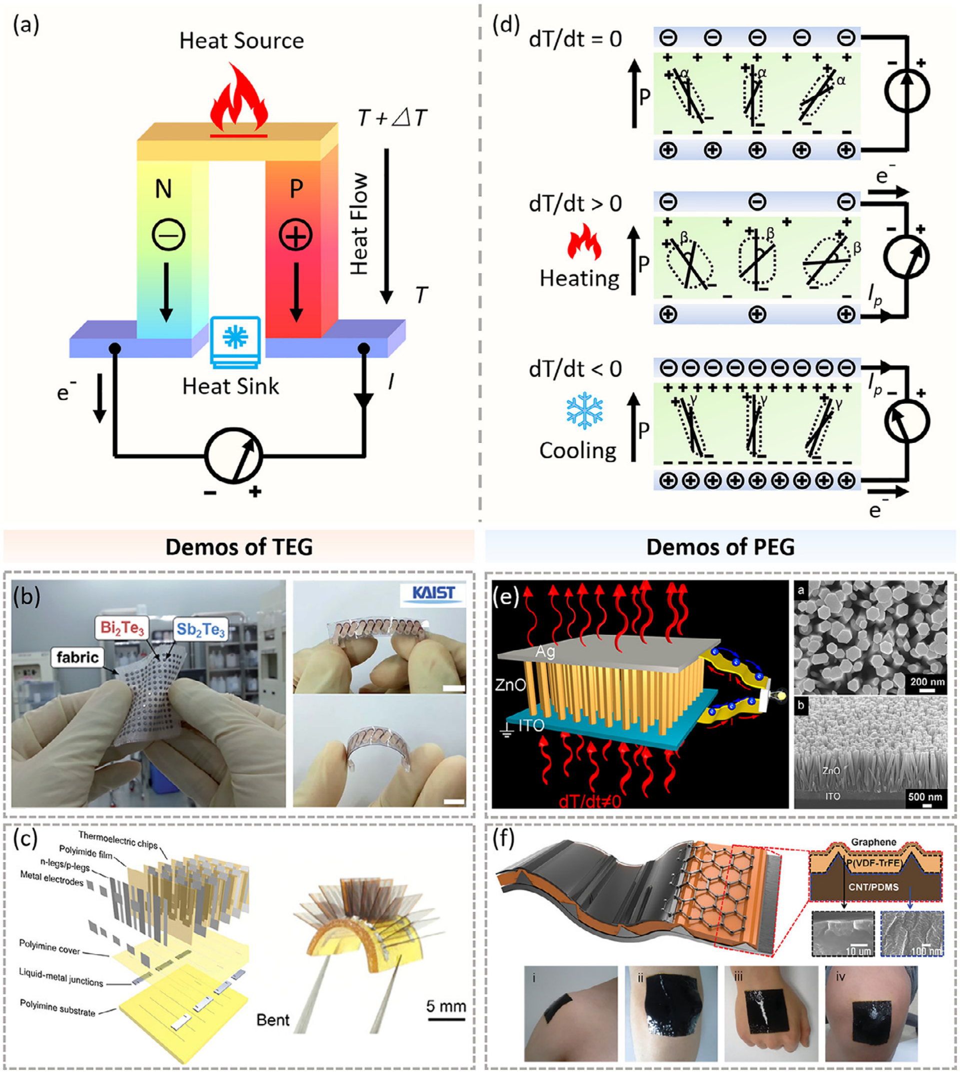

Fig. 2. Thermal energy harvesting of the human body, from principle to demos of TEG and PEG. (a) Principle of TEG. (b) A flexible TEG based on glass fabric and self-sustaining structure. (c) A wearable TEG utilizing a “soft motherboard-rigid plugin modules” architecture. (d) Principle of PEG. (e) A PEG based on ZnO nanowire arrays. (f) A highly stretchable PEG which can be directly attached to the human skin.

amount of induced charge on the electrode is reduced, leading to the flow of electrons. When the temperature decreases, the electric dipole oscillates in a smaller angle range due to the lower thermal activation energy, leading to the increasing spontaneous polarization. As a result, the amount of induced charge on the corresponding electrode increases and causes electrons to flow in the opposite direction [20,21].

The second-order pyroelectric effect describes the charge caused by the strain induced by thermal expansion, which exists in ZnO, CdS, and other wurtzite structure materials with piezoelectric effect. The temperature change causes the deformation of the material firstly, and then a piezoelectric potential is generated due to the piezoelectric effect, driving the flow of electrons in the external circuit. The corresponding output is related to the piezoelectric coefficient and thermal deformation of the material. If the temperature change rate remains unchanged, PEG usually generates pyroelectric charges with the same amount and the opposite polarity when temperature rises and falls [21,22].

3.1.2.2. *Demos of PEG.*

Yang et al. demonstrated the first pyroelectric nanogenerator (PyNG) based on ZnO nanowire arrays [23] (Fig. 2e). The bottom indium tin oxide (ITO) electrode serves as the growth substrate of ZnO nanowire arrays, and the silver film serves as the top electrode. The fabricated pyroelectric nanogenerator can produce a 5.8 mV and 120.4 pA voltage/current pulse when the temperature rapidly rises from room temperature 295 to 304 K.

Lee et al. presented a flexible and highly stretchable pyroelectric nanogenerator constructed by P(VDF-TrFE) polymer, polydimethylsiloxane (PDMS)-carbon nanotubes composite and graphene nanosheets [24] (Fig. 2f). This highly stretchable PyNG can be directly attached to the human skin and generate a voltage pulse up to 400 mV when the temperature changes rapidly between high and low positions.

3.1.3. *Applications of thermal energy harvesting*

After collecting the human body’s thermal energy and converting it into electricity, the thermal energy harvesting devices can be used as the power supply for some low-power electronics. Simultaneously, these thermal energy harvesting devices can also be used as self-powered temperature sensors due to the certain relationship between the output and the temperature difference. Here some representative works of the thermal energy harvesting devices are introduced in terms of the applications of TEG and PEG.

3.1.3.1. *Applications of TEG.*

Sun et al. demonstrated a stretchable all-fabric TEG based on woven thermoelectric fibers [25] (Fig. 3a). The π-type thermoelectric modules are woven through doped carbon nan-

Fig. 3. Applications of thermal energy harvesting technology. (a) A stretchable all-fabric TEG based on woven thermoelectric fibers. (b) Thermoelectric units array integrated with a T-shirt and a wrist strap. (c) A stretchable and shape-adaptive TEG integrated with a force sensor. (d) A self-powered temperature–pressure dual-parameter sensor array based on microstructure-frame-supported organic thermoelectric materials. (e) A PyNG consisted of a single lead zirconate titanate microwire. (f) A highly stretchable PyNG based on micropatterned architectures. (g) A flexible transparent tribo-piezo-pyroelectric hybrid generator for physiological monitoring. (h) A self-powered breathing sensor based on a PVDF film integrated with a mask.

otube fibers wrapped with acrylic fibers alternately. The 3D fabric TEG without substrate is stretchable and fully aligned with the direction of heat flow, benefited from the elasticity of interlocked thermoelectric modules. When the temperature difference is 44 K, the peak power density of the textile TEG can reach 70 mWm^{-2}, which is sufficient to drive some low-power electronics.

Li et al. used the organic thermoelectric polymer PEDOT:PSS and the 3D spacer fabric to build a thermal energy harvester [26] (Fig. 3b). The device consists of 100 thermoelectric units integrated with a T-shirt that can obtain an output voltage of 203 mV when the temperature difference is 40 K. A thermoelectric wrist strap was presented to harvest energy from the body heat, which can light an LED at an ambient temperature of 25 °C. They also demonstrated a wearable, self-powered temperature-pressure sensor array that can be prepared on a large scale. The temperature detection resolution and response time of the sensor are 0.1 K and 1 s respectively.

Yang et al. presented a stretchable and shape-adaptive TEG (S-TEG) for human body heat collection, which can be applied to complex and dynamic surfaces of heat sources [27] (Fig. 3c). The thermoelectric elements p-type (Sb_2Te_3) and n-type (Bi_2Te_3) are fabricated into cuboids through hot-pressing and connected with a wavy serpentine structure to form thermocouples. The S-TEG consists of 10 × 10 thermocouples array that can generate an output power of 0.15 mW/cm^2 when the temperature difference is 19 K. The S-TEG attached to the wrist can harvest the body heat and provide a voltage to drive a force sensor for the finger motion detection.

Zhang et al. fabricated a self-powered temperature–pressure dual-parameter sensor based on independent thermoelectric and piezoresistive effects [28] (Fig. 3d). The device constructed by microstructure-frame-supported organic thermoelectric materials can work under a natural temperature gradient without external power supply. The temperature resolution and pressure sensitivity of the sensor can reach 0.1 K and 28.9 kPa^{-1} respectively. They also demonstrated an e-finger integrated 1350 pixels sensor array on a fabric frame of with an area of 2 × 3 cm^2.

3.1.3.2. Applications of PEG.

Yang et al. presented a pyroelectric nanogenerator consisted of a single lead zirconate titanate (PZT) micro/nanowire [29] (Fig. 3e). When the temperature increases from 296 to 333 K, the device can produce an output of 60 mV and 0.6 nA. A liquid crystal display is lighted up by the device under a large change in temperature (∼180 K). Obviously, such a large temperature difference is not suitable for human thermal energy harvesting, but it can be used as a self-powered sensor to detect the temperature of fingertips.

Lee et al. fabricated a highly stretchable PyNG, which is composed of pyroelectric material P(VDF-TrFE), PDMS elastomer, and Ag/AgNWs electrode [30] (Fig. 3f). Making use of micropatterned architectures and different thermal expansion coefficients of materials, the output performance of PyNG has been greatly improved. When the temperature difference is 22 K and the rate of temperature change is 105 K s^{-1}, the stretchable PyNG can produce an output voltage of 2.5 V and a current density of 570 nA cm^{-2}. By storing the energy from PyNG in a capacitor, LEDs and LCD screens can be driven to operate.

Sun et al. demonstrated a flexible transparent tribo-piezo-pyroelectric hybrid generator for human body energy harvesting and physiological monitoring [31] (Fig. 3g). A leaf venation-like silver nanowires network is prepared as high-performance transparent electrodes (TEs) to fabricate the hybrid generator. A visual thermometer is also presented by integrating the transparent hybrid generator with a thermochromic liquid crystal film. When the wearer breathes weakly and normally at an ambient temperature of 15 °C, the device can produce 25V and 35V output voltage respectively, meanwhile turns red and green accordingly.

Xue et al. presented a self-powered breathing sensor based on a wearable PyNG, which is fabricated by a PVDF film covered electrodes on both sides and an N95 respirator [32] (Fig. 3h). The PVDF film is embedded in the middle of the respirator to sense the airflow exhaled by a subject. When the wearer breathes at 5 °C ambient temperature, the PyNG can produce 42 V/ 2.5 μA output signals due to the temperature fluctuation. The high output performance PyNG can be used to monitor human breathing status and ambient temperature.

3.1.4. Comparison of TEG and PEG

Thermal energy harvesting technologies have made great progress in recent years. These technologies have unique advantages in the practical application of human body thermal energy harvesting, but there are also relevant critical issues. Here we summarize them and put forward some promising solutions by comparing TEG with PEG (Table. 1).

The human body is a natural constant heat source. The human body consumes a large amount of energy every day to maintain a constant body temperature and emits heat to the surrounding environment all the time. Therefore, the thermal energy from the human body can be recycled and utilized as a continuous energy source. Most importantly, this form of energy harvesting does not cause any negative impact on the human body itself, so human heat is an ideal energy source which can be continuously utilized at any moment. Nevertheless, there are still some limitations in the actual use of human heat. First of all, the energy conversion efficiency of TEG and PEG is limited by the second law of thermodynamics (Carnot efficiency). A high energy conversion efficiency requires a large temperature difference. Since normal human body temperature is stable at 36–37 °C, the temperature difference that can be used for energy harvesting mostly comes from the temperature difference between the human body and the external environment. Therefore, it is usually impossible to achieve a large temperature difference unless in extremely cold environment. In addition, although the temperature inside the human body is more constant, it is difficult to directly build the temperature difference with the outside, so that TEGs and PEGs are hardly used *in vivo*.

TEGs are currently the main way to harvest thermal energy from the human body. TEGs adopt an all-solid-state energy conversion method without chemical reaction or fluid medium, which have the advantages of no noise, no vibration, no wear, no medium leakage, small size, light weight, and long service life during the generation process. Despite these advantages, there are still some critical issues for TEGs. TEGs rely on a spatially graded distribution of temperature. Compared with PEGs, TEGs are more dependent on the heat exchange between the human body and the external environment. In addition, TEGs are generally composed of multiple sets of semiconductor thermocouples in series and parallel, which leads to complex structure and high cost.

PEGs can only harvest thermal energy that changes in temperature over time, so there are relatively few applicable scenarios for human body thermal energy harvesting, such as the non-continuous breathing heat from mouth and nose. However, PEGs can be used as ideal self-powered sensors, particularly suitable for detecting human activities and temperature changes. Compared with TEG, PEG generally has a simple device structure and relatively high output voltage, but it is not as stable as the former. When the temperature is higher than the Curie temperature, the spontaneous polarization of the pyroelectric materials will dissipate. In addition, the extreme high humidity atmosphere also attenuates its performance.

In summary, TEGs and PEGs currently applied on human body thermal energy harvesting can only provide relatively low output power with low energy conversion efficiency. Increasing the thermal contact surface and using an efficient power management system can appropriately improve the output and conversion efficiency. For TEGs, the core content of current research is to continue in-depth study of thermoelectric conversion materials, develop high thermoelectric figure of merit (ZT) thermoelectric materials with high Seebeck coefficient, high conductivity and low thermal conductivity [33]. In addition, increasing the number of series and parallel thermocouples to build a more efficient thermopile for space utilization, establishing an appropriate structure to match the heat flow direction, and using an auxiliary heat dissipation unit to improve the heat collection efficiency can also partly improve the output performance of TEGs [34,35]. For PEGs, developing pyroelectric materials with high pyroelectric coefficient, further optimizing the device's structure, and taking advanced packaging technology are promising methods.

3.2. Chemical energy harvesting of the human body

The collection and conversion of chemical energy in the human body are usually accompanied by chemical reactions as well as the transfer of electrons in chemical substances. We mainly introduce two kinds of human chemical energy harvesting technology, biofuel cell (BFC) and

Table 1
Comparison of TEG and PEG, from advantages, critical issues to promising solutions.

	TEG	**PEG**
Advantages (Shared)	Human body as natural constant heat source Utilization of human waste heat No negative effects on the human body	
Advantages (Individual)	No mechanical wear No chemical reaction Long-term stability	Simple structure Relatively high output voltage Sensitive to temperature changes
Critical issues (Shared)	Limited by Carnot efficiency Small available temperature difference Low energy conversion efficiency	
Critical issues (Individual)	Limited by temperature gradient Relatively complex structure Relatively high cost	Limited by temperature fluctuation Limited by Curie temperature High-humidity impact
Promising solutions (Shared)	Increased thermal contact surface Efficient power management system	
Promising solutions (Individual)	High ZT value thermoelectric materials innovation Increase the number of thermocouples Auxiliary heat dissipation	High pyroelectric coefficient materials innovation Structure optimization Good encapsulation

hydrovoltaic effect generator (HEG). The former technology uses human body fluids like glucose and lactate as energy substances to convert electrical energy, while the latter utilizes the interaction between nanomaterials and water molecules to convert electrical energy through evaporation energy and humidity changes.

3.2.1. Biofuel cell

3.2.1.1. Principle of BFC. Biofuel cell is a kind of energy harvesting device that uses the redox reaction of energy substances in living organisms to generate electricity. Biofuel cells can be divided into enzymatic fuel cells (EFCs) and microbial fuel cells (MFCs) according to the catalyst types [36]. MFCs use living microorganisms as catalysts, while EFCs use oxidoreductases as catalysts. Although MFC has better stability with long working life, considering that living microorganisms are used in the human body, there is a certain risk of infection. Meanwhile, the diffusion rates of reactants/products/electrons in MFC are limited by biofilm, leading to a relatively low power generation performance. Therefore, EFC is currently the main research direction of biofuel cells for human chemical energy harvesting.

The working mechanism of EFC is elaborated by taking glucose biofuel cell as an example, which is shown in Fig. 4 (a). The anode of EFC uses glucose as fuel substrate, glucose oxidase or glucose dehydrogenase as catalyst, while the cathode uses oxygen as oxidant, laccase or bilirubin oxidase as catalyst [37]. At the same time, ferrocene acts as redox mediator. Carbon nanotubes or conducting polymers with good conductivity are usually used as carriers of biological enzymes, while inert metals or carbon materials are used as base electrodes. When the glucose biofuel cell works, the glucose oxidase on the anode catalyzes the oxidation of glucose to gluconolactone, while the electrons are transferred to the electrode through ferrocene and then reach the cathode through the external circuit. On the surface of the cathode, oxygen combines with the protons and the electrons transferred from the anode, and is reduced to water under the catalytic action of laccase. In the whole working process of glucose biofuel cell, the chemical reaction equations at anode and cathode are as follow:

$$\text{Anode}: \ C_6H_{12}O_6 + 2OH^- \rightarrow C_6H_{12}O_7 + H_2O + 2e^-$$

$$\text{Cathode}: \ \frac{1}{2}O_2 + H_2O + 2e^- \rightarrow 2OH^-$$

The simplified overall chemical reaction equation is as follows:

$$\text{Overall}: \ C_6H_{12}O_6 + \frac{1}{2}O_2 \rightarrow C_6H_{12}O_7$$

It can be seen that the power generation process of biofuel cell is actually the process of electrons transfer from anode to cathode through redox reactions of substances. When the fuel substrate is sufficient and the activity of the enzyme is maintained, the biofuel cell can produce continuous direct-current electricity.

3.2.1.2. Demos of BFC. Bandodkar et al. reported a soft e-skin based on biofuel cells for scavenging chemical energy from human sweat [38] (Fig. 4b). An island-bridge structure is used to fabricate anode and cathode of biofuel cells, endowing the device with good stretchability and stability. The wearable e-skin-based biofuel cell can produce a power density of 1.2 mW cm^{-2} at 0.2 V by scavenging lactate from human sweat, which is able to power a Bluetooth Low Energy (BLE) radio and LED with the help of a DC–DC converter.

Pankratov et al. designed a mediator-free and membrane-less glucose biofuel cell based on a tubular graphite electrode that simulates human veins [39] (Fig. 4c). The tubular glucose biofuel cell is connected with a peripheral venous catheter inserted into a volunteer's superficial vein. In the case of simulating human venous blood flow, the device obtains a maximal power of 0.74 μW at 0.16 V from the real blood of the human body, which is capable of driving an electronic ink display to operate directly. Despite using a simulated vein, this work verified the feasibility of biofuel cells operating in real human blood for the first time.

3.2.2. Hydrovoltaic effect generator

3.2.2.1. Principle of HEG. Hydrovoltaic effect is a recently emerging scientific concept in the energy field. It is a general term for the phenomenon that the water-energy is converted to electrical energy by the interaction between nanomaterials and water molecules [40,41]. When low-dimensional materials such as carbon nanotubes and graphene interact with water molecules in different ways, a series of various electricity generation effects occur at the solid-liquid interface. Among the effects, the electrokinetic effects that have been proposed in an early stage rely on external input of mechanical work, which includes streaming potential, drawing potential, waving potential, and flow-induced potentials [40,42]. Recently, electricity generation effects induced by water evaporation and humidity have been presented. Since these two electricity generation effects can completely rely on the natural water evaporation and the humidity in ambient to generate electricity without the need of additional input of mechanical work, they have become the hotspots of current research of hydrovoltaic power generation [43,44].

The water evaporation-induced power generation can be attributed to the interaction between water molecules and nanomaterials. In the evaporation process, the flow of water molecules in the gap of nanomaterials induces the generation of voltage and current, which is similar to the traditional streaming potential. Taking porous carbon nanomaterials as an example, the relevant mechanism is shown in Fig. 4(d). The channel wall between the treated nanocarbon layers is naturally negatively charged, which will attract the hydronium ions in water and form an electric double layer on the surface. At the same time, the electrical double layers formed at the surface of the channel wall will overlap with each other due to the small size of the micro/nano-channel (the electric

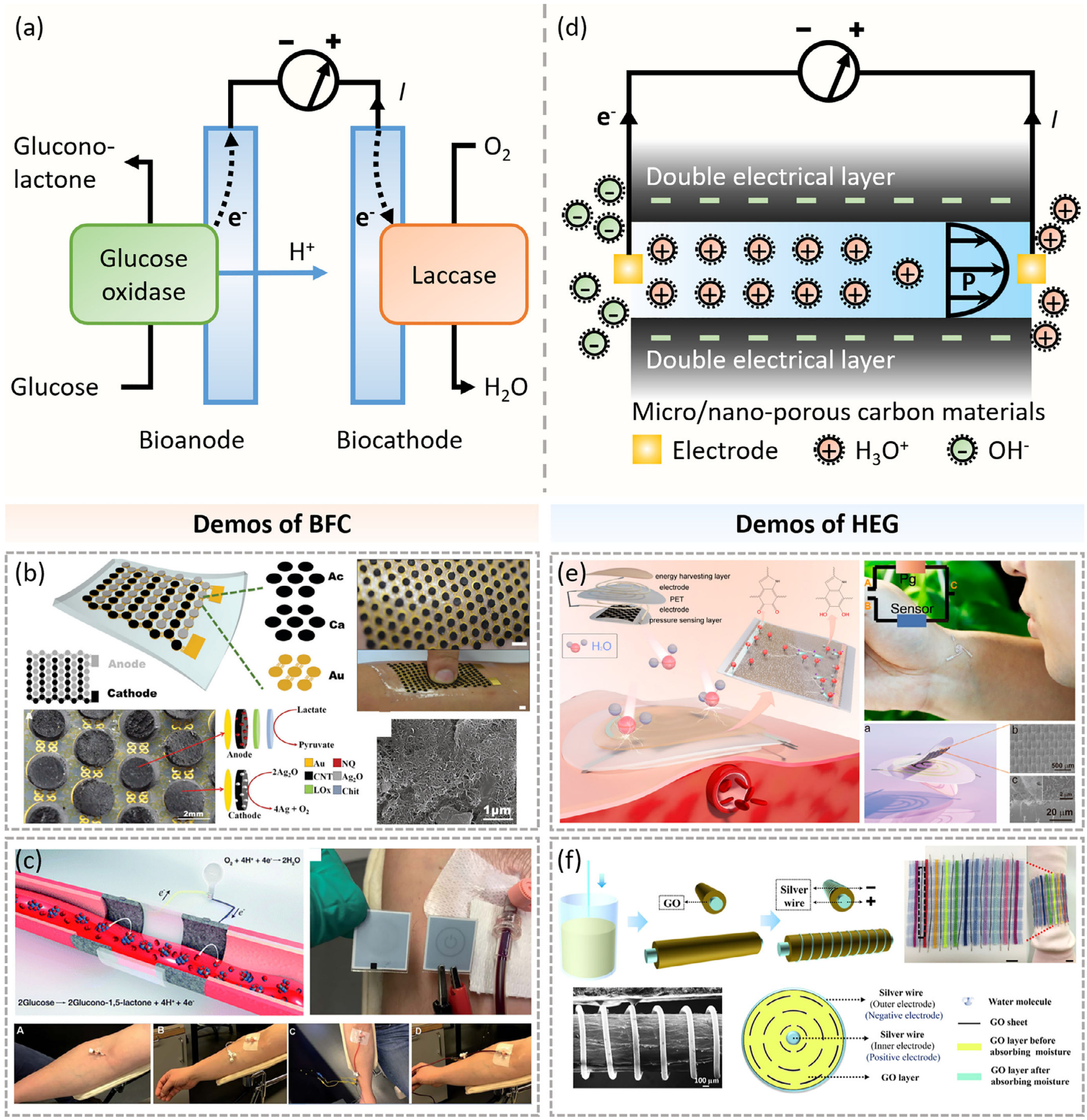

Fig. 4. Chemical energy harvesting of the human body, from principle to demos of BFC and HEG. (a) Principle of BFC. (b) A soft e-skin based on BFCs for scavenging energy from human sweat. (c) A tubular glucose BFC operating in real human blood. (d) Principle of HEG. (e) A moisture-enabled power generator operated by water vapor from human breath. (f) A coaxial fiberform HEG for moisture energy collection.

double layers will overlap when the Debye length of the liquid is larger than the width of the microchannel), which makes the whole channel relatively repel anions (OH^-) with the same charge. When water evaporates, the hydronium ions in the channel will move in the direction of water flow continuously under the pressure gradient in the channel, resulting in the accumulation of charges in the direction of water flow and producing a streaming potential accompanied with current output [40].

Humidity-induced power generation can be performed by environmental relative humidity changes. The main mechanism of the humidity to electricity conversion process is dependent on reversible changes between hydration and dehydration, resulting in the release of free hydrated ions by pre-formed gradient distributed ionizable groups. When exposed to moisture, driven by the concentration gradient, free hydrated ions will migrate directionally from the high concentration zone to the low concentration zone, resulting in electricity output [43,45].

3.2.2.2. Demos of HEG. Xue et al. found that when water evaporated on the surface of the annealed and plasma-treated carbon black film, continuous DC voltage and current are generated in a natural environment [46]. The induced voltage and short-circuit current reach up to 1.0 V and 150 nA, and the duration exceeds 160 hours. By connecting four devices in series, the output voltage can reach 4.8V and successfully power an LCD display.

Li et al. presented a moisture-enabled power generator based on a porous polydopamine layer modified by gradient hydroxy group [47] (Fig. 4e). The porous membrane can capture moisture from ambient, promote hydration and ion transport under the action of polar functional groups. A moisture-induced potential will generate due to the plenty of gradient-distributed free cations and locally restricted anions on the membrane. The device can generate an open-circuit voltage of 0.52V and a power density of 0.246 mW cm^{-2} when relative humidity varies from 5% to 95%.

Shao et al. demonstrated a fiberform hygroelectric generator (FHEG) for moisture energy collection [48] (Fig. 4f). The coaxial FHEG consists of a core silver wire, a shell of graphene oxide (GO) layer and another silver wire twined on the shell. The silver serves as an electrode while GO layer serves as the power generation layer. The FHEG can produce an open-circuit voltage of 0.3 V and a power density of 0.21 μW cm^{-1} under 70% humidity change. This kind of hygroelectric generator can be woven into any shape and integrated with fabric for wearable energy harvesting devices.

3.2.3. Applications of chemical energy harvesting

Chemical energy harvesting devices can convert the human body's chemical energy into electricity to power some low-power electronics. Since the output of BFCs correlates with the levels of certain metabolites in body fluids, BFCs can also act as self-powered biochemical sensors to detect concentrations of substances such as glucose or lactate. For hydrovoltaic power generation devices, they can act as self-powered humidity sensors due to their output is highly correlated with humidity. Some representative works of the chemical energy harvesting devices are introduced in this section containing the applications of BFC and HEG.

3.2.3.1. Applications of BFC. Yu et al. reported a flexible, fully perspiration-powered electronic skin (PPES) for in-situ multiplex metabolism detection [49] (Fig. 5a). PPES is powered by high-efficiency lactate biofuel cells, which can obtain 3.5 mW/cm^{-2} power density output from untreated human sweat, and maintain stable performance for 60 hours of continuous operation. When integrated with multimodal chemical sensors, PPES can continuously monitor metabolic analytes ($NH4^+$, urea, glucose, and pH) in real-time. A human-machine interaction interface was also demonstrated for assistive robotic control by integrating PPES with strain sensors.

Wang et al. presented a wearable textile-based glucose biofuel cell utilizing moisture management fabric (MMF) [50] (Fig. 5b). MMF composed of polyester is a fabric widely used in sportswear, which has the characteristics of rapid water absorption and evaporation. The biofuel cells constructed by MMF can generate an output voltage of 1.08 V and a maximum power of 80.2 μW due to the high-speed flow of sweat, which ensures the sufficient supply of fuel and the efficient transportation of molecules. By integrating 6 MMF-based biofuel cells stacked in series into a bandage, an electronic watch is successfully powered.

Jeerapan et al. reported a wearable self-powered sensor for detecting glucose or lactate content in human sweat based on a stretchable textile-based biofuel cell [51] (Fig. 5c). Using stretchable engineered conductive ink and screen-printing technology, the preset serpentine structure electrode can be printed on a highly ductile fabric. On this basis, a single enzyme and membrane-free biofuel cell can be constructed on a sock. The self-powered sensor built on the sock can detect the concentration of metabolites in sweat with good sensitivity and stability.

Bandodkar et al. demonstrated a wireless passive sweat analysis platform inspired by biofuel cells [52] (Fig. 5d). The platform integrates biofuel cell sensors, colorimetric analysis, near-field communication, and soft microfluidics, which can detect the concentration of lactate, glucose and chloride, pH value in human sweat and sweat rate/loss simultaneously and efficiently. After two days of human trials, comparing the concentration of glucose and lactate from sweat analysis platform and blood, results show that the platform has the potential to be used in non-invasive semi-quantitative detection of physiological status.

For the sake of safety and experimental ethics, there are few studies on BFC harvesting chemical energy from the human body *in vivo*, but many related studies have been validated in animals. Implantable BFCs have achieved remarkable results in animal experiments in recent years. In 2010, Cinquin et al. conducted the first implantable enzyme biofuel cell in a living organism, the BFC implanted in the retroperitoneal space of a rat can produce 6.5 μW output power at 0.13 V [53]. In 2011, Miyake et al. inserted a needle anode of a BFC into the blood vessel of a rabbit ear, generating an output power of 0.42 μW at 0.56 V [54]. In 2013, MacVittie et al. implanted BFC into lobster and achieved an open circuit voltage of 0.54 V and a short circuit current of 1 mA, by connecting two BFCs in series, an electronic watch was driven successfully [55]. In 2016, Shoji et al. implanted BFC into the back of a cockroach, the insect-mountable BFC produced a maximum power output of 333 μW, which can drive both an LED device and a wireless sensor [56]. In 2019, Bollella et al. implanted a small size (2× 3× 2 mm3) BFC into the hemolymph of a slug and successfully drove the supporting microelectronic sensor system autonomously [57]. In 2021, Lee et al. implanted a BFC and an animal brain stimulator (ABS) in a pigeon, the implanted BFC can generate an output power of 0.08 mW *in vivo* and supply to the ABS for intermittent neurostimulation [58]. In summary, implantable BFCs are constantly improving in terms of conversion efficiency, output power, stability and sustainability. The exciting results obtained in animal experiments are the basis for the real application of implantable BFCs in the human body and clinical medicine.

3.2.3.2. Applications of HEG. Qin et al. found that silicon nanowire arrays can also be used to collect the energy from water evaporation and convert it into constant electricity [59] (Fig. 5e). A hydrovoltaic device is fabricated with silicon nanowire array as the active layer, graphite and silver as the cathode and anode, respectively. The open-circuit voltage, short-circuit current density and output power density that the device can generate are 400 mV, 55 μA cm^{-2} and 6 μW cm^{-2} respectively, when the relative humidity is 45% and the ambient temperature is 65 °C. A light emitting diode can be powered by 6 devices in series at room temperature.

Zhang et al. designed a wearable self-powered perspiration analyzing site based on the coupling of enzymatic reaction and hydrovoltaic effect [60] (Fig. 5f). The device consists of ZnO nanowire arrays modified by lactate oxidase and a flexible PDMS substrate integrated with microfluidics. When the device is attached to human skin, sweat will flow into the ZnO nanowire arrays through the microchannels and generate a direct current signal due to the hydrovoltaic effect. The lactate in the sweat will react with the lactate oxidase on the ZnO nanowire and further affect the electrical output, which can reflect the concentration of lactate of sweat.

Mandal et al. presented a moisture-induced self-biased electronic sensor, which is fabricated by protein films of gelatin molecules [61] (Fig. 5g). The gelatin protein film serves as the active material for power generation. The device shows a significant electrical response when the relative humidity exceeds 55%. A smart mask is constructed based on the sensor, which can monitor the wearer's breathing state by sensing the relative humidity in breathing airflow. In addition, the sensor can also monitor the humidity distribution on the surface of the finger to evaluate the state of wound healing.

Shen et al. designed a self-powered portable gas analyzer for detecting the alcohol concentration in exhaled breath, which is consisted of a

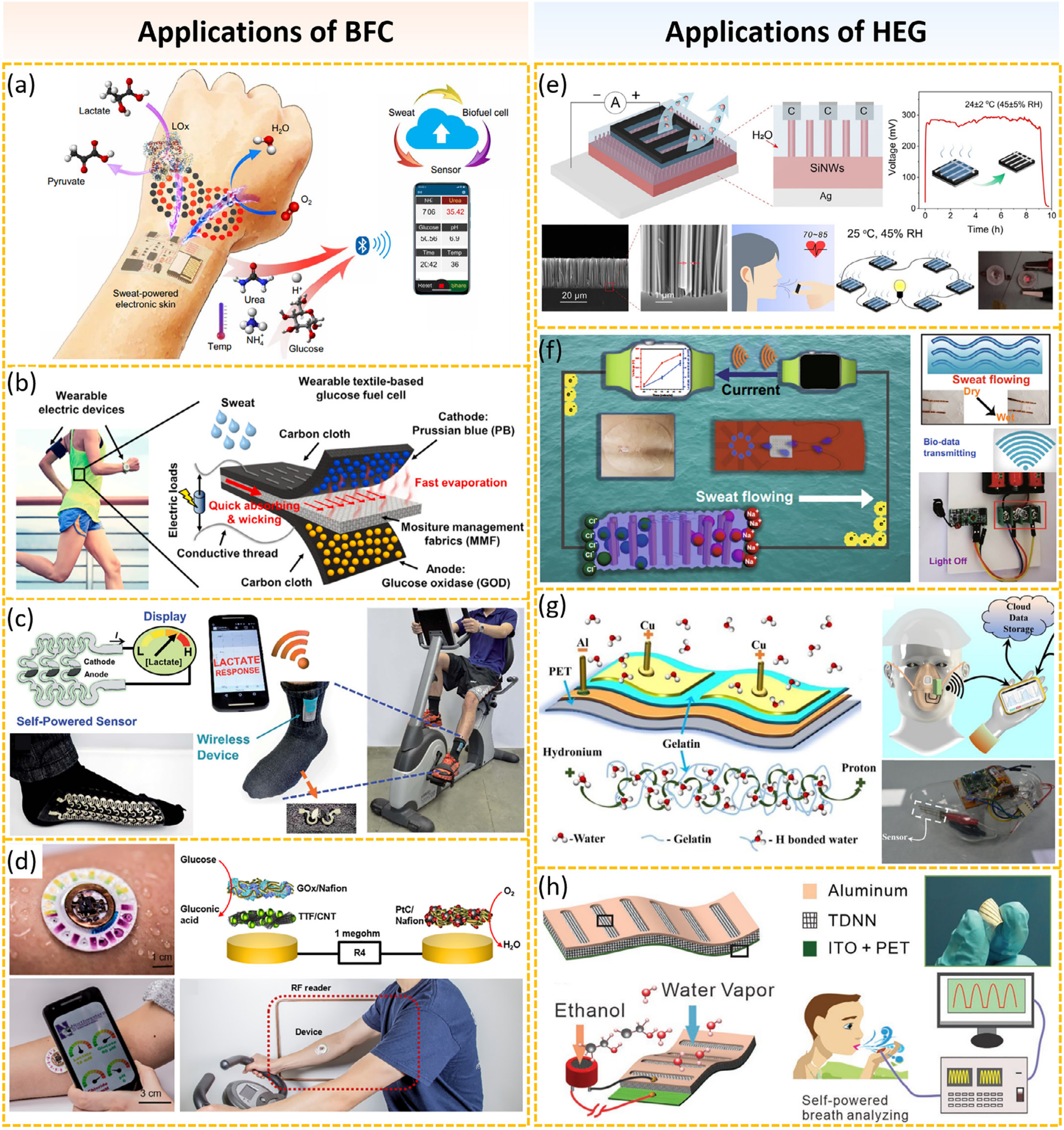

Fig. 5. Applications of chemical energy harvesting technology. (a) A flexible, fully perspiration-powered electronic skin for in-situ multiplex metabolism detection. (b) A wearable textile-based glucose BFC utilizing moisture management fabric. (c) The self-powered sweat sensor built on sock using a stretchable textile-based BFC. (d) A wireless passive sweat analysis platform inspired by BFCs. (e) A hydrovoltaic device fabricated with silicon nanowire arrays. (f) A wearable self-powered perspiration analyzing site based on enzymatic reaction and hydrovoltaic effect. (g) A smart mask based on a moisture-induced self-biased respiration sensor. (h) A self-powered gas analyzer for detecting the alcohol in exhaled breath based on a HEG.

hydroelectric nanogenerator (HENG) and a commercial ethanol sensor [62] (Fig. 5h). HENG which uses TiO_2 nanowire networks as the active layer, can generate 0.5 V output voltage and 0.7 $\mu W\ cm^{-2}$ maximum power density from the exhaled breath. When HENG connects with the ethanol sensor, the voltage signal output by the ethanol sensor shows a certain linear relationship with the ethanol concentration ranging from 50 to 1000 ppm.

3.2.4. Comparison of BFC and HEG

Whether the biofuel cell that has been studied for many years or the recently proposed hydrovoltaic effect, they both have advantages and problems in application of chemical energy harvesting from the human body. Here we summarize the advantages and problems and propose some possible solutions for reference (Table. 2).

Table 2
Comparison of BFC and HEG, from advantages, critical issues to promising solutions.

	BFC	HEG
Advantages (Shared)	Direct-current output characteristics High current density	
Advantages (Individual)	Wide range of energy substances High conversion efficiency Mild reaction conditions	Sufficient source of moisture Harmless to the human body Relatively good stability
Critical issues (Shared)	Low output voltage Constrained Sustainability	
Critical issues (Individual)	Relatively poor stability Limited by the oxidation-reduction potential Biosafety to be further verified	Relatively low output Relatively simple applications No general mechanism explanation
Promising solutions (Shared)	Multiple devices in series Step-up transformer	
Promising solutions (Individual)	Increase catalytic efficiency Intermittent working Mediator-free BFC Good encapsulation	Hydrophilicity regulation Surface chemical modification In-depth exploration of universal mechanism

The human body is rich in chemical energy substances, which exist in body fluids or organs in the form of glucose, lactate, vitamin C and so on. Biofuel cells can directly convert the chemical energy of these energy substances into electrical energy through electrochemical reactions under the action of catalysts. The energy conversion of biofuel cells is not limited by the Carnot cycle, which allows biofuel cells to have a relatively high energy conversion efficiency. Furthermore, biofuel cells have the advantages of a wide range of substrate sources, mild reaction conditions and diverse catalyst types. However, the current research and application of biofuel cells are still in an immature stage in view of the problems including low output power, poor stability, and short service life. Additionally, when biofuel cells are implanted into organisms for *in vivo* application, the oxygen content contained in the body could be much lower than that *in vitro*, which may lead to insufficient oxidation and a limited energy conversion efficiency [63, 64].

The effective way to solve these problems is to find more suitable enzyme catalysts, corresponding fixed carriers and redox mediators, so as to increase the catalytic efficiency, realize faster electron transfer between the catalyst and the electrode while ensuring good stability and working life of the biofuel cells. Although biofuel cell usually obtains a high current density, the output voltage is usually lower than 1 V limited by the oxidation-reduction potential [65,66]. In practical application, multiple biofuel cells connected in series or a step-up transformer is required to make the output voltage of biofuel cells achieve the threshold operating voltage of general commercial electronics. In order to prevent the leakage of enzymes and redox mediators from affecting the human body, dialysis bags are usually used for packaging biofuel cells, which will increase the size and complexity of the device. Therefore, mediator-free biofuel cell is one of the current research hotspots and trends. The most important point which is often ignored in current research, is that when using biofuel cells to convert the chemical energy of the human body, priority needs to be given to whether this energy conversion will affect the normal physiological functions of the human body. It is because the human body itself needs a large number of energy substances to supply the corresponding energy to cells, tissues, organs as well. For diabetic patients, the excessive glucose content in blood can provide sufficient reaction substrates for the electrochemical reaction of biofuel cells. However, for healthy people with normal blood glucose and hypoglycemic patients whose blood glucose levels are already lower than normal, it is necessary to consider whether the use of biofuel cells will have a negative impact on their body, which requires a large number of biological *in vivo* experiments and clinical trials to verify. It could be sensible strategy to use intermittent working mode, such as operating during the period of blood glucose rise after meals.

The water content in the human body is approximately 70% of the body weight, while a large quantity of water still needs to be ingested every day. In addition to being excreted through urine, part of water will be excreted in the form of sweat evaporation and respiration to maintain the dynamic balance of water in the body. The evaporation of human sweat and the humidity change from breathing are ideal energy sources for electricity generation by hydrovoltaic effect. This kind of energy belongs to the ‘waste energy’ discharged by the human body spontaneously and therefore does not have any impact on the human body when conducting electric energy conversion. This new power generation method does not need any additional energy input and any mechanical moving parts, which can be long-term used on the human body for its safety and reliability. At present, the technology of utilizing hydrovoltaic effect for electrical energy conversion is still in infancy, the relevant conversion efficiency and output power are still relatively low. Although some studies have shown that the performance of HEG can be improved by controlling the hydrophilic and hydrophobic interface as well as surface chemical modification [43]. But more importantly, further in-depth exploration to refining a universal mechanism of hydrovoltaic effect is needed, which will provide guidance for enhancing the energy conversion efficiency of HEG and improving the corresponding output voltage and current density. In addition, current research on HEG applied to the human body is relatively basic. How to design the HEG applicable to the human body, and how to make better use of the evaporation energy and the humidity energy from the human body, are also critical issues that need to be considered. Considering that most of the suitable application scenarios need to directly contact with the skin of the human body, it will be an ideal approach to design a comfortable wearable HEG to help dehumidify and generate electricity at the same time.

3.3. *Mechanical energy harvesting of the human body*

The collection of mechanical energy of the human body can be traced back to more than one hundred years ago, the first hand generator based on electromagnetic induction was invented, which is the first time that human beings have consciously converted their own mechanical energy into electrical energy. Later, some radios and flashlights driven by human motion were invented successively. The traditional electromagnetic power generation devices are usually large and heavy, operating under a high frequency, which may bring burdens to the human body when collecting human body mechanical energy passively. Although there are some excellent research works on human mechanical energy harvesting based on electromagnetic generators (EMG) [67–71], the relevant working principle will not be elaborated here since it is well known. The mechanical energy from the daily activities of the human body is usually low-frequency and unconscious. In this section, we mainly introduce two newly emerging mechanical energy harvesting technologies, piezoelectric nanogenerator (PENG) and triboelectric nanogenerator (TENG),

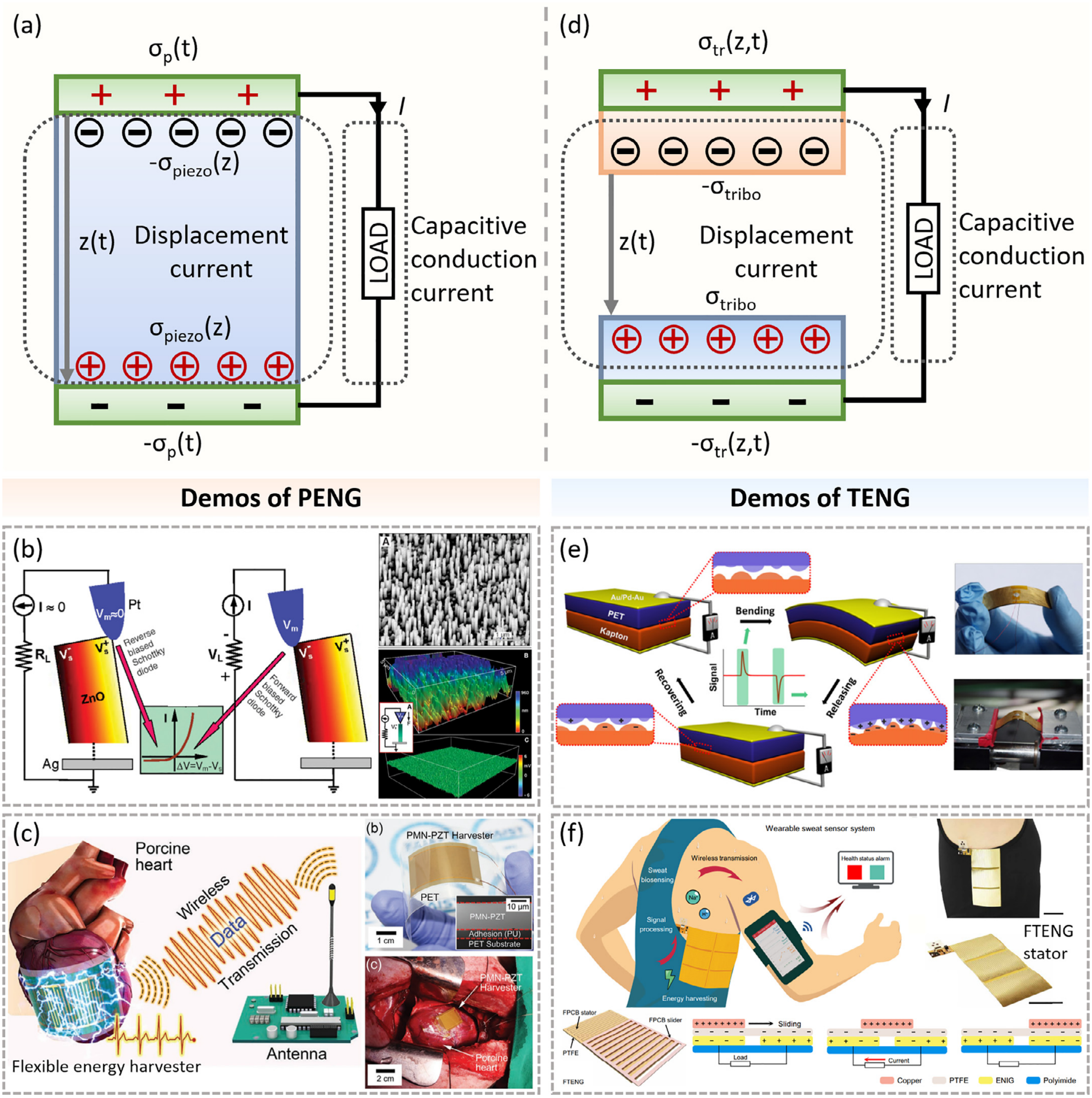

Fig. 6. Mechanical energy harvesting of the human body, from principle to demos of PENG and TENG. (a) Principle of PENG. (b) The first PENG based on ZnO nanowire arrays. (c) Collected biomechanical energy from a porcine's heart by a biocompatible piezoelectric energy harvester. (d) Principle of TENG. (e) The first TENG based on two stacked thin polymer films. (f) A fully self-powered wearable sweat analysis system driven by a freestanding-mode TENG.

which are especially suitable for distributed, mobile, low frequency, and micro energy harvesting and conversion.

3.3.1. Piezoelectric nanogenerator

3.3.1.1. Principle of PENG. Piezoelectric nanogenerator is a mechanical energy-electric energy conversion device based on the piezoelectric effect. PENG utilizes the piezoelectric polarization charges and time-varying electric field to drive the flow of electrons in a circuit [72]. The working principle of PENG based on the displacement current model is shown in Fig. 6(a). Displacement current is generated inside the generator, while capacitive conduction current is generated in the external circuit.

Piezoelectric materials are usually crystal materials with asymmetric structure. The generation of the piezoelectric effect is closely related to the generation of electric dipoles in piezoelectric materials [73]. A simple PENG is constructed by covering the top and bottom electrodes on two surfaces of insulated piezoelectric material. When the piezoelectric material is deformed by external force along a specific direction (take Z-axis as an example), the relative displacement of positive and negative ions in the unit cell causes the positive and negative charge centers to no longer coincide, forming electric dipoles and causing the macroscopic polarization of the crystal. In this case, equivalent piezoelectric polarization charges with opposite polarity are generated at both ends of the piezoelectric material, and the density of the polarization charge increases with the applied force [74,75]. The polarization charge density at both ends of the piezoelectric material is expressed by $\sigma_{\mathrm{piezo}}(\mathrm{z})$, which is a function of the thickness z of the piezoelectric material. The electrostatic potential generated by the polarization charges drives the free electrons to flow from one electrode to another through the external circuit to balance the potential, thereby causing a current to be generated in the circuit and realizing the conversion from force to electricity. The charge density of free electrons on the corresponding electrode is expressed by $\sigma_{\mathrm{p}}(\mathrm{t})$, which is a function of the time t. When a periodic external force is applied to PENG to make it continuously deform and recover, a periodic alternating current output will be produced.

3.3.1.2. Demos of PENG. In 2006, Wang et al. proposed the first piezoelectric nanogenerator based on ZnO nanowire arrays to realize the electrical energy conversion from tiny vibration (Fig. 6b), which opened up the field of micro/nano-energy [76]. Since then, various high-performance nanogenerators have been developed and used for the collection of mechanical energy from the environment and the human body.

Yang et al. improved the previously PENG with vertically aligned ZnO nanowire array structure and designed a flexible PENG based on a laterally packaged piezoelectric fine wire [77]. Both ends of a single ZnO nanowire are fixed on the metal electrodes, and the entire device is packaged on a flexible substrate. When the device is stretched and released, the single piezoelectric wire can generate an output voltage of 50 mV at a strain of 0.05–0.1%.

Li et al. demonstrated a PENG based on a single ZnO nanowire for biomechanical energy harvesting in vivo [78]. A PENG manufactured by a ZnO nanowire with 100–800 nm diameter and 100–500 μm length is implanted into a rat's diaphragm and heart. The device can obtain a voltage of 3 mV and a current of 30 pA on average from a rat's heartbeat. Although such an output is relatively small, it verified the possibility of PENG collecting biomechanical energy *in vivo* for the first time.

Kim et al. presented a biocompatible flexible energy harvester based on single-crystalline PMN-PZT [79] (Fig. 6c), and verified the biomechanical energy harvesting of the high-performance piezoelectric energy harvester in a large animal model (a porcine). The implanted device can generate an open-circuit voltage of 17.8 V and a short-circuit current of 1.75 μA from the contraction and relaxation of the porcine heart. In addition, a wireless signal transmission is successfully realized by the energy collected *in vivo*.

3.3.2. Triboelectric nanogenerator

3.3.2.1. Principle of TENG. Triboelectric nanogenerator is a mechanical energy-electric energy conversion device based on the coupling of triboelectrification and electrostatic induction, which use the time-varying electric field caused by the surface electrostatic charges to drive the flow of electrons [72]. Four fundamental working modes of TENG are vertical contact-separation mode, in-plane sliding mode, single-electrode mode and free-standing triboelectric-layer mode [80]. Taking the most typical vertical contact-separation mode TENG as an example, the corresponding working principle based on the displacement current model is shown in Fig. 6(d). Displacement current is generated inside the generator while capacitive conduction current is generated in the external circuit.

The back of two dielectric materials with different electron affinity are covered with metal electrodes. When the two dielectric materials come into physical contact driven by an external force, the electrostatic charges on the surface of the two materials will be transferred due to triboelectric effect, which leads to the inner surface of the two materials carrying equivalent number of dissimilar charges [81]. These charges are non-moving static charges, the corresponding surface charge density is expressed by σ_{tribo}. With the increase of contact times between the two dielectric materials, the surface static charge density finally reaches saturation, which is independent of the distance z between the two materials. The electrostatic field formed by the triboelectric charges drives electrons to flow through the external load, resulting in the accumulation of free electrons in the electrodes on the back of the dielectric material. The corresponding charge density of free electrons on the electrodes is expressed by $\sigma_{\mathrm{tr}}(\mathrm{z,t})$, which is a function of the separation distance z(t) between the two dielectric materials [82]. This is the process that TENG converts mechanical energy into electrical energy. When a periodic external force is applied on TENG to make the two friction layers contact and separate continuously, a periodic alternating current will be produced.

3.3.2.2. Demos of TENG. In 2012, Zhong Lin Wang's group proposed the first triboelectric nanogenerator by stacking two thin polymer films with deposited metal electrodes on the top and bottom separately [83] (Fig. 6e). The flexible TENG generates an output voltage of 3.3 V and a power density of 10.4 mW/cm^3 from mechanical deformation. Since then, the research boom of new era energy and self-powered system based on TENG has started.

Kim et al. demonstrated a wearable TENG based on 2D power generation fabrics [84]. A fiber-structured TENG is prepared by assembling an Al wire with a PDMS tube, which are both covered with vertically aligned nanowires nanotextured surface. The wearable TENG is weaved by the power generation fibers onto a waterproof fabric for scavenging energy under harsh environments, obtaining a high output performance of 40 V, 210 μA and 4 mW.

Wang et al. designed a helix-belt structured TENG for collecting the mechanical energy generated by human motion [85]. The tube-like TENG with a symmetrical structure can harvest mechanical energy from various directions and generate a high surface charge density of 250 μC m^{-2}. The TENG built in outsoles or clothes can collect energy from walking or jogging, and continuously power an electronic watch and fitness tracker.

Zou et al. presented a bionic stretchable nanogenerator (BSNG) for underwater human mechanical energy harvesting [86]. The BSNG is manufactured by mimicking the structure of ion channels of electrocyte in electric eel, which can generate an open circuit voltage over 10 V when stretched underwater. By integrated with a diving suit and wireless signal transmission module, BSNG can also be used for underwater motion monitoring or undersea emergency rescue.

Song et al. demonstrated a wireless fully self-powered wearable sweat analysis system [87] (Fig. 6f), which is seamlessly integrated a high-performance freestanding-mode TENG (FTENG), sweat sensor patch, high-efficiency power management and Bluetooth Low Energy module on a flexible printed circuit board. The FTENG can generate an output power up to 416 mW m^{-2}, which is enough to drive the entire system to operate independently without any other external power supply during on-body human trials.

3.3.3. Applications of mechanical energy harvesting

The mechanical energy from human activities and organ movements can be converted into electricity by mechanical energy harvesting devices to drive some low-power portable devices and electronic medical devices. These mechanical energy harvesting devices can also be used as self-powered sensors to detect the human motions and physiological signals of the human body. Some representative works of the mechanical energy harvesting devices are introduced including the applications of PENG and TENG.

3.3.3.1. Applications of PENG. Lu et al. reported a flexible all-polymer piezoelectric fiber based on thermoplastic piezoelectric nanocomposites using thermal drawing technique [88] (Fig. 7a). The proposed piezoelectric fiber with a spiral geometry structure is fabricated by a soft hollow polycarbonate core encircled by a spiral multilayer, which consists of alternating layers of piezoelectric nanocomposites (PVDF, BaTiO3, PZT,

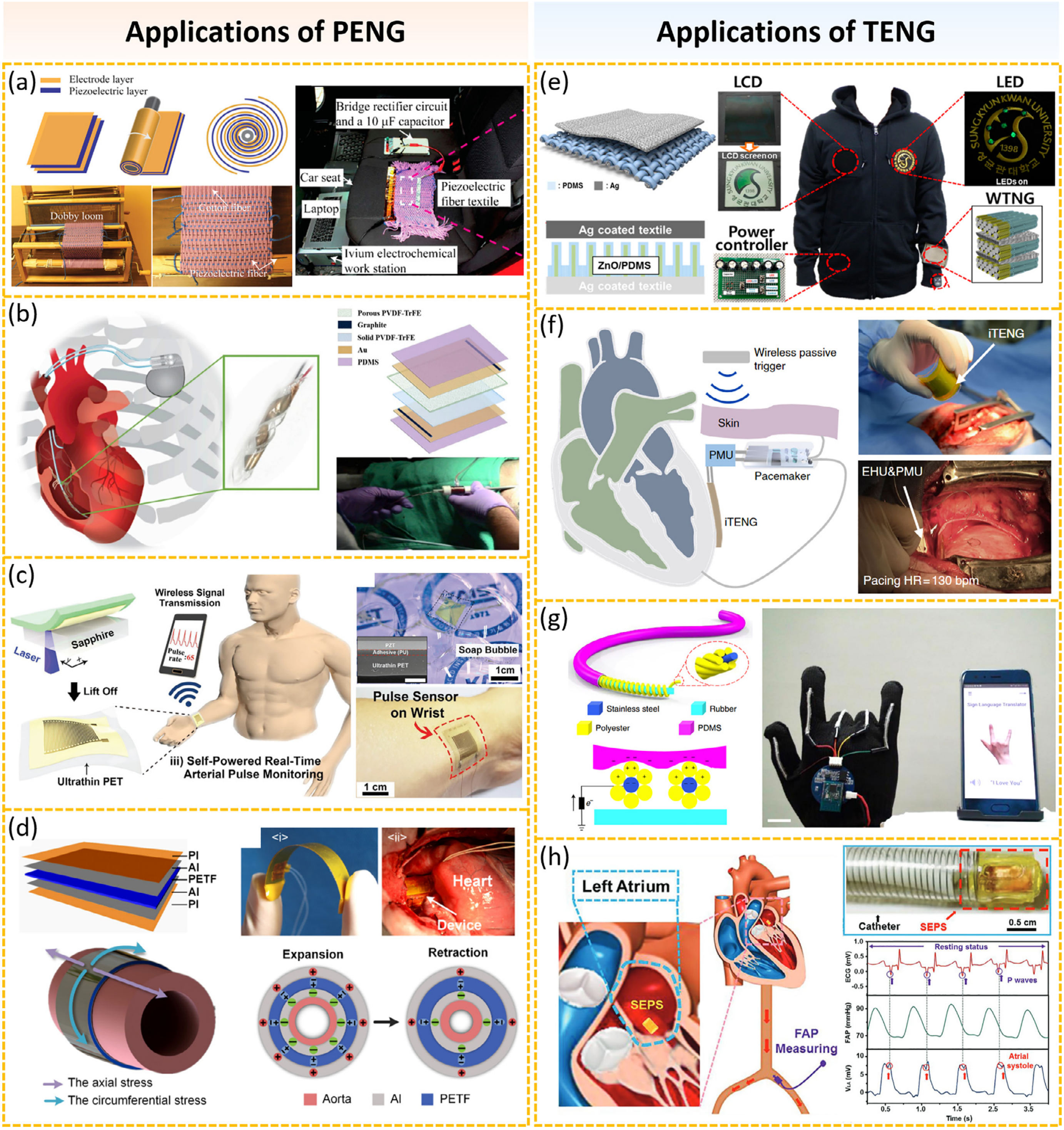

Fig. 7. Applications of mechanical energy harvesting technology. (a) Energy harvesting textiles based on flexible all-polymer piezoelectric fiber. (b) A porous piezoelectric thinfilm assembled with the lead of a pacemaker for cardiac mechanical energy harvesting. (c) An ultrathin epidermal piezoelectric sensor for real-time pulse monitoring. (d) A self-powered blood pressure monitor based on a piezoelectric thinfilm wrapped around the ascending aorta of a porcine. (e) A fabric wearable TENG based on silver-coated textile and PDMS nanopatterns. (f) A symbiotic cardiac pacemaker integrated by an implantable TENG and a commercial pacemaker. (g) A wearable sign-to-speech translation system based on stretchable sensor arrays and machine learning. (h) A transcatheter self-powered endocardial pressure sensor based on a miniaturized TENG.

CNT) and a conductive polymer. When the fiber is stretched or bent, it can effectively generate piezoelectricity, with an output voltage of 6 V. The fibers can be woven into energy harvesting textiles to collect mechanical energy in daily life, such as wearable clothing or car seat cushions.

Dong et al. proposed a cardiac mechanical energy harvesting strategy by integrating the energy harvesting device with the existing pacemaker lead [89] (Fig. 7b). The strategy is compatible with the pacemaker lead implantation surgery and does not contact the heart directly, so it will not affect cardiovascular function. A porous piezoelectric thinfilm of

PVDF-TrFE is manufactured with a self-wrapping helical configuration to assemble with the lead of a pacemaker. The device is implanted in a porcine to verify the feasibility of the energy harvesting strategy, obtaining an output voltage of 0.6 V and 1.2 V under normal and intensified cardiac contractions respectively.

Park et al. proposed an ultrathin epidermal piezoelectric sensor for real-time monitoring radial/carotid pulse signal [90] (Fig. 7c). The flexible piezoelectric pulse sensor based on a high-quality PZT thin film exhibits a high sensitivity of 0.018 kPa^{-1} and a short response time of 60 ms. When attached to human skin conformally, the device can convert the tiny vibration of human pulse into electrical signal output. A real-time wirelessly pulse signal transmission system is also demonstrated by integrated with a Bluetooth transmitter and an MCU.

Cheng et al. reported a self-powered blood pressure monitoring system, which is mainly constructed by a piezoelectric thinfilm of polarized PVDF (200 μm) [91] (Fig. 7d). After simulation and in vitro tests, the output of the device is highly correlated with pressure changes. The piezoelectric thinfilm with flexible encapsulation is implanted into a porcine and wrapped around the ascending aorta, achieving real-time monitoring of blood pressure in vivo. The system exhibits good linearity ($R^2 = 0.971$) and a sensitivity of 14.32 mV/mmHg, which can be used to identify the state of normotensive and hypertensive.

3.3.3.2. Applications of TENG. Seung et al. reported a fabric wearable triboelectric nanogenerator (WTNG) with high output performance and mechanical robustness [92] (Fig. 7e). The flexible and foldable WTNG is fabricated by a silver-coated textile and PDMS nanopatterns based on ZnO nanorod arrays formed on another silver-coated textile template. One WTNG can produce an output of 120 V and 65 μA under a compressive force of 10 kgf. A four-layer-stacked WTNG can produce a higher output of 170 V and 120 μA under the same force. By collecting human mechanical energy, WTNG can drive commercial LEDs and LCD screen successfully. In addition, a keyless vehicle entry system based on WTNG is also demonstrated without any external power sources.

Ouyang et al. demonstrated a symbiotic cardiac pacemaker (SPM) inspired by the symbiosis phenomenon in biology [93] (Fig. 7f). The symbiotic pacemaker constructed by an implantable triboelectric nanogenerator and a commercial pacemaker is implanted into a large animal model for experiment. SPM obtains an open circuit voltage of 65.2 V from the heartbeat of a porcine, and the collected energy successfully achieves cardiac pacing and corrected arrhythmia *in vivo*. The energy collected from each heartbeat can reach 0.495 μJ, which is higher than the threshold energy required for cardiac pacing (0.377 μJ for humans). This work is of great significance for delaying the service life and even completely getting rid of the limitation of batteries for commercial pacemakers.

Zhou et al. presented a wearable sign-to-speech translation system based on stretchable sensor arrays and assisted by machine learning, which can translate gestures into speech in real-time [94] (Fig. 7g). The system is integrated yarn-based stretchable sensor arrays with a wireless printed circuit board. The yarn-based stretchable sensing unit is a kind of TENG, which can sense the movement of human fingers and convert it into electrical signal output in a wide strain range of up to 90%. Through machine learning analysis of 660 obtained sign language gesture recognition patterns, the system achieves a high recognition rate of 98.63%.

Liu et al. demonstrated a transcatheter self-powered endocardial pressure sensor (SEPS), which is integrated by a miniaturized triboelectric nanogenerator (TENG) and a surgical catheter [95] (Fig. 7h). The SEPS exhibits good linearity ($R^2 = 0.997$) with pressure and a sensitivity of 1.195 mV $mmHg^{-1}$. When implanted into the left ventricle and the left atrium of a porcine in a minimally invasive way, SEPS can real-time accurately monitor the endocardial pressure *in vivo*. In addition, cardiac arrhythmias can also be detected by SEPS according to sudden changes of endocardial pressure.

Tan et al. designed a self-charge universal module (SUM) according to the size of AA battery for motional energy collection and storage [96]. SUM integrates three kinds of energy harvesting devices including TENG, PENG and EMG, and stores the collected energy in a small lithium battery through a power management unit. Under the working frequency of 5 Hz, the output power density of SUM can reach 2 mW g^{-1}. Integrating 4 SUMs with a knee pad, the energy collected by the wearer from jogging for 10 minutes can drive a commercial GPS to work continuously for 0.5 h. In addition, different numbers of SUMs can be assembled to adapt to various portable electronics.

3.3.4. Comparison of PENG and TENG

Among the convertible energy sources available to the human body, mechanical energy is the most accessible and studied energy harvesting source currently. The advantages, problems and possible solutions of PENG and TENG for mechanical energy harvesting of the human body are summarized (Table. 3). Mechanical energy is a kind of energy source with the largest external output power of the human body, which can be obtained from the daily movements of the human body and the comparatively small biomechanical motions of muscles or organs. Generally speaking, the mechanical energy from the human's daily movements, such as walking and arms swinging, has the characteristics of noncontinuity and large output power. The mechanical energy from the body's internal organs, such as heartbeat and lung movement, has the characteristics of continuity and small output power.

PENG and TENG have natural advantages in collecting low-frequency mechanical energy due to their unique structure and working principle, which are suitable for collecting mechanical energy from various parts of the human body [97]. Compared with the traditional electromagnetic generators, they have the advantages of light weight, free size, good flexibility and simple structure. TENG and PENG can convert the low-frequency mechanical energy from the human body into pulsed alternating-current (AC) output with high voltage and low current. Although the voltage can reach up to hundred volts, the corresponding current is usually on the order of microamperes, so the converted electricity is safe and reliable for the human body. Since the AC pulse electricity cannot be used directly in general, some supporting power managements and energy storages are also required for better use of the converted electricity. Specifically, a rectifier circuit is first used to convert AC to DC, then a DC/DC step-down converter is needed to lower the output voltage and increase the output current, and finally the electric energy is stored in some energy storages such as capacitors for further applicaions [9,98].

Another important issue to be considered is how to balance the energy collection efficiency with the burden of these energy collection devices on human limbs and organs when collecting mechanical energy from the human body, which can be considered from two aspects. The first is how to capture the mechanical energy of the human body as insensibly as possible. Passive behaviors are carried out by the human body autonomously and unconsciously, such as breathing, heartbeat, and arm swing when walking. These passive behaviors are ideal sources of mechanical energy for harvesting because they will not affect active works. To collect the mechanical energy from passive behaviors without being perceived by the human body, it is essential to minimize the burden of energy harvester on human tissues or organs to integrate energy harvesting processes with the passive behaviors of the human body. It requires full consideration of the characteristics of human movements, as well as the structural features of organs and tissues in various parts of the human body, so as to design a gentle, conformal and comfortable energy harvester for the human body. For PENG, PVDF film, ZnO nanowire arrays, $BaTiO_3$ elastic composite and other flexible and biocompatible piezoelectric materials can be selected to replace the traditional hard and lead-containing PZT piezoelectric ceramics [99,100]. TENGs have a large range of materials that can be chosen, and diverse structure designs due to the multiple working modes. Natural materials can be used for fabricating implantable and absorbable TENGs, while elastic electrode

Table 3
Comparison of TENG and PENG, from advantages, critical issues to promising solutions.

	PENG	TENG
Advantages (Shared)	Abundant mechanical energy from the human body Applicable for low-frequency working conditions High output performance	
Advantages (Individual)	Simple structure Relatively stable	Low cost Multiple working modes Wide selection of materials
Critical issues (Shared)	Alternate-current pulse output characteristics Balance of energy collection efficiency and burden on the human body Mechanical loss	
Critical issues (Individual)	Relatively high cost Biocompatibility of PZT piezoelectric ceramics	Air breakdown Output performance affected by ambient humidity
Promising solutions (Shared)	Rectifier circuit to convert AC to DC DC/DC step-down converter The capture of negative work from the human body Choice of fatigue resistant materials	
Promising solutions (Individual)	High-property piezoelectric materials innovation Multi-layer three-dimensional stacking	Surface modification Charge-excitation Flexible packaging Structure optimization

materials can be used for fabricating wearable and conformal TENGs [101]. In addition, TENGs with unique structures can be designed according to the suitable binding sites for specific parts of the human body [102–104]. Another solution is to try to capture the negative work generated by the human body. The human body produces both positive and negative work by muscles during activities. The metabolically generated energy is consumed when muscles do positive work, while little energy is consumed when doing negative work usually. Therefore, to reduce the burden of the human body and the consumed metabolic energy, capturing the negative work produced by human movements is an ideal energy harvesting strategy.

Although PENG and TENG are considered as promising biomechanical energy harvesting approaches, their output power and energy conversion efficiency still need to be further improved. For PENG, new materials with high piezoelectric property and new structural designs can further improve the energy conversion efficiency. Recently, a breakthrough has been made in output performance by designing a PENG using a three-dimensional intercalation electrode [105], with a maximum current density of 290 μA cm^{-2}. For TENG, the output performance can be further improved by micromachining and modifying the surface of the friction layer with microstructures and functional groups. Meanwhile, designing more reasonable and efficient structures is another effective way. Surface charge density is an important factor affecting the output performance of TENG. Recently, it has been shown that the surface charge density of TENG can be effectively improved by quantifying contact status and establishing the air-breakdown model of charge-excitation TENGs [106]. Additionally, the output performance of TENG is significantly attenuated under a high humidity environment due to the sensitivity of TENG to humidity. Therefore, suitable encapsulation materials and advanced packaging technology are essential to ensuring the safety, stability and reliability for TENG working inside or outside the human body [98]. Another issue to be considered is that mechanical energy harvesting devices are generally subjected to deformation, friction and other mechanical loss during their working period, which results in mechanical fatigue and material wear of the devices and further affects their service life. Therefore, selecting materials with better fatigue resistance, investigating methods to enhance the mechanical properties of materials, and designing devices with better robustness structures are promising solutions.

4. Strategies for interaction between energy harvesting devices and the human body

When harvesting energy from the human body, different energy harvesting strategies are used based on the characteristics of different energy sources and specific body parts. Meanwhile, these converted electric energy sources have their own appropriate applications according to the magnitude of output power. For the energy harvesting devices with large converted electricity, the electricity can be stored in energy storages and supplied to electronic medical devices when necessary. While the energy harvesting devices with small electricity acquirement can be directly used as self-powered sensors to capture the physiological signals of the corresponding parts of the human body, or directly used as stimulators to stimulate the nerves and muscles of specific parts of the human body. Strategies for interaction between various energy harvesting devices and the human body are summarized from the two aspects of wearable and implantable applications, shown in Fig. 8.

4.1. Wearable strategies

People's lives are inseparable from clothing. Besides keeping warm, clothing also has the meaning of fashion and beauty. Clothes, pants, socks, shoes are closely related to people's daily life, so the integration of various energy harvesting techniques with various wearing supplies is the simplest way to combine with the human body. In this regard, many researchers have made attempts and achieved effective results. For example, the T-shit made based on TEG can be used to collect thermal energy of the human body [18], the socks made based on biofuel cells can be used to detect sweat metabolites of the human body [51], and the shoes made based on TENG and EMG can be used to collect mechanical energy of foot movement [107]. Besides clothing, a variety of wearable devices have been integrated into people's lives in recent years, the most typical of which are smart bracelets and smart glasses. The skin patch sensors based on TENG and PENG can be effectively integrated with these intelligent wearable devices to capture physiological signals of the human body such as pulse and blood pressure [90,108]. In addition, with the emerging of some new technologies, TENG-based electronic skin [109], biofuel cell-based electronic tattoo [110] and microneedle sensor [111] have also been developed to collect corresponding physiological signals of the human body. Combining these energy harvesting devices with the human body in a wearable way is one of the main trends for current research, which needs to be simple and efficient without obvious burden or any damage to people.

4.2. Implantable strategies

With the advancement of modern medicine and the electronic industry, various implantable electronic medical devices have been developed to treat relevant diseases and prolong people's lives. Therefore, apart from the applications of wearables, related research and exploration in

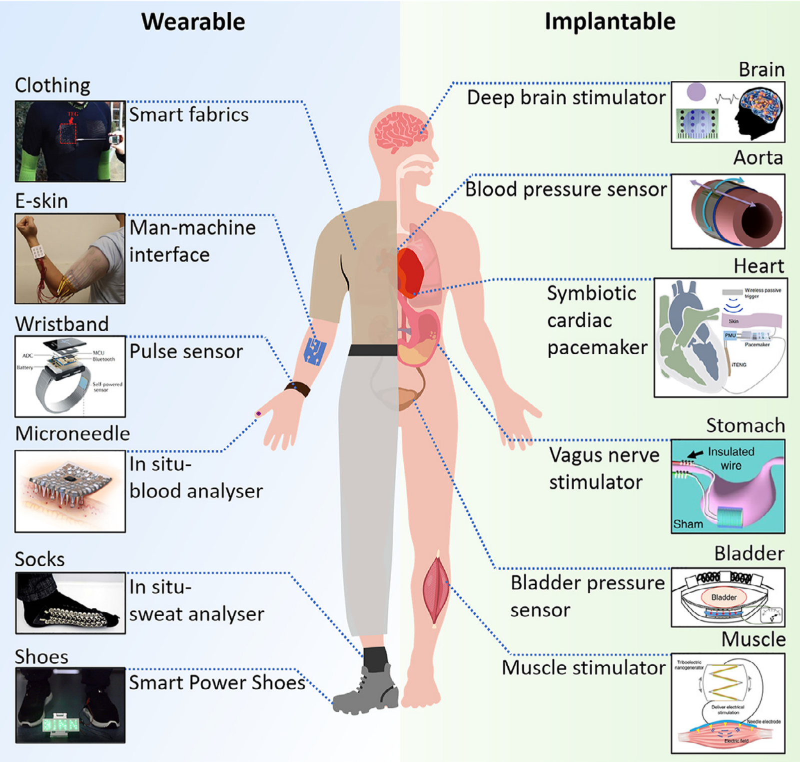

Fig. 8. Strategies for interaction between various energy harvesting devices and the human body.

living organisms, is another major research direction of energy harvesting device interacting with the human body. In view of the requirements for strict medical evaluation and approval to implant devices into the human body, most of the current research is based on animal experiments. Many studies have been carried out in small animals such as rats. For example, TENG has been shown to be connected with rat brain nerves for neuroregulation [112]. The TENG implanted into the stomach of rats can be driven by the movement of the stomach to stimulate the gastric vagus nerve and control the weight of rats [113]. The TENG implanted into the bladder of rats can detect the pressure of the bladder and assist urination [114,115]. The TENG connected with the leg muscles of a rat can stimulate muscle movement [116,117]. In addition to small animals, some studies have been verified in large animals. For example, the PENG implanted into the ascending aorta of porcine can monitor blood pressure in real-time [91]. The TENG implanted into the pericardium of porcine can collect energy from the heartbeat of porcine and supply it to a commercial pacemaker [93]. In addition to PENG and TENG, there are also many studies that have implanted biofuel cells into various organisms to collect chemical energy in organisms, which have been verified in insects [118], snails [119], lobsters [55], rats [120] and so on. Although significant results have been achieved in animal experiments, the implantable energy harvesting devices are still far from practical use in human body. The biocompatibility and biosafety of the devices require to be further verified, and the efficiency of energy harvesting *in vivo* needs further improvements.

5. Self-powered closed-loop bioelectronic system

Closed loop is the basic mode of all life processes in nature. In a closed-loop system, the feedback information is taken from the state of the system and is the basis for decision-making. The state of the system is changed through decision-making control, and the new system state further affects future decisions, the process of which is continuous and cyclic. The human body is a natural closed-loop system. The human body perceives the external environment through receptors located in various parts of the body. The most typical senses including vision, hearing, olfaction, taste and touch, which are all pathways for the human body to acquire extrinsic information. The information from receptors feeds back to the nervous system of the human body, and the brain sends instructions for further corresponding behaviors, thus forming a closed-loop control system.

In addition to the closed-loop of the perception and feedback of the external environment, the internal physiological system of the human body is composed of many closed-loops. For example, when the blood glucose of the human body rises after a meal, the secretion of insulin in the body will simultaneously increase to decrease blood glucose appropriately. When blood glucose returns to a certain level, the secretion of insulin will decrease, thus realizing the regulation of blood glucose concentration in the body in a closed-loop. When the physiological system of the human body is in disorder due to illness, it is unable to accurately recognize the physiological status of the human body, or cannot normally transmit the physiological signals to the relevant nervous system, so that normal physiological feedback adjustment closed-loop cannot be achieved. At this time, appropriate treatments need to be intervened externally to restore the physiological feedback regulation of the human body to normal.

Here, we put forward a self-powered closed-loop bioelectronic system (SCBS) (Fig. 9), which could be compatible with the natural closed-loop of the human body. SCBS will change the way that existing wearable electronics and implantable medical electronic devices interact with the human body into a symbiosis relationship. Under the assistance of SCBS, the physiological state of the human body can be automatically regulated to optimal, and the physiological system can be repaired actively when disorders occur.

A complete closed-loop bioelectronic system needs sensing units that can accurately acquire the physiological state information of the system in real-time, and functional units that can make corresponding feedback to the physiological signals obtained by the sensing units. With the

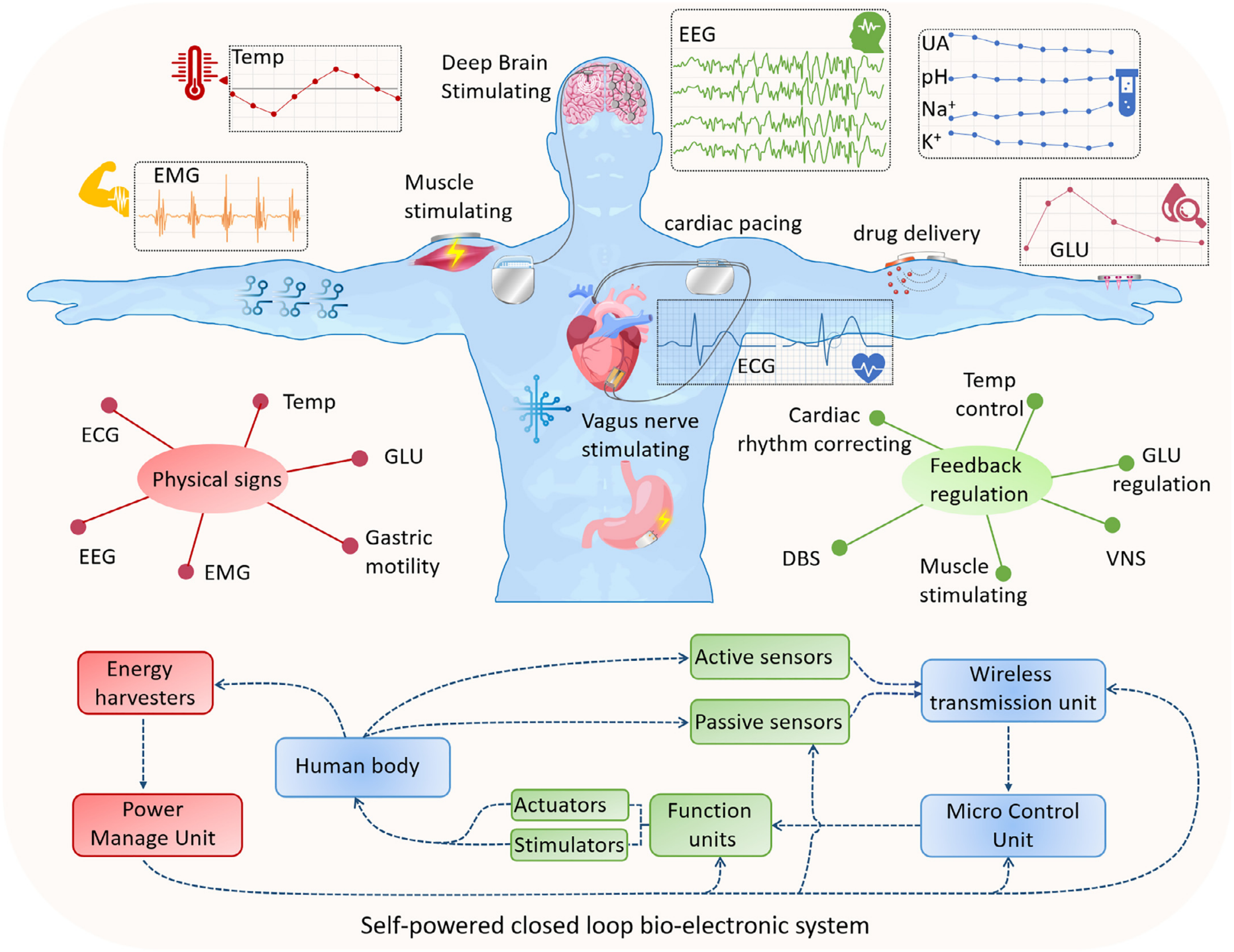

Fig. 9. Schematic of Self-powered closed-loop bioelectronic system.

advancement of modern medicine and the electronic industry, various health monitoring products and electronic medical devices emerge in an endless stream. At present, health monitors and electronic medical devices mainly work independently, and act as human body sensors and corresponding function units respectively. In addition, due to the limitation of battery capacity, the service life of the device is limited in application, which makes it difficult to achieve long-term monitoring and treatment of the human body in real-time. In recent years, electronic devices are gradually reducing power consumption, and the energy harvesting technology from the human body is constantly evolving, which makes it possible for the entire closed-loop bioelectronic system to be self-powered while the human body itself acts as a power source to drive continuous operation of the entire system. In one closed-loop of SCBS, various energy flows from the human body are collected by energy harvesting devices and converted into electricity. Through the power management unit, the electricity can be stored effectively and provided to the energy-consuming units at any time. The self-powered sensor without additional energy supply can monitor the physiological state of the human body in real-time and transmit the physiological signals to the micro-control unit via a wireless transmission unit. Once the physiological state exhibits abnormality, the micro control unit will send instructions to the corresponding function units, thereby exerting feedback regulation on the relevant organs or nerves of the human body until the physiological state returns to normal.

There are multiple ‘signal-feedback regulation’ loops in SCBS. For example, the EMG signals of the human body can be monitored through electronic skin. When muscle fatigue occurs, the muscle stimulator can apply electrical stimulation to the relevant muscles to relieve the fatigue state. The EEG signals of the human body can be monitored through brain electrodes in real-time. When abnormal EEG signals such as epilepsy or other symptoms are detected, the brain pacemaker will apply appropriate electrical stimulation pulses to the corresponding brain nuclei to alleviate the symptoms. The sensors implanted into the pericardium and ascending aorta can monitor the state of heartbeat and blood pressure. When arrhythmias occurs, the pacemaker will apply electric stimulation pulses to the myocardium to correct the rhythm return to normal. With a sensor implanted into the gastric wall, the gastric motility of the human body can be monitored. When gastric motility is abnormal, the gastric stimulator will stimulate the vagus nerve in the stomach to regulate gastric motility. The blood glucose concentration of the human body can be monitored by a microneedle sensor. When the blood glucose is too high and does not drop for a long time, the percutaneous drug release device will release an appropriate dose of insulin to make the blood glucose return to a normal level. The body temperature can be monitored by an electronic tattoo. When the body surface temperature is too high, the intelligent fabric will adjust to the heat dissipation mode to make people feel comfortable, while when the body surface temperature is too low, it will adjust to the heating mode

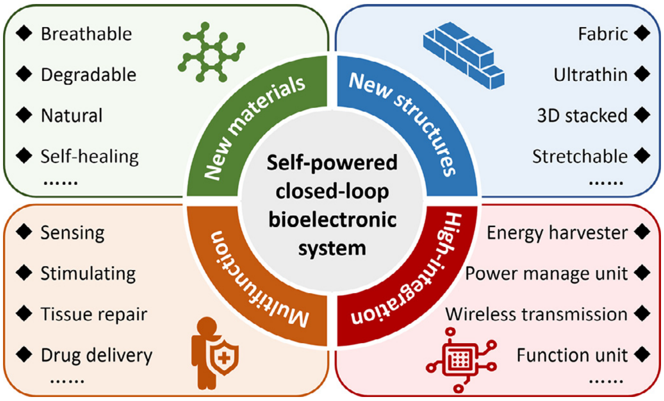

Fig. 10. Future development trends and demands of self-powered closed-loop bioelectronic system.

to make people feel warm. These signal-feedback regulation loops are only cited examples to discuss the possible operation mechanisms of SCBS, which are an outlook of the future at present. In order to truly construct SCBS and realize a series of functions, it still needs long-term scientific exploration as well as collaborative efforts across multiple research fields.

6. Future development trends and demands of SCBS

In recent years, the continuous development of materials with new characteristics and structures designed with new functions have endowed traditional electronic devices with diversified functional characteristics and a comfortable way of interaction with the human body. At the same time, the continuous progress of microfabrication technology and microelectronics enables these novel electronic units to be integrated efficiently for miniaturization and intelligence. The continuous improvement of these fields makes the realization of a self-powered closed-loop bioelectronic system further possible. Here, the future development trends in four aspects including material, structure, function and integration are summarized and discussed according to the construction requirements of the self-powered closed-loop bioelectronic system (Fig. 10).

In terms of material and structure, materials with appropriate characteristics and the structures with unique features can be selected according to the specific application scenarios and requirements. In case of directly fitting human skin, the wearable devices can be fabricated by breathable materials [121], woven structure [25] or ultra-thin structure [90] for good comfort. For devices that need to be implanted into the human body for short-term service, degradable [122] and natural [123] materials can be chosen, so that they can be degraded by themselves and absorbed by the human body after completing the missions. In application to the joint parts of the human body that need to bear large strain for a long time, self-healing materials [124] and stretchable structures [125,126] can be used to manufactured corresponding devices, so that they can stretch and contract with the movement of the human body and repair themselves in case of fatigue damage. In addition, when there is a certain space for utilization but the output performance of a single device is insufficient, the corresponding functional properties of the device can be further enhanced by adopting a three-dimensional stacking structure [127].

In order to achieve the relevant closed-loop, the functions of the devices must be diversified. There must be multimodal sensors that can collect various physiological parameters of the human body, as well as performing units that can feedback and adjust the corresponding physiological state, such as nerve and muscle stimulators [117], tissue and wound repair devices [128], transdermal drug release patches [129] and so on. In terms of integration, energy harvester and power management unit that will provide power for the entire system must first be effectively integrated to ensure the normal and stable operation of the entire system. Then the function units including various sensor units and performing units, wireless transmission unit and micro control unit, also need to be connected together in an appropriate way [87,130], so as to achieve a complete closed-loop of the whole system [131]. On the premise of guaranteeing human comfort and system stability, high integration, miniaturization, multi-function and intelligence are the future development trends of SCBS.

7. Conclusions

With the development of the electronic industry, mobile health care and Internet of things technology, everything in the world can be connected together in an informationized way. The world's energy structure is undergoing tremendous changes today. In addition to the traditionally large-scale accumulated energy sources for the development of human society, distributed, mobile, and divergent small energy sources are also needed in this Internet of Things era, namely new era energy. Actually, everyone contains inexhaustible energy, and the human body itself is a typical form of new era energy. In recent years, the research on human body energy harvesting has made significant progress, some low-power electronic medical devices and portable devices are successfully powered by energy from the human body itself.

This review summarizes three major energy flow sources contained within the human body, which are thermal energy, chemical energy and mechanical energy. In view of the characteristics of the three energy flows, corresponding energy harvesting technologies are introduced successively: thermoelectric generator and pyroelectric generator for harvesting thermal energy, biofuel cell and hydrovoltaic generator for harvesting chemical energy, piezoelectric nanogenerator and triboelectric nanogenerator for harvesting mechanical energy. Some typical demos and applications of various energy harvesting technologies to the human body are enumerated respectively. The advantages and critical issues of various energy harvesting technologies are summarized, and promising solutions are proposed. The strategies of interaction between various energy harvesting devices and the human body are summed up from two aspects of wearable and implantable applications. Finally, a self-powered closed-loop bioelectronic system (SCBS) is put forward for the first time, and the demands and future development trends of SCBS are further analyzed.

SCBS is a way of the human body mutualistic symbiosis with various wearable and implantable electronic devices in the future. Humans rely on these electronic devices to enhance themselves and serve as an energy source guarantee for the operation of these electronic devices. However, many problems remain to be addressed for the actual realization of the complete self-powered closed-loop. First of all, the energy conversion efficiency of current human body energy harvesting technologies needs to be further improved. Meanwhile, balancing the energy harvesting efficiency and the burden of the relevant harvesting technology on the human body is a key issue for all human body energy harvesting technologies. In the future, multiple energy harvesting methods coexist with complementary advantages is a main trend of developments. Secondly, due to the long-term operation in the organism to achieve a symbiotic state, the biocompatibility of the devices and the stability of the system require a large number of animal experiments and clinical trials to verify. Finally, the existing portable, wearable devices and implantable electronic medical devices are mostly independent and incoherent from each other, which increases the complexity of the entire system and makes it difficult to control and manage. With the emergence of artificial intelligence and new communication methods, future intelligent electronic devices will be connected together through body area networks [132,133], uniformly managed by a microprocessor chip, which is similar to the 'brain' of the entire system. This will greatly improve the efficiency of SCBS and simplify the complexity of the system, so that *in vivo* and *in vitro* devices can work synergistically to adjust the physiological state of the human body to optimal in real-time. Although the road to building a self-powered closed-loop bioelectronic system is full of challenges, it is accompanied by great opportunities as well. The future of SCBS is full of hope and has great prospects for applications. It is believed that with the joint efforts of researchers in various fields, SCBS will become a reality one day and change the existing lifestyles of human beings.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

Acknowledgments

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Author contributions

Yang Zou, Lin Bo and Zhou Li proposed original conceptualization. Yang Zou investigated the related works, prepared the figures and wrote the article. Zhou Li supervised the manuscript. All authors have read and approved the content of the manuscript.

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