

Bio-energy-powered microfluidic devices

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ABSTRACT

Bio-microfluidic technologies offer promising applications in diagnostics and therapy, yet they face significant technical challenges, particularly in the need for external power sources, which limits their practicality and user-friendliness. Recent advancements have explored innovative methods utilizing body fluids, motion, and heat to power these devices, addressing the power supply issue effectively. Among these, body-motion and body-heat-powered systems stand out for their potential to create self-sustaining, wearable, and implantable devices. In this Perspective, we focus on the principles and applications of hydrovoltaic cells, biofuel cells, and piezoelectric and triboelectric nanogenerators. Recent strides in energy conversion efficiency, coupled with the development of biocompatible and durable materials, are driving innovation in bio-integrated electronics. Integration with bio-microfluidic platforms further enhances the linkage to the human body and the potential of these devices for personalized healthcare applications. Ongoing research into these areas promises to deliver sustainable and user-friendly solutions for continuous monitoring, diagnostics, and therapy, potentially revolutionizing the landscape of healthcare delivery.

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I. INTRODUCTION

Bio-energy-powered microfluidic devices represent a cutting-edge frontier in the convergence of biology and engineering. By combining pressure, electrode mobility, and capillary action,^{1–4} with some microvalve and pressure pumps, and the channel structure is specially designed, it is capable of accurately driving the fluid to flow in the micro-current control channel. When the fluid flows in the microfluidic channel, the fluid itself will bring driving energy, pressure energy, and even thermal energy.

Figure 1 shows microfluidic devices and microfluidic channels, as well as the power supply methods of the four most representative bio-microfluidic devices. Wireless microfluidic actuation is achieved using signals transmitted by smartphones through specific wireless power transmission circuits,⁵ such as circuits designed at Near-Field Communication (NFC) frequencies [Fig. 1(a)].⁶ Designing microfluidic channels of specific shapes and sizes can accurately guide and restrict the flow path of liquids at the micrometer scale, which can achieve better microfluidic control and application effects. Using fluorescent dyes, spontaneous capillary flow can be

Microfluidic devices

① Power generator ② Microfluidic channel Sensors/Actuators

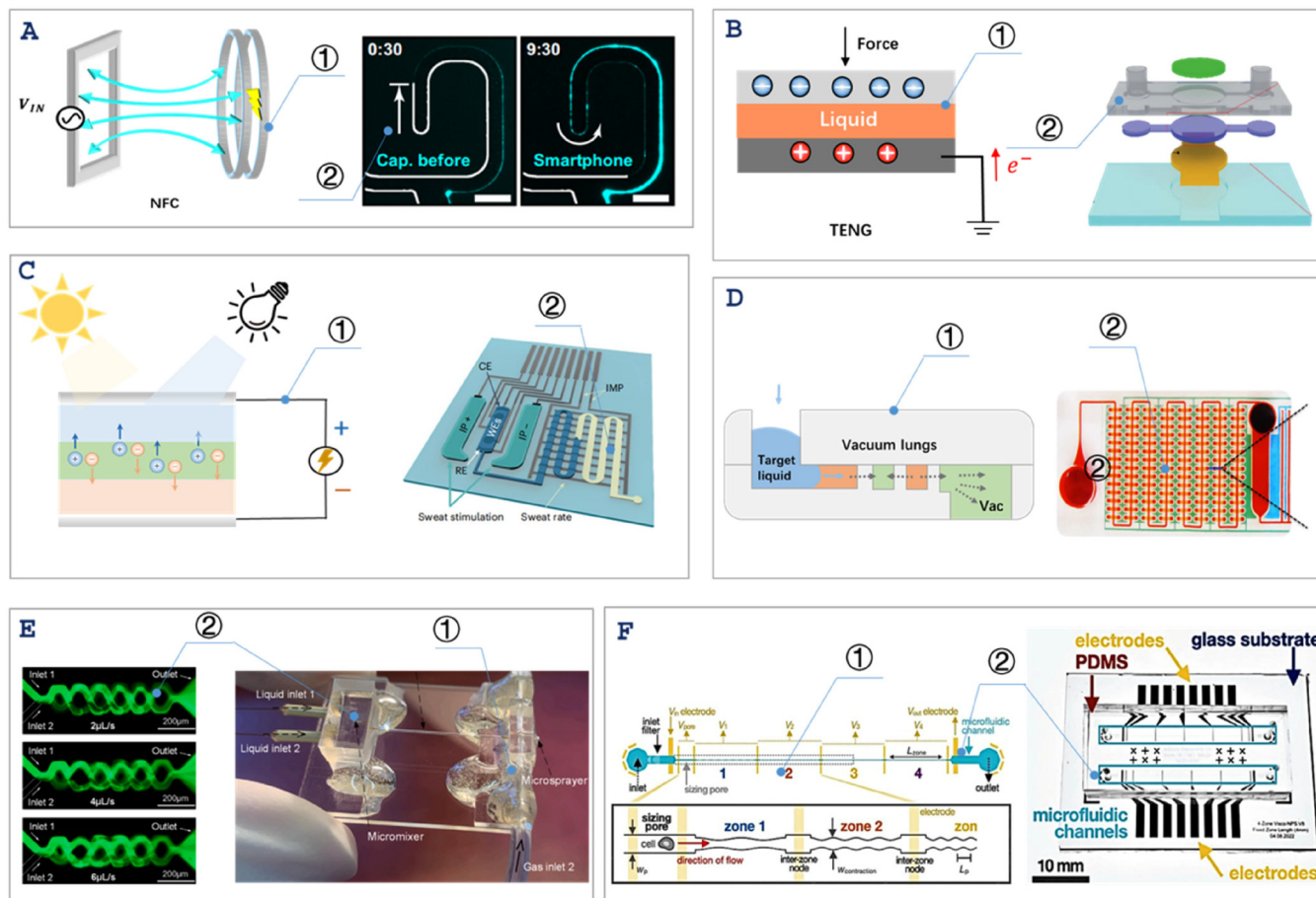


FIG. 1. Microfluidic devices. (a) Power supply by a wireless power transmission circuit. Reproduced with permission from Ertsgaard *et al.*, *Nat. Commun.* **13**, 1869 (2022); licensed under a Creative Commons Attribution (CC BY) license.⁶ (b) Friction power generation. Reproduced with permission from Kim *et al.*, *J. Mater. Chem. A* **6**, 14069 (2018). Copyright 2018 Royal Society of Chemistry.⁷ (c) Solar power supply (photoelectric power generation). Reproduced with permission from Min *et al.*, *Nat. Electron.* **6**, 630 (2023). Copyright 2023 Springer Nature.⁸ (d) Vacuum battery. Reproduced with permission from Yeh *et al.*, *Sci. Adv.* **3**, 3 (2017); licensed under a Creative Commons Attribution (CC BY) license.⁹ (e) Power supply by gas pressure. Reproduced with permission from Bhattacharjee *et al.*, *Cell* **187**, 782 (2024). Copyright 2024 Elsevier.¹⁴ (f) Power supply by voltage. Reproduced with permission from Lai *et al.*, *Adv. Sci.* **11**, 43 (2024); licensed under a Creative Commons Attribution (CC BY) license.¹⁵

observed in the channel under the interaction of surface tension and electric field. Triboelectric nanogenerator (TENG) technology is also a common self-powered microfluidic device [Fig. 1(b)].⁷ This microfluidic device uses PDMS to make microfluidic channels for carrying target liquid. Triboelectric charging occurs when the top electrode contacts the PDMS channel. In this process, the bottom electrode plays an important role in the transfer of electrons and interaction with the PDMS channel to generate electrical signals. The electrodes distributed in the microfluidic channels will

collect sweat, and the electrodes and various biosensors will continuously monitor and analyze various physiological indicators of sweat (such as sweat rate, glucose, pH value, sodium ions, etc.) [Fig. 1(c)].⁸ This module converts ambient light (such as indoor and outdoor lighting) into electrical energy to power the entire wearable device. Microfluidic devices can also be self-powered through a vacuum battery system integrated into the chip [Fig. 1(d)].⁹ When the liquid in the chip needs to flow, the air trapped in the chip will diffuse through the PDMS wall of the

vacuum component (vacuum lung) similar to the alveolar structure, thereby generating suction and achieving fluid pumping. The vacuum battery is not a real power generation, but a vacuum area with holes created in advance on the chip to store vacuum potential energy. It can replace traditional chemical batteries and realize self-powering of microfluidic devices. The system's self-maintenance has a broad application prospect through integrated engines and micro-flow control devices, which can change various fields, from chemistry and physics to biology and medicine.^{10–13} The bottom two sets of pictures are from articles published in the last year. Different from the previous four power generation methods, the power generation method of this microfluidic device mainly uses nitrogen (N₂) as the gas source and generates stable spray by controlling the gas pressure to ensure that the microsyringe can spray the reaction products stably [Fig. 1(e)].¹⁴ The other microfluidic device is powered by a DC voltage applied to both ends of the microfluidic channel, using the pressure difference to drive the cell to move in the microfluidic channel [Fig. 1(f)].¹⁵

Bio-microfluidic devices offer numerous advantages, including biocompatibility, precise control over fluid flow, and the ability to mimic physiological environments.¹⁶ However, powering these devices in a sustainable and biocompatible manner remains a challenge. Traditional chemical batteries are not only bulky, but also need to be replaced frequently, and may pose environmental concerns due to their non-biodegradable nature.¹⁷ Therefore, using green power instead of traditional chemical batteries is the current research hotspot. The main technologies such as hydrovoltaic cells, piezoelectric and triboelectric nanogenerators, electromagnetic generators, and thermoelectric generators mentioned in this article are mainly mentioned in various aspects such as self-power supply, micro-dimensional, biocompatibility and green environmental protection, and high conversion rates, with many breakthroughs.^{18–20} By replacing traditional chemical batteries, equipment self-power supply is realized. For example, water voltage batteries that can use body fluids (or sweat) to power generation, use heart-beating mechanical energy to transform into electrical energy and use the temperature difference between the human body and the environment.^{21–23} Most inorganic piezoelectric materials are usually rigid, brittle, difficult to process, and may even contain toxic elements, making it difficult to meet the flexibility and degradability requirements of biological microfluidic devices. Therefore, in recent years, various types of biodegradable materials with biocompatibility that can be used in microfluidic devices have become a major focus of research in the relevant fields.^{18,24,25} Yang *et al.* developed a method for making high-quality crystalline thin films of piezoelectric-glycine crystals.¹⁸ The films prepared using the method developed by Yang *et al.* exhibited excellent uniformity, integrity, and flexibility. The thin films exhibit a significant piezoelectric response on a macroscopic scale and maintain high stability in aqueous environments. This can effectively improve the performance of sensors and actuators used in integrated and automated microfluidic devices; in addition, this material is naturally biocompatible and degradable (water-soluble), provides a safer, greener option for implantable microfluidic devices and helps alleviate environmental concerns.

This is where bio-energy-powered microfluidic devices come into play. By harnessing energy from biological sources, such as

body heat, body fluids, or even the metabolic activity of cells, these devices offer a self-sustainable and environmentally friendly alternative.²⁶ The integration of bio-energy harvesting mechanisms with bio-microfluidic platforms not only handles the power supply issue but also opens up new ways for creating truly autonomous and implantable biomedical devices.

Traditional energy supply forms (such as traditional chemical batteries) cannot meet the requirements of microfluidic devices in terms of biocompatibility, energy supply stability, and sustainability. In this review, we will explore the various energy supply forms of bio-energy-powered microfluidic devices, their underlying principles, and their potential applications in healthcare, diagnostics, and environmental monitoring. We will also explore the obstacles and upcoming trends in this fast-developing domain, highlighting the potential of bio-energy-powered microfluidics to revolutionize the way we interact with and utilize biological systems.

II. PERSPECTIVES

Based on the limitations of traditional chemical batteries mentioned in the introduction, we hope to combine emerging water photovoltaic technology, various nanogenerators, and thermoelectric generators with various energy sources contained in the human body to achieve efficient, green, and sustainable self-powered microfluidic devices. Next, we will introduce the development status of microfluidic devices from three parts: body fluid-driven, body motion-driven, and body heat-driven microfluidic devices, as well as related technical principles, applications, challenges, and opportunities.

A. Body-fluid-powered bio-microfluidics devices

Body fluids, including sweat, tears, and even water itself, present a novel and sustainable energy source for powering bio-microfluidic devices.^{27–29} This emerging field, is often referred to as “hydrovoltaics.” Hydrovoltaics technology mainly generates electricity through direct interaction between water and nanomaterials. Various new power generation devices have been discovered that use various forms of water to generate electricity (such as falling water droplets,^{30,31} water evaporation,^{32–35} moisture absorption,³⁶ etc.), which are different from traditional hydroelectric power generation devices.³⁷ In addition to hydrovoltaics technology, microorganisms are also an important component of the energy conversion part of bio-microfluidic devices driven by body fluids. Microorganisms can not only be combined with reverse osmosis systems (REDs) to generate electricity using ion gradients but can also be used as oxidizing components in biofuel cells.³⁸ They mainly leverage the unique properties of body fluids and innovative materials to generate electricity, offering promising applications in wearable and implantable medical technologies.

1. Principles and technologies

- Hydrovoltaic cells: These cells are emerging energy conversion devices. It works based on a variety of physical and chemical mechanisms. It mainly uses the interaction between various forms of water, such as moisture, flowing water, rainwater, water that wets the surface through capillary action and then

evaporates,^{31,33,39,40} and the interaction with specific material interfaces to generate voltage and current.^{41–44} The key to its energy conversion lies in the interaction between water and material interfaces. The flow of water can bring more opportunities for water to contact with materials, enhance the transfer and separation of charges, and thus affect the output performance of the battery. When water contacts materials with specific surface chemical properties, charge separation will occur on the surface of the material. For example, graphene or graphene oxide,⁴¹ its surface will adsorb ions in water after contact with water, thereby forming a charge layer on the surface of the material and generating a potential difference. Through reasonable channel, structure, and interface design, the electrode of the hydrovoltaic battery can be prepared as part of the microfluidic channel, or the structure of the hydrovoltaic battery can be set next to or at the bottom of the microfluidic channel, so that water can interact with the material of the hydrovoltaic battery while flowing in the microfluidic channel. Recent advancements have led to the development of protein-based hydrovoltaic cells which offer enhanced biocompatibility compared to traditional materials.⁴³ These cells utilize protein hydrogels, which are inherently compatible with biological systems, reducing the risk of tissue irritation or immune response.^{45,46}

- Reverse electrodialysis (RED): RED systems harness the salinity gradient between different body fluids (e.g., sweat and tears) to generate electricity through ion exchange membranes.⁴⁷ Due to the concentration difference, the anions and cations on the high-salinity side will move to the low-salinity side through the anion and cation exchange membranes, respectively, and this directional movement of ions forms an ion current. In existing research, RED systems can be combined with microbial fuel cells (MFCs) to improve the utilization of bioenergy.⁴⁸ Using the salinity gradient to directly convert energy into electricity provides a relatively straightforward conversion pathway. With the benefits of sustainability and renewability, this technology is greener and cleaner than using traditional materials. However, the use of salinity gradients between body fluids such as sweat and tears to generate electricity through ion exchange membranes is still in a very early stage of research, and there are currently no mature application examples.
- Biofuel cells: These cells employ enzymes or microorganisms to catalyze the oxidation of biomolecules present in body fluids, converting chemical energy into electricity. Research on biofuel cells has made significant progress in recent years.^{49–52} Compared with traditional fuel cells that use non-biological catalysts such as precious metals, biofuel cells rely on substances in the body to catalyze reactions for energy conversion; they have enhanced biocompatibility, making them potentially suitable for implantable devices. In biofuel cells, both the supply of fuel and the generation of reactants involve the flow and transmission of fluids. For example, when using wastewater and organic waste,⁵³ these substances need to flow in the anode chamber so that they can fully contact with microorganisms and enzymes and undergo oxidation reactions, and then undergo reduction reactions in the cathode chamber to form water, thereby completing the entire battery reaction. It is only necessary to design a suitable

microfluidic channel on the microfluidic device, and these microorganisms and enzymes can use fuel in the electrolyte to achieve energy conversion. To solve the problem that the stability of biofuel cells is affected by factors such as the activity of biocatalysts and fuel supply, artificial enzyme catalysts with high activity and stability have been developed to replace natural enzyme catalysts.^{54,55} At the same time, new optimizations have been made in the battery structure to improve the utilization rate of fuel and the output efficiency of electrical energy.^{56,57} In addition, the combination with other technologies has also enabled biofuel cells to develop toward miniaturization, intelligence, and multifunctionality.^{58,59}

2. Applications in bio-microfluidics

Body-fluid-powered devices provide sustainable energy by using biological fluids such as tears, perspiration, or interstitial fluid (Fig. 2). Exciting opportunities arise when these devices are integrated with bio-microfluidic platforms:

- Self-powered contact lenses: Contact lenses that integrate hydrovoltaic cells and bio-microfluidic chips use microfluidic devices to sample biomarkers in tears, such as glucose,⁶⁰ to quickly monitor patients' blood sugar levels and send the monitored data to external devices via wireless transmission. These contact lenses are composed of hydrogels and other biocompatible polymer materials, such as polydimethylsiloxane (PDMS), and can offer a potential solution for powering vision correction, drug delivery, or health monitoring features.^{61–63} This approach could reduce the need for external batteries, thereby increasing user comfort and ease of use.⁶⁴
- Wearable biosensors: Based on the principles of hydrovoltaic cells, this can be applied to wearable devices, such as wearable glucose meters (Fig. 2), or sweat-powered biosensors can track biomarkers such as glucose, lactate, or electrolytes, offering real-time health insights.^{65,66}
- Implantable devices: Body-fluid-powered micro-batteries, such as biofuel cells, can provide sustainable energy for pacemakers, neurostimulators, or drug delivery pumps.⁶⁷ The biocompatibility of materials is particularly crucial for implantable applications to ensure long-term safety and functionality within the body.^{68–70} These micro-batteries do not require frequent battery replacement compared to batteries used in traditional implantable devices, improving patient outcomes and reducing healthcare costs.

Figure 2 shows some of the practical applications of fluid-driven bio-microfluidic devices in bioelectronics. “Body fluids” can come from eyes (tears), skin (sweat), various biological tissues (interstitial fluids), etc. [Fig. 2(a)]. These “body fluids” generally contain various ions, and the movement of ions can generate electric current [Fig. 2(b)]. For example, using the RED system, the need for self-power supply can be achieved. Or through the water in these “body fluids,” when it comes into contact with proteins and other special materials, such as water vapor and the surface of graphene oxide, the interaction between the material surfaces will generate an electric potential difference [Fig. 2(b)], realizing energy

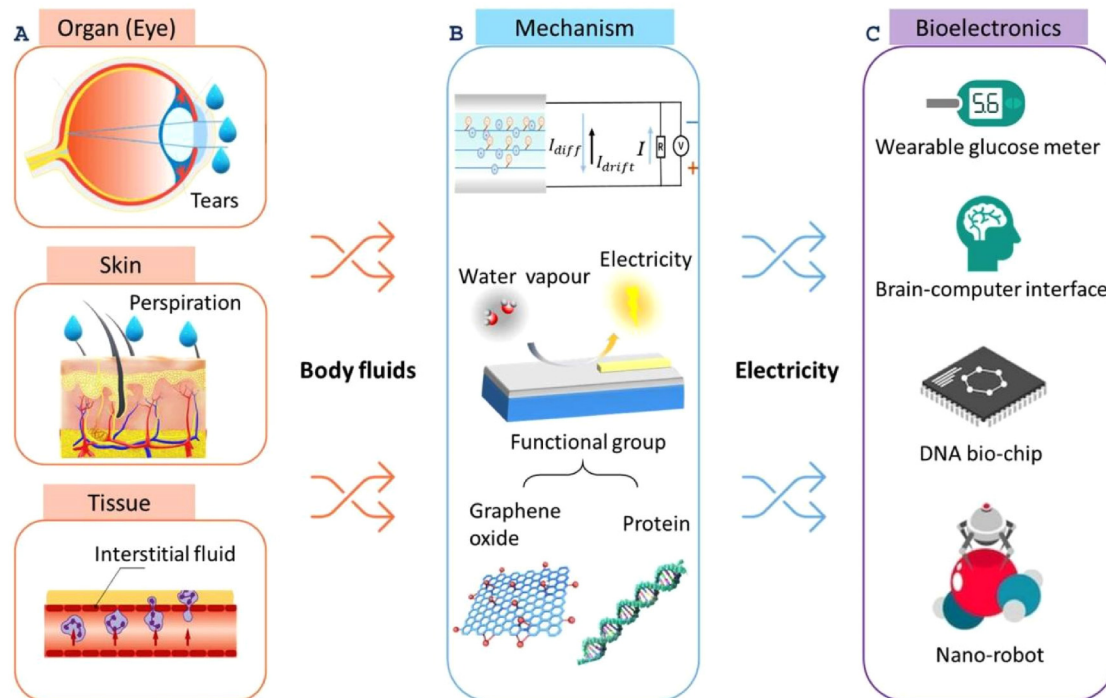


FIG. 2. Introduction to the energy source, power generation principle, and practical applications of fluid-driven microfluidic devices. (a) Various body fluids such as tears, sweat, and interstitial fluid can serve as energy sources for bioelectricity generation. (b) The mechanism of using body fluids as an energy source for bioelectricity generation involves proteins and other special materials. (c) Practical applications in bioelectronics include wearable glucose meters, brain-machine interfaces, DNA biochips, and nano-robots.

conversion and power generation. These potential sources of bioelectricity and specific power generation mechanisms provide broad application prospects for bioelectronics [Fig. 2(c)]. For example, wearable blood glucose meters can achieve convenient and real-time monitoring of human blood glucose with the help of fluid-driven microfluidic technology; in the field of brain-computer interface, they provide energy support for sustainable and efficient interaction between the brain and external devices; DNA biochips use this technology to achieve accurate detection and analysis of biological information; nanorobots can also rely on bioelectricity to drive and perform complex tasks such as disease diagnosis and treatment *in vivo*.

3. Challenges and future directions

While body-fluid-powered bio-microfluidic devices hold immense potential, several challenges need to be addressed for broader adoption and effective deployment of this technology in healthcare, diagnostics, and environmental monitoring:

- **Enzyme immobilization:** In some implantable devices, enzyme immobilization techniques may be applied. For example, in continuous blood glucose monitoring (CGM) sensor, glucose reactive enzyme and glucose oxidase (GOx) are fixed to single-wall carbon nanotubes (SWCNTs) to construct glucose sensor to

detect glucose concentration.⁷¹ Enzyme immobilization technology can solve the problems that natural enzymes are unstable in solution, easy to be affected by environment and difficult to be reused. However, the immobilization process itself will also have a certain impact on enzyme activity, and some chemical cross-linking agents or immobilization methods may have a certain degree of impact on the active site of GOx. When the enzyme is adsorbed and immobilized on the surface, there may be some problems such as enzyme leakage and random orientation affecting the activity. In addition, the implantable device will also be affected by the internal environment, the cells and tissues around the implantation site may have a certain physical effect on the immobilized enzyme, such as phagocytosis of the cell or extrusion of the tissue, which may destroy the connection between the enzyme and the carrier.⁷²

- **Power output:** The current power output of hydrovoltaic cells and other technologies is relatively low, limiting their applications. Enhancing energy conversion efficiency, especially for protein-based cells, is a key priority. Enhancements in materials and electrode design are pivotal for achieving higher yields, fostering advancements that could broaden their utility in sustainable energy solutions and biomedical applications.
- **Material optimization:** While protein-based materials demonstrate promising biocompatibility, their application potential is contingent on enhancing electrical conductivity, mechanical

stability, and long-term durability. Ongoing research in material science aims to optimize these properties, ensuring suitability for diverse applications such as biomedical implants and sustainable energy devices. The successful integration of protein-based materials into various technologies relies on achieving a balance between these factors, ultimately expanding their practicality and reliability.

- **Device integration:** To successfully combine body-fluid-powered modules with microfluidic systems, device architectures, especially those incorporating protein-based components, must be miniaturized and optimized. This integration necessitates meticulous engineering to guarantee efficient energy transfer, dependable performance, and compatibility with established microfluidic technologies. Successfully achieving this could unlock novel applications in healthcare and environmental monitoring.
- **Safety and regulation:** Ensuring the safety and regulatory compliance of body-fluid-powered devices, especially for implantable applications, is paramount. Rigorous testing and validation of protein-based materials are necessary to address potential concerns related to biodegradation and immune response.

Body-fluid-powered bio-microfluidic devices, particularly those utilizing protein-based materials, represent a promising and sustainable approach to powering next-generation medical technologies. By harnessing the energy inherent in our bodily fluids and leveraging the biocompatibility of proteins, we can create wearable, implantable, and self-powered systems that offer continuous monitoring, personalized therapy, and improved patient outcomes. Overcoming current challenges will unlock the full potential of this exciting field and revolutionize healthcare delivery.

B. Body-motion powered bio-microfluidics device

Human kinetic energy, encompassing everyday activities such as walking, jumping rope, running, and even the beating of our hearts, harbors a vast reservoir of untapped energy. Transforming this mechanical energy into electrical power not only holds the potential to energize wearable and implantable medical devices but also to unlock new possibilities in the realm of bio-microfluidics.

1. From kinetic to electric energy

- **Walking, jumping rope, running:** The kinetic energy generated by these motions can be converted into electricity through piezoelectric materials and electromagnetic induction. For instance, embedding piezoelectric materials in shoe soles could transform each step's impact into an electrical signal (Fig. 3). As the wearer walks, the pressure exerted on the soles compresses the piezoelectric materials, generating an electrical charge that can be harvested and stored. This electricity can power small electronic devices such as fitness trackers or health monitors, reducing the need for external batteries. Additionally, integrating these materials into running shoes or jump ropes can harness the more significant kinetic energy produced during these activities, providing a sustainable power source for various wearable technologies. This innovative approach not only enhances the functionality of everyday footwear but also promotes energy efficiency and sustainability in wearable technology.
- **Heartbeat, pulsation, eye movement:** The mechanical energy produced by the heart's contractions can similarly be harnessed through piezoelectric or triboelectric methods

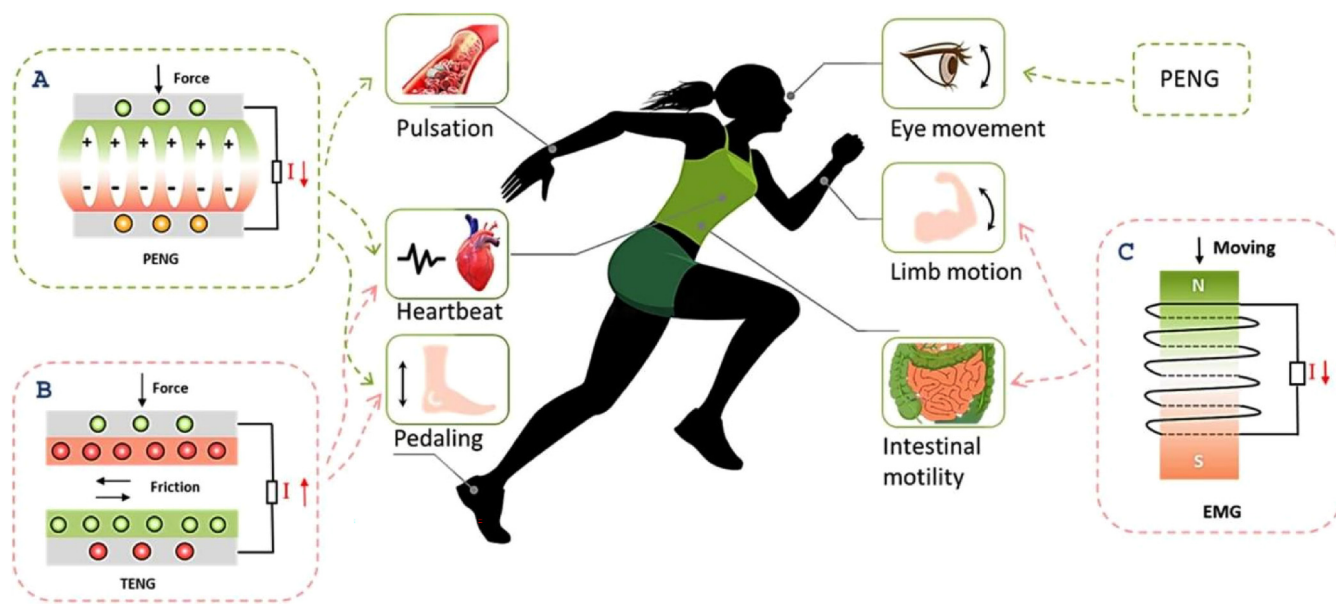


FIG. 3. Introduction to the principles of three types of power generators that can convert human kinetic energy, with human movements. (a) The principle of a piezoelectric nanogenerator, which can convert mechanical pressure into electrical energy. (b) The principle of a triboelectric nanogenerator, which can convert pressure and friction into electrical energy. (c) The principle of an electromagnetic generator, which can convert motion into electrical energy.

- (Figure 3), providing a sustainable power source for implantable devices such as pacemakers. Additionally, the kinetic energy generated by eye movements can be converted into electricity using similar technologies. Tiny piezoelectric generators, for instance, may be included in contact lenses or eyeglass frames to convert mechanical energy into electrical signals with each blink or eye movement. These developments show how common physical motions may be used to power a variety of wearable and medical devices, improving their ease and sustainability.
- Limb motion, intestinal motility: Through electromagnetic induction, the kinetic energy produced by these motions may be effectively transformed into electrical energy. Wearable devices such as armbands and knee braces can have electromagnetic generators (EMGs) installed in them to record the mechanical motion of a person's moving limbs. A coil of wire and a moving magnet are usually found in these devices (Fig. 3); as the limb moves, the magnet moves in relation to the coil, creating an electric current. This generated electricity can be used to power wearable health monitors or fitness trackers, reducing the reliance on batteries. The utilization of bodily motions for energy harvesting showcases the potential of transforming everyday activities into a sustainable power source.
- Figure 3 shows the power generation principles of three different generators, which use body movements such as walking, jumping, running, limb movements, heartbeats, and weak human activities such as pulse, eye movement, and intestinal peristalsis as potential energy sources. Piezoelectric nanogenerators (PENGs) [Fig. 3(a)] and electromagnetic generators (EMGs) [Fig. 3(c)] convert the pressure and vibration generated by these movements and movements into electrical energy through piezoelectric effect and electromagnetic induction, respectively. The illustration shows two operating modes of triboelectric nanogenerators (TENGs) [Fig. 3(b)]: vertical contact-separation mode and lateral sliding mode, which can easily collect the mechanical energy generated by human body movement.

a. Triboelectric nanogenerators (TENGs). TENGs, a prospective energy harvesting device, exhibit immense potential in the conversion of human kinetic energy.^{73,74} Their operating principle relies on triboelectrification and electrostatic induction, boasting a simple structure, diverse material options, and high power output. The core of the work of TENGs is to convert various forms of mechanical energy, such as the energy generated by human body movements, vibrations, weak activities, etc., into electrical energy, powering miniature sensors and wearable devices.⁷⁴ In the design and preparation of microfluidic equipment, select electrode materials that match TENGs and adapt to the structure of the microfluidic channel and the characteristics of the fluid, and integrate the electrodes onto the microfluidic chip through photolithography, printing, and other technologies. Currently, through material innovation and structural optimization, such as designing novel structures such as three-dimensional structures, layered structures, and nanostructures, the performance of TENGs has been significantly improved, enabling it to meet the needs of more practical applications.^{75–77}

b. Piezoelectric nanogenerators (PENGs). PENGs are nano-scale devices that utilize the piezoelectric effect to transform mechanical energy into electrical energy. Characterized by their ability to generate electricity from mechanical stress or vibrations, PENGs utilize piezoelectric materials that produce an electric charge when deformed [Fig. 3(b)]. Their basic principle is that when a piezoelectric material is subjected to an external mechanical force, the positive and negative charge centers inside the material will be relatively displaced, resulting in polarization, which will generate a potential difference across the material. If electrodes are connected to the two ends of the material, a current path can be formed to convert mechanical energy into electrical energy. Piezoelectric polymer materials with good performance have always attracted much attention, such as polyvinylidene fluoride (PVDF).^{78–80} PENG structures that can match the size and shape of microfluidic devices are designed and integrated into microfluidic channels or chips. Therefore, PENGs are widely used in powering small electronic devices, sensors, and wearable technology, offering a sustainable and efficient energy solution for various applications.^{78,81,82} From the power generation principle of PENGs, it can be seen that the application scenarios of PENGs are relatively limited, requiring external mechanical vibration or pressure to generate electricity. At the same time, the output power of PENGs is relatively low, which makes it difficult to meet the needs of high-power biological microfluidic devices.

c. Electromagnetic generators (EMGs). EMGs can convert mechanical energy into electrical energy through electromagnetic induction. They typically feature a coil of wire and a moving magnet. When the magnet moves relative to the coil, it induces an electric current within the coil [Fig. 3(c)]. EMGs are characterized by their high efficiency and durability. They are widely used in power generation, including wind turbines, hydroelectric dams, and various portable power applications.^{83–85} EMGs can be made using processes such as lithography, etching, deposition, and miniaturized magnet materials, and integrated into microfluidic devices.⁸⁶ The electricity generated by EMGs can be used to drive micropumps for precise drug delivery or as a power source for biosensors. If EMGs can be embedded in wearable sensors, the kinetic energy generated by body movement can be converted into electrical energy. However, the current application of EMGs in microfluidic devices is not widespread and still faces many technical challenges. For example, how to achieve efficient electromagnetic conversion in a limited space while ensuring the stability and reliability of the generator, and how to develop new materials that not only have biocompatibility, corrosion resistance, and thermal conductivity but also meet electromagnetic performance requirements. Due to size limitations, the output power of micro-EMGs is usually low, and for wearable devices or implantable medical devices, the volume and weight of EMGs are strictly limited, which is not as good as other ways to obtain energy, such as TENGs,⁸⁷ which have high output power, good stability, and ease of use.

2. Applications in bio-microfluidics

The synergistic integration of human kinetic energy-powered devices with bio-microfluidic platforms enables real-time

monitoring and diagnosis of physiological parameters, enhancing personalized healthcare. This convergence offers exciting opportunities for the application of bio-microfluidic technologies:

- **Implantable drug delivery:** Combined with motion-driven biosensors, these bio-microfluidic devices could enable self-powered drug delivery systems that respond to physiological cues or patient activity levels.⁸⁸ Powered by human kinetic energy, these implantable drug delivery systems offer the potential for autonomous drug release, eliminating the reliance on external power sources.^{89,90} For instance, a patient's movements could activate medication release when required, optimizing therapeutic outcomes and minimizing adverse effects.⁹¹ This approach holds particular promise for managing chronic conditions such as diabetes or heart disease, where precise and timely drug delivery is crucial. Additionally, such devices could enhance patient adherence and convenience by reducing the need for frequent manual intervention.
- **Point-of-care diagnostics:** Wearable health monitors driven by body movement are revolutionizing the field of health monitoring and diagnostics by tracking signs, such as heart rate and glucose levels, in real-time through devices that can be worn on the skin or integrated into clothing. This enables users and healthcare professionals to promptly address any health concerns⁹² based on feedback provided by these devices.
- One significant advancement in these gadgets is the removal of batteries in favor of generating energy through motion (kinetic energy harvesting). This independence improves the eco-friendliness of these devices. Cuts down on the need for frequent upkeep tasks. Making them more convenient for prolonged usage periods. The constant flow of data recorded by these gadgets facilitates the detection of health issues and enables prompt medical attention as well as tailored treatment strategies.⁹³
- Moreover, combining these biosensors with health (mHealth) platforms widens their usefulness by allowing remote monitoring and telemedicine services, connecting patients with healthcare providers effectively for ongoing assistance in distant or underserved regions, and improving healthcare accessibility.⁹⁴ The applications have been showcased in areas such as preventing asthma with respiration-based nanogenerators⁹⁵ as well as conducting cancer point-of-care testing using materials inspired by nature.⁹⁶ These devices' ability to work seamlessly with health systems makes them essential tools for the advancement of convenient and preventive healthcare practices.
- **Lab-on-a-chip systems:** The emergence of microfluidic technology has made it possible to create portable, self-sufficient lab-on-a-chip systems. Traditional drug development takes a long time and is costly. Microfluidic chip labs have the advantages of miniaturization, integration, high throughput, and automation. They can screen and analyze a large number of drug candidates in a short period of time, improving the efficiency and success rate of drug discovery.^{97,98} These integrated systems combine preparation, analysis, and diagnosis of samples with other laboratory tasks onto a single chip. These gadgets may function without an external power supply by using TENGs as a power source, which improves mobility and user-friendliness. Microfluidic chips can integrate functional units such as sensors,

controllers, and communication modules, providing a flexible platform for on-site analysis and decision-making, which is particularly useful for customized treatment, environmental monitoring, and rapid disease identification. They provide a flexible platform for on-site analysis and decision-making and are especially useful for customized treatment, environmental monitoring, and quick illness identification. At present, there are still many technical challenges in the manufacturing, integration, and detection of lab-on-a-chip systems, but overall, microfluidic chip lab technology has important application value and development prospects in both chemistry and medicine.

3. Challenges and future directions

Although bio-microfluidic systems driven by human kinetic energy have enormous promise, several issues need to be resolved before their full potential can be realized.

- **Energy conversion efficiency:** Enhancing the efficiency of mechanical-to-electrical energy conversion is a key focus. This entails optimizing materials and device designs to maximize energy capture and conversion rates. Innovative piezoelectric and triboelectric materials, coupled with novel engineering approaches, are necessary to improve performance. Moreover, integrating these technologies with existing energy storage solutions will ensure a consistent and dependable power supply for bio-microfluidic applications, even during periods of reduced mechanical input.
- **Miniaturization and biocompatibility:** Developing miniature and biocompatible energy harvesting components is essential for implantable and wearable devices. These components must be small enough to integrate seamlessly into the human body or onto wearable platforms without causing discomfort. Moreover, the materials used must be biocompatible to prevent adverse reactions, including tissue irritation or immune response. Innovations in nanotechnology and material science are key to achieving these goals, enabling the creation of tiny, efficient, and safe energy harvesters that can power advanced biomedical devices.
- **Long-term reliability:** Ensuring the prolonged stability and resilience of these devices in the human body is a key consideration. Devices must withstand the dynamic and often harsh physiological environment without degrading performance. This requires robust materials and designs that resist biofouling, mechanical wear, and chemical degradation. Long-term biocompatibility studies and rigorous testing protocols are essential to validate these devices' reliability over extended periods, ensuring that they can provide consistent and safe performance in medical applications.

Human kinetic energy-powered bio-microfluidic devices represent a promising frontier in both energy harvesting and biomedical engineering. By harnessing the energy of our movements, we can create self-powered, personalized medical devices that seamlessly integrate with our lives, revolutionizing healthcare and improving patient outcomes.

C. Body-heat-powered bio-microfluidics devices

Body heat, a ubiquitous and continuous energy source, different parts of the human body having varying temperatures (Fig. 4),

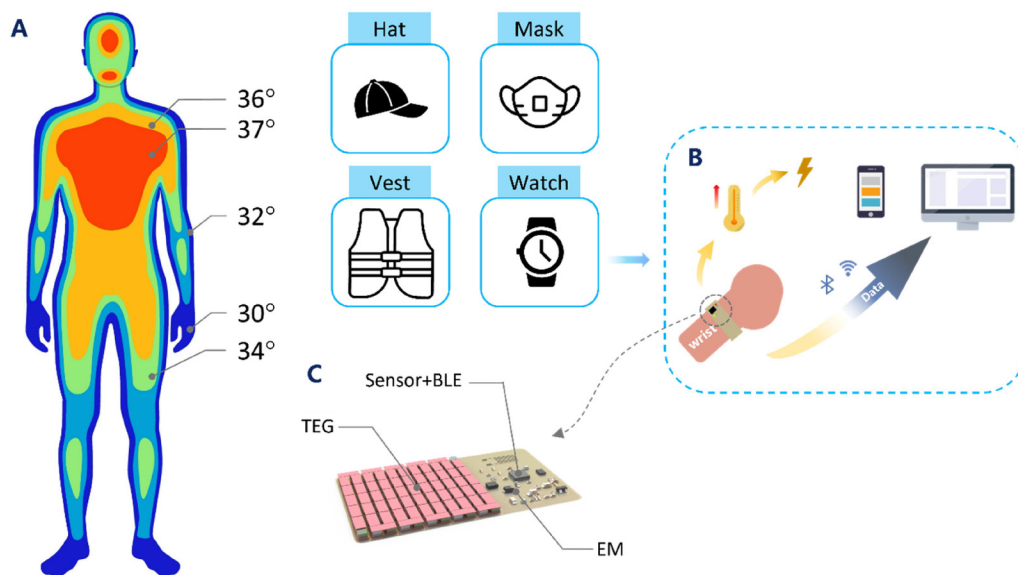


FIG. 4. Introduction to the application scenarios of microfluidic devices powered by body heat. (a) The temperatures of different parts of the human body. (b) A bracelet that uses the temperature differential between the human body and the environment as an energy source. (c) The main components that enable the bracelet's functions, including a thermoelectric generator (TEG), energy management (EM) electronics, a bluetooth low energy (BLE) wireless chipset, and sensors.

offers a unique opportunity for powering bio-microfluidic devices.⁹⁹ This emerging field aims to leverage the thermal contrast between the human body and the surroundings to drive various microfluidic operations, enabling self-powered and autonomous biomedical applications.^{100,101}

1. Principles and technologies

- **Thermoelectric generators (TEGs):** TEGs, based on the Seebeck effect, convert temperature gradients into electricity. The Seebeck effect occurs when a thermal gradient between two dissimilar conductive materials produces a voltage. By positioning TEGs in contact with the skin, they can harness body heat and utilize the temperature difference between the body and the environment to generate power. This electricity can then drive microfluidic pumps, sensors, and other components in bio-microfluidic devices,^{102,103} enabling continuous and self-sustained operation without external power sources, and enhancing their practicality for wearable and implantable medical applications.^{104,105}
- **Thermopneumatic actuators:** These devices utilize the expansion of gases or liquids when heated to create mechanical motion. The principle involves heating a contained gas or liquid, causing it to expand and generate pressure, which then drives mechanical movement. Body-heat-driven thermopneumatic actuators can power microfluidic valves, mixers, and drug delivery systems. By converting body heat into mechanical energy, these actuators enable precise control of microfluidic processes, ensuring efficient and targeted operation of biomedical devices without the need for external power sources.

- **Shape-memory alloys (SMAs):** SMAs exhibit a unique property of returning to their original shape when heated. Body heat can trigger SMA-based actuators for microfluidic flow control and other functions. These materials are currently used in various applications, including medical stents, eyeglass frames, and actuators in aerospace engineering. In bio-microfluidics, SMAs can precisely control fluid movement and enable responsive, self-regulating systems.

2. Applications in bio-microfluidics

The integration of body-heat-powered devices with bio-microfluidic platforms presents a wide range of possibilities, enhancing functionality and sustainability across various biomedical applications:

- **Wearable diagnostics:** In addition to biomarkers in sweat, tears, or tissue fluid, body temperature is also an important physiological health indicator. Wearable biosensors can diagnose the health or recovery of patients from changing body temperature. If these device sensors are integrated with thermoelectric generators, the need for external batteries can be eliminated.^{106,107} In addition to harvesting energy from body heat, energy conversion can be based on the Seebeck effect, utilizing the temperature difference between the environment and the human body to drive sensors and Bluetooth devices (Fig. 4). Yang *et al.* developed a flexible thermoelectric generator and energy management electronic device driven by body heat based on the Seebeck effect. This system can achieve reliable data transmission in short periods using minimal temperature differentials between the environment and the human body.¹⁰⁸

- **Implantable drug delivery:** Body-heat-driven drug delivery systems can offer personalized and on-demand release of therapeutics, responding to physiological cues. These systems harness the thermal energy from the body to trigger the release of medications precisely when needed, enhancing treatment efficacy and reducing side effects. Such smart drug delivery mechanisms are particularly beneficial for managing conditions requiring precise dosing, such as diabetes or cancer, ensuring optimal therapeutic outcomes, and improving patient compliance.
- **Point-of-care testing:** Portable microfluidic devices that utilize body heat for power offer the potential for rapid diagnostics at the point of care or in remote locations. By harnessing body heat to conduct intricate biochemical assays, these devices eliminate the reliance on external power sources, making them well-suited for deployment in resource-limited environments. They can swiftly analyze samples such as blood or saliva, delivering immediate diagnostic results. This capability is vital for prompt medical intervention and enhancing healthcare access in underserved areas.
- **Organ-on-a-chip systems:** Microfluidic components powered by body heat can facilitate precise temperature regulation and fluid flow within organ-on-a-chip models, thereby enhancing their physiological accuracy. Leveraging body heat as a power source, researchers can develop more realistic and dynamic models of human organs for applications such as drug testing and disease modeling. This approach improves the simulation of *in vivo* conditions, leading to a deeper understanding of human physiology and potentially contributing to the development of more effective treatments.
- **At the operational level,** systems contain intricately crafted channels that precisely regulate and steer fluid motion, as well as effectively control ion and particle transportation within a

confined setting. These channel-regulated conditions make them highly effective in facilitating the movement of currents by leveraging electrochemical processes synergistically. In terms of energy propagation applications, such microfluidic pathways have the potential to be harnessed to direct the flow of charge-carrying fluids as a means to power miniature-scale generators efficiently. The flow of ions in these channels can imitate circuits and facilitate energy transfer within the system, like how conductive wires work in electronic setups. This concept may be a helpful guide for creating compact and effective energy-generating setups that depend on the controlled movement of ions in areas such as bioelectronics or wearable devices (Table I).

3. Challenges and future directions

While research into flexible wearable technology, customized healthcare, and sustainable autonomous systems holds enormous promise for body-heat-driven bio-microfluidic devices, there are still several issues that need to be resolved before their full potential can be realized.

- **Efficiency enhancement:** Improving the conversion rate of body heat into usable electrical energy is crucial for the widespread adoption of these devices. Advances in thermoelectric materials and device design are needed to maximize energy output and ensure reliable power supply under varying thermal conditions.³⁵
- **Miniaturization and integration:** Developing compact and efficient energy harvesters that seamlessly integrate with existing microfluidic systems is essential for their widespread application.³⁶ This requires innovative miniaturization techniques that enable incorporation into wearable or implantable devices without compromising user comfort or functionality.

TABLE I. Comparison of energy harvesting approaches for micro-fluidic biosensors. PV, photovoltaic; TEG, thermoelectric generator; MEG, moisture-enabled electric generator; TENG, triboelectric nanogenerator; PENG, piezoelectric nanogenerator; EMF, electromagnetic field energy harvesting.

Category	Materials	Dimension	Linkage to body	Power density	Application scenarios	Reference
PV	Perovskite	20 × 27 × 4 mm ³	E-skin	6.08 mW cm ⁻²	Wearable biosensors	8
	PNTz4T	20 × 20 mm ²	Textile	1.2 mW cm ⁻²	Washable electronics	109
	FAPbI ₃	3 × 3 mm ²	E-skin	19.3 mW cm ⁻²	Flexible electronics	110
TEG	Bi _{0.5} Sb _{1.5} Te ₃ /Bi ₂ Te _{2.8} Se _{0.3}	6 × 25 cm ²	On-finger	12.5 μW	Sports wristband	111
	Bi ₂ Te ₃	3 × 8 cm ²	On-wrist	13.6 μW cm ⁻²	Wireless monitoring	112
MEG	PEDOT (p)/TiS ₂ (n)	15 × 15 mm ²	On-ankle	10 μW cm ⁻²	Wearable patch	113
	GO/PVA/PEG	15 × 2 cm ²	Textile	3 W m ⁻²	Athlete rehabilitation	44
TENG	GO/PDDA	5 × 5 cm ²	Textile	90 mW m ⁻²	Face mask	114
	Cu/protein/Al	8 × 8 mm ²	Tape	164 μW cm ⁻²	Location tracking	43
	PVA-2D-TMDs/PU/telfon	...	Tape	138 mW cm ⁻²	Electronic charging	115
PENG	PA conductive yarn	60 × 78 mm ²	Fabric	3.8 mW cm ⁻²	Illumination	116
	Al/PET/PTFE/Cu	50 × 75 mm ²	Backpack	3.7 mW cm ⁻²	Illumination	117
EMF	PVDF-g-MA	...	Fabric	3.15 μW cm ⁻²	Nanogenerator	118
	Glycine-PVA	10 × 10 mm ²	Biodegradable films	667.2 μW cm ⁻³	Implants	82
	PVDA matrix	75.0 × 42.7 × 0.15 mm ³	E-skin	0.6 μW cm ⁻²	Sign-language interpretation	119
EMF	Cu/polyimide	61 × 39 mm ²	Patch	19.6 μW cm ⁻²	Health monitoring	5
	Cu/Nd ₂ Fe ₁₄ B	Φ10 × D115 mm ²	Bracelet	3.34 mW cm ⁻²	Movement tracking	120
	MXene (Ti ₃ C ₂ T _x)	38 × 25 mm ²	Patch	5 μW cm ⁻²	Wireless power transfer	121

TABLE II. Summary and comparison of body-energy-driven energy generators.

Generator type	Linkage to body	Materials	Generator volume (mm ³)	Power (μ W)/ power density (W m ⁻²)	Reference
Thermoelectric energy generators	Direct contact to body skin	SiGe, Au;	...	142 nW	122
		Bi ₂ Te ₃ ;	2954.45	192.6	123
		Bi ₂ Te ₃ , Au, Cu;	...	4860/4660	124
		PDMS;	2954.45	176.1	125
Electromagnetic energy generators	Wearable devices	CNCs;	...	125 pW	126
		PMMA;	8000	422	127
		PDMS, NdFeB;	600	115.1	128
		PCB;	1700	0.4	129
		NdFeB;	2400	61.6	130
		ABS, NdFeB;	100 878	5000	131
		...	539 000	80 870	132
Piezoelectric energy generators	Hydrogels	MgZr, AlN;	2.45×10^{-4}	1.3	133
		PMN-PT, Si;	4.18×10^{-4}	7.182	134
		PZT, SOI;	4.006×10^{-4}	11.56	135
		PMN-PZT;	1.06×10^{-1}	14.7	136
		AlN;	0.0127	60	137
		PVDF;	...	0.315	118
		GO/PVA;	...	7.5×10^{-4}	138
Moisture-enabled electric generators	Microfluidic channels	GO, Au;	16	4.05×10^{-3}	139
		PSSA/PAA-CMC/carbon, Cu wire/Au;	50	1.8×10^{-3}	140
		GO/PVA, Ag/FTO;	...	0.78	141
		PDDA ink, C-Al	6	0.104	142

- Thermal management: Effective heat dissipation is critical for long-term performance and user comfort. Implementing advanced thermal materials^{37–39} and passive cooling mechanisms can prevent device overheating, ensuring stable operation and user satisfaction.
- Biocompatibility and safety: Rigorous testing and validation are required to confirm the long-term biocompatibility and safety of materials used in these devices. This includes assessing their interaction with bodily fluids and tissues, as well as addressing potential issues such as material degradation and biofouling.

Body-heat-powered bio-microfluidic devices can fulfill their potential as a sustainable and revolutionary technology for healthcare and other fields by tackling these obstacles. These gadgets have the potential to improve patient care and results by enabling decentralized healthcare solutions, continuous health monitoring, and tailored treatment through ongoing innovation and research.

Table II shows four types of generators that can be used in microfluidic devices and wearable devices, including thermoelectric energy generators, electromagnetic energy generators, piezoelectric energy generators, and moisture-enabled electric generators. Thermoelectric energy generators can directly contact human skin to collect heat or generate electricity using temperature differences. It has a certain power output and can meet the needs of some low-power devices, but it is relatively large and has certain requirements for application scenarios. The second is the electromagnetic energy generator, which can generate relatively high power and has good

power density within a certain range. It has a large volume difference and has limited application scenarios in micro-biosensors. Then, there is the piezoelectric energy generator, which is relatively small in size and is also one of the most common ways to power microfluidic devices and wearable devices. It can achieve a high power density. The moisture-enabled electric generator is very small in size and can generate electricity using humidity in the air or evaporated water. It has great advantages in many specific application scenarios (such as in body fluids or humid environments), but its power output is generally low and there is a lot of room for development in material and structural innovation.

III. CONCLUSIONS

In conclusion, we have looked at various bioenergy-driven microfluidic devices, their underlying theories, and their possible uses in environmental monitoring, healthcare, and diagnostics. Bio-energy-powered microfluidic devices are very promising because of their deep integration of cutting-edge technologies such as biotechnology and nanotechnology. In addition to more accurately mimicking the milieu within living things, these devices may do real-time monitoring of physiological processes and disease signs at the microscopic level, enabling early diagnosis and targeted medication formulation and administration.

However, this field also faces numerous challenges and areas for improvement. First, the efficiency of converting bioenergy into the power required for microfluidic devices needs to be enhanced.

Additionally, to be applicable for wearable and implantable flexible equipment, more functions need to be integrated into smaller spaces. Beyond that, biocompatibility and stability are indispensable. Yet, current research shows that materials that combine biocompatibility with stable electrical energy conversion are quite limited.

Nevertheless, we believe that in the future, microfluidic devices are expected to break through material limitations based on achieving high integration and intelligence. The development of new materials with superior biocompatibility and durability will enable devices to operate stably, accurately, and efficiently in complex and dynamic environments within living organisms. They will also achieve perfect integration with human tissues and cells, bringing unprecedented breakthroughs in disease treatment and prevention, and truly ushering in a new era of personalized medicine.

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AUTHOR DECLARATIONS

Conflict of Interest

The authors have no conflict of interest.

Author Contributions

Yuhan Li: Writing – original draft (lead); Writing – review & editing (equal). **Chuangyi Xu:** Writing – original draft (supporting); Writing – review & editing (supporting). **Yifan Liao:** Writing – original draft (supporting); Writing – review & editing (supporting). **Xiao Chen:** Writing – original draft (supporting); Writing – review & editing (supporting). **Jiang Chen:** Writing – original draft (supporting); Writing – review & editing (supporting). **Fan Yang:** Funding acquisition (equal); Writing – original draft (supporting); Writing – review & editing (supporting). **Mingyuan Gao:** Funding acquisition (equal); Writing – original draft (equal); Writing – review & editing (lead).

DATA AVAILABILITY

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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