PENG-Based Non-Invasive Medical Sensors

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Piezoelectric nanogenerators (PENGs) not only are able to harvest mechanical energy from the ambient environment or body and convert mechanical signals into electricity but can also inform people about pathophysiological changes and communicate this information using electrical signals, thus acting as medical sensors to provide personalized medical solutions to patients.

Keywords: piezoelectric nanogenerator ; non-invasive sensor ; medical application

1. Sensing Mechanism

The distinctive properties of piezoelectric materials have driven their rapid development in many fields, among which sensing technology based on the piezoelectric effect is one of the most fruitful areas. At the root, the piezoelectric effect is due to the mechanical stress in the lattice of a piezoelectric material that changes the distance between the center of the positive and negative charges, thus changing the original dipole moment and resulting in a polarized charge on the surface of the piezoelectric material.

One type of sensing is mechanical, monitoring motions, respiratory rate, and pulse rate, to name a few examples. After the device is attached to a person, the PENG is pulled and bent when subjected to mechanical forces, and its upper surface experiences tensile stress. Meanwhile, the lower surface of the PENG experiences compressive stress, which deforms the piezoelectric layer, thereby generating a polarized charge. The resulting electric field attracts or repels electrons in the electrodes, and an electrical signal, the response of the mechanical force to the PENG, is generated when an external circuit is connected in order to allow the generated electrons to move from the electrode surface to the bottom electrode. Due to the flexibility of the PENG, it will return to its initial state once the external force is removed. Once the stress state is reversed, the electrons gathered at the bottom electrode will return to the top electrode, generating an opposite electrical pulse. Thus, the compression and release of the PENG can generate cyclic alternating piezoelectric signals during human movement, respiration, and in pulse. In addition, the layered baklava structure is sensitive to stress changes. This sensor does not involve biochemical reactions and relies on the physical properties of the material itself. Another type is biosensing, monitoring aspects such as body fluids and gas molecules. Owing to the coupling of the piezoelectric effect and molecular sensitivity properties, the piezoelectric output of the PENG can serve as both a power source and a sensing signal. The surface of the piezoelectric material has a high density of point defects, such as oxygen vacancies, which provide adsorption sites for the target molecules and form an adsorption layer [1]. When subjected to an external force, the material surface can generate a high local charge density and a strong electrostatic field, which dissociates the adsorbed molecules into ions. The ion, in turn, releases a proton to the neighboring molecule, thus resulting in the charge transfer generated by the Grotthuss chain reaction [2]. Overall, when the PENG is compressed and deformed, both the ions in the adsorbed layer and the electrons inside the piezoelectric material can move in a directional manner, shielding the polarized charge on the surface of the piezoelectric material and thus reducing the piezoelectric output of the device [3][4][5].

The electromechanical coupling behavior of piezoelectric materials can be described by the following equation:

$$T_{ij} = c^{E}_{ijkl} S_{kl} - e_{kij} E_k \tag{1}$$

$$D_i = e_{ikl} S_{kl} + k^{s}_{ij} E_k \tag{2}$$

where *S*, *T*, *D*, and *E* are the mechanical strain, mechanical stress, potential shift, and electric field, respectively. ekji, kSij, and cEijkl are the piezoelectric constant, dielectric constant, and elastic constant, respectively. The superscript “*E*” indicates a constant electric field, and "*S*" indicates a constant strain [6]. Equation (1) describes the inverse piezoelectric effect, i.e., the strain or displacement that occurs when an electric field is applied to a piezoelectric material. Equation (2) describes the direct piezoelectric effect, where an electrical charge is generated when an external force is applied to the material. This effect is used for sensing and energy harvesting. Equations (1) and (2) can be represented explicitly in matrix form:

$$\begin{bmatrix}\sigma_{11}\\ \sigma_{22}\\ \sigma_{33}\\ \sigma_{23}\\ \sigma_{31}\\ \sigma_{12}\end{bmatrix}=\begin{bmatrix}c_{11} & c_{12} & c_{13} & 0 & 0 & 0\\ c_{12} & c_{22} & c_{13} & 0 & 0 & 0\\ c_{13} & c_{13} & c_{33} & 0 & 0 & 0\\ 0 & 0 & 0 & c_{44} & 0 & 0\\ 0 & 0 & 0 & 0 & c_{55} & 0\\ 0 & 0 & 0 & 0 & 0 & c_{66}\end{bmatrix}\begin{bmatrix}\varepsilon_{11}\\ \varepsilon_{22}\\ \varepsilon_{33}\\ 2\varepsilon_{23}\\ 2\varepsilon_{31}\\ 2\varepsilon_{12}\end{bmatrix}-\begin{bmatrix}0 & 0 & e_{31}\\ 0 & 0 & e_{32}\\ 0 & 0 & e_{33}\\ 0 & e_{24} & 0\\ e_{15} & 0 & 0\\ 0 & 0 & 0\end{bmatrix}\begin{bmatrix}E_1\\ E_2\\ E_3\end{bmatrix} \quad (3)$$

$$\begin{bmatrix}D_1\\ D_2\\ D_3\end{bmatrix}=\begin{bmatrix}0 & 0 & 0 & 0 & e_{15} & 0\\ 0 & 0 & 0 & e_{24} & 0 & 0\\ e_{31} & e_{32} & e_{33} & 0 & 0 & 0\end{bmatrix}\begin{bmatrix}\varepsilon_{11}\\ \varepsilon_{22}\\ \varepsilon_{33}\\ 2\varepsilon_{23}\\ 2\varepsilon_{31}\\ 2\varepsilon_{12}\end{bmatrix}-\begin{bmatrix}k_{11} & 0 & 0\\ 0 & k_{22} & 0\\ 0 & 0 & k_{33}\end{bmatrix}\begin{bmatrix}E_1\\ E_2\\ E_3\end{bmatrix} \quad (4)$$

where σ denotes mechanical stress, ε is the strain, and k denotes the dielectric constant under constant strain. Since the elastic, piezoelectric, and dielectric constants depend on other constants, many piezoelectric materials can be understood as transversely isotropic.

2. Material Selection of PENGs for Energy Harvesting and Sensing

The applications of PENGs for sensing and energy harvesting have expanded rapidly over the last few decades. Most of the reported works are based on inorganic piezoelectric materials, such as zinc oxide, or other materials, such as polymers, with high voltage electrical coefficients, and composites are also widely used.

2.1. Inorganic Piezoelectric Materials

The most widely used inorganic piezoelectric materials include ZnO, PZT, $BaTiO_3$, MoS_2, and $BiFeO_3$. Zinc oxide is an excellent piezoelectric material and is commonly used to fabricate sensor devices and transistors. The flexibility, biosafety, and piezoelectric effect render ZnO a promising candidate for non-invasive sensors [7][8].

For example, Nour et al. proposed a piezoelectric nanogenerator (PENG) based on zinc oxide (ZnO) nanowires [9]. They prepared the PENG by hydrothermally growing ZnO nanowires on a paper substrate. The device can harvest energy from low-frequency motion (footsteps) for self-powered pressure sensors.

Owing to its low cost, high piezoelectric performance, and stable thermal properties, PZT is widely applied. Niu et al. developed a high-performance PZT-based stretchable piezoelectric nanogenerator (HSPG) [10]. They adopted a mixing technique instead of the conventional stirring technique to blend the PZT into silicone rubber. The tensile rate was increased to 30%, and the output performance was significantly improved. The device can be conformally attached to the body to obtain kinetic energy by deformation.

As lead is toxic and can pollute the environment and harm health, some lead-free piezoelectric materials have been developed. For example, Baek et al. designed a lead-free PENG based on $BaTiO_3$ nanowire arrays (BaTiO NWs) [11]. They adopted a two-step hydrothermal method to grow BaTiO NWs on a Ti substrate. To measure the piezoelectric energy of the individual $BaTiO_3$ single grains, they transferred the NWs to a flexible substrate and connected the NWs to a Au electrode pad. When the device was pressurized with a finger, the output voltage and current values were 90 V and 1.2 µA, respectively.

The MoS_2 with semiconducting and piezoelectric properties may also serve as a candidate material for piezoelectric devices. Han et al. developed a MoS_2-based PENG ([12]. They fabricated S-treated monolayer MoS_2 nanosheets on a sapphire substrate by the CVD method and then transferred them to PET. They compared the performance of the PENG before and after the S treatment, and the results showed that the piezoelectric output of the s-treated MoS_2-based PENG was significantly increased. This can be attributed to the fact that the S treatment process effectively passivates the S vacancies, reduces the free carriers, and prevents the shielding effect. Therefore, the piezoelectric output of the S-treated MoS_2-based PENG was significantly increased compared to the original MoS_2.

BFO possesses excellent physical properties but is one of the least studied lead-free chalcogenide materials used for piezoelectric applications. Sankar et al. fabricated a $BiFeO_3$ (BFO) by the sol–gel method and obtained spherical BFO nanoparticles after annealing at 100–500 °C [13]. Then, they prepared a sandwich structure piezoelectric device (graphene/$BiFeO_3$-PDMS/graphene). The output voltage of the device could reach 0.4 V when finger pressure was exerted.

Due to the huge market demand for piezoelectric products, piezoelectric materials and devices are advancing rapidly and exhibiting a higher biocompatibility, piezoelectric properties, and transconductance efficiency compared to conventional piezoelectric materials, such as PZT and BT. In addition, piezoelectric metamaterials are a strategy that can be used to achieve high-performance, lead-free piezoelectricity. Ceramic sheets can be transformed into piezoelectric metamaterials by chemical inhomogeneities, which may be caused by the formation and diffusion of oxygen vacancies during the reduction process. Furthermore, the novel stretchable structures of inorganic piezoelectric films have been explored in order to render them stretchable, with wavy and flexural geometries being examples.

2.2. Piezoelectric Polymers

Piezoelectric polymers are carbon-based materials. Owing to their specific molecular structure and orientation, they can exhibit piezoelectricity. They are softer than ceramic materials and possess the advantages of simplicity, flexibility, and a low density for energy harvesting. Polymers with a semi-crystalline structure can exhibit piezoelectricity due to the microscopic crystals distributed in the amorphous body, including PVDF, P(VDF-TrFE), cellulose, PLA, polyamides, paraxylene, etc. [14][15]. Piezoelectricity can also be observed in amorphous or non-crystalline polymers, resulting from the presence of dipoles in their molecular structure, which form at temperatures above the glass transition temperature (Tg) of the polymer. Such polymers include nylon, polyimide, polyurethane, polyurea, etc. [16].

PVDF and P(VDF-TrFE) are the most commonly used piezoelectric polymers [17]. Owing to their piezoelectricity, flexibility, and biocompatibility, they have great potential for medical sensing. There are α, β, γ, and & phases in PVDF, in which the β phase is closely related to the piezoelectricity. Moreover, the α phase can transform into the β phase by stretching. For example, Khadtare et al. fabricated a flexible piezoelectric nanogenerator for the real-time monitoring of muscle activity using PVDF film as the active layer [18]. The device had an excellent flexibility, stability, and transparency. The output voltage and current could reach 7.02 V and 1.11 μA, respectively, during the stretch–release process at 8 Hz. In addition, the device could be adhered to the finger in order to monitor human muscle movement through the piezoelectric response obtained from finger flexion and release.

2.3. Piezoelectric Polymer Nanocomposites

By adding fillers with high-voltage electrical properties to polymers, it is possible to obtain piezoelectric polymer composites with their advantages, which are the high-voltage electrical constants of the fillers and flexible properties of the polymers.

Yang et al. fabricated a piezoelectric pressure sensor based on PDA@BTO/PVDF film [19]. They first modified barium titanate (BTO) with polydopamine (PDA), homogeneously mixed it with polyvinylidene fluoride (PVDF), and, finally, prepared the piezoelectric sensor by the surface solution casting method. The voltage output was significantly enhanced by 13.3 times in comparison to the original PVDF, exhibiting a promising power supply capability. Furthermore, the signals of joint flexion and human motion could be monitored.

Shi et al. developed a flexible $BaTiO_3$/PVDF-TrFE-based PENG [20]. They fabricated PMMA@$BaTiO_3$ NWs by the atom transfer radical polymerization (ATRP) method and used them as the piezoelectric reinforced phase to prepare PVDF-TrFE nanocomposites by the electrostatic spinning method. The compatibility of PVDF-TrFE with the PMMA material greatly improved the dispersion of the $BaTiO_3$ nanowires and stress transfer at the interface, thus significantly improving the output performance of the PENG.

Singh et al. fabricated a PVDF/$NaNbO_3$/RGO flexible composite film and investigated its piezoelectric response ([21]. The results indicated that it had the same degree of β phase as the bare PVDF, but the nanogenerator based on the composite film had a higher voltage signal (output voltage of 2.16 V and current of 0.383 a). This result originated from the presence of $NaNbO_3$ and RGO, which enabled the easier alignment of the dipoles of the PVDF. Moreover, the piezoelectric properties of $NaNbO_3$ itself were also responsible.

3. Design Criteria of PENG-Based Non-invasive Sensors

3.1. Performance Improvement Strategy

The goal of improving the performance of PENG-based sensors is mainly to improve the flexibility, sensitivity, and piezoelectricity of the device. The commonly employed methods include the use of materials with high voltage coefficients, the development of composite thin film materials, changing the micromorphology of the material, the addition of dopants, and the selection of a suitable substrate. Materials with high voltage electrical coefficients and composite thin film materials have been mentioned previously, and the remaining methods are comprehensively analyzed in this section to provide a guide for the development of high-performance PENG-based non-invasive sensing devices.

Micromorphology

By controlling the process conditions, different micromorphological materials such as nanowires, nanoribbons, nanorods, nanotubes, etc., can be prepared. Different micromorphologies of the same piezoelectric material have great impacts on the performance of piezoelectric sensors [22].

Navale et al. prepared graded ZnO nanowires (BNWs) and nanorods (NRs) on glass substrates by the surface thermal evaporation method [23]. The prepared ZnO NRs and BNWs were used as sensing materials for the detection of toxic nitrogen dioxide (NO_2). The ZnO sensors had a high response to NO_2, with a maximum response of 622 and 101% and fast response and recovery time values at 200 °C. Moreover, the ZnO sensor responded to very low exposure to NO_2 gas (1 ppm). The excellent stability and reproducibility of the response enables ZnO with nanostructures to be widely applied in the development of wearable sensors.

Koka et al. synthesized a $BaTiO_3$ nanowire array that can be applied for vibration sensing and vibration energy harvesting [24]. They adopted a two-step hydrothermal reaction method to control the growth of titanate NW arrays and then convert the titanate NW arrays into $BaTiO_3$ NW arrays as precursors, while maintaining the nanowire shape. The arrays possessed a tetragonal phase, thus exhibiting ferroelectric and piezoelectric properties. At a lower resonant frequency (170 Hz), the $BaTiO_3$ NWs exhibited a superior output voltage response of up to 345 mV when excited by sine-wave-based acceleration.

Dopants

To improve the properties of sensing devices, various dopants have been developed, such as metallic elements, graphene, etc. Their addition to piezoelectric materials can significantly increase the piezoelectric coefficient (d33) [25].

Chen and his team designed a graphene-based pressure sensor [26]. The device exhibited a sensing behavior for static signal measurements that originated from the piezoelectric-potential-induced transient electron flow e). Furthermore, owing to the high carrier mobility of the graphene, the device possessed a high sensing performance (sensitivity of up to 9.4×10^{-3} kPa^{-1}, response time of 5–7 ms) and excellent flexibility, making it suitable for wearable health sensors.

Song et al. prepared an in-plane deformation field sensor array based on ZnO thin film by the RF sputtering method [27]. With the doping of the lithium metal element in ZnO, the sensitivity of this device was 100 times higher than that of ordinary strain sensors. This can be attributed to the lower conductivity of the doped ZnO that reduced the shielding effect of the polarized charge and also prevented the mutual crosstalk between the individual sensing units, allowing each sensing unit to share the same highly sensitive film.

Substrate

The performance of PENG-based sensors depends mainly on the piezoelectric material. However, the substrate can also significantly affect its performance. Currently, the main suitable substrates used to improve the performance of devices are PET and PDMS.

Gao et al. proposed a $BaTiO_3$-based flexible piezoelectric nanogenerator [28]. They adopted PET as the substrate of the device, which exhibited a higher output performance than the other substrates of the piezoelectric nanogenerator. Owing to the excellent flexibility of PET, the device was deformed by the solution under the external force and thus efficiently converted mechanical energy into electrical energy. Moreover, the insulating properties of PET reduced the energy loss in the process of the charge flow, thus improving the output performance of the device.

Yan et al. prepared a $BaTiO_3$-based flexible piezoelectric nanogenerator [29]. They selected polydimethylsiloxane (PDMS) as the substrate, and the output current of the device was up to 261.40 nA. The output of the device was increased by the excellent insulating property of PDMS, which reduced the energy loss during transmission. Furthermore, its flexibility protected the piezoelectric material from contamination and provided protection against mechanical damage to the device. Therefore, PET and PDMS are excellent candidates for the preparation of PENG-based sensor substrates.

3.2. Comfortability and Durability Enhancement Method

Owing to the long-term contact of the PENG-based non-invasive sensor with the wearer's skin, its comfortability and durability are also very important. Generally, relatively rigid piezoelectric materials cannot establish a highly conformal contact with the skin and result in the discomfort of the wearer. Polymer piezoelectric materials and composite piezoelectric materials possess an excellent elasticity and flexibility, making them a favorable choice. Furthermore, the introduction of microstructures to the film surface in order to increase the contact area is also a promising option.

Siddiqui et al. fabricated a lead-free flexible PENG by the electrospinning technique [30]. The nanofibers in the device consisted of a composite of P(VDF-TrFE) and $BaTiO_3$ nanoparticles (BT NPs), which were embedded in elastomeric PDMS to fabricate the PENG. When positioned inside the shoe, the elastomeric PDMS dissipated the applied force uniformly and avoided the pressure body's direct contact with the soft polymeric fibers, thus reducing local damage and fragility and improving wearer comfort and the device's durability.

3.3. Biocompatibility Assurance

Biocompatibility is a basic requirement for PENG non-invasive sensors. Although lead (Pb)-based ceramics such as PZT exhibit high electrical coefficients, their brittleness, rigidity, and toxicity limit their application in non-invasive sensing devices. Lead-free ceramics, such as $KNbO_3$, $NaNbO_3$, etc., have an excellent biocompatibility and can thus serve as PZT ceramic replacements. Furthermore, while most polymeric piezoelectric materials have an excellent biocompatibility, their piezoelectricity is relatively weak. The development of piezoelectric composites, which have the advantages of both organic and inorganic materials, could partially solve this problem.

They grew amorphous-phase $KNbO_3$ (KN) films on TiN/polyimide/poly (ethylene terephthalate) substrates at a low temperature (350 °C). The PENG exhibited an excellent output performance (~2.5 V, ~70 nA) under strain and strain rates of 0.76% and 0.79%/s, respectively. Moreover, the KN films possessed an excellent reliability and biocompatibility, making the material an outstanding candidate for self-powered medical devices.

Deng et al. proposed a self-powered piezoelectric sensor (PES) for the monitoring of pressure sensing and bending motion [31]. They fabricated cowpea-structured PVDF/ZnO nanofibers using an electrostatic spinning technique. The device had both the piezoelectric effect and polymer flexibility. Furthermore, it could work in both the compression and bending modes, with excellent flexibility, a high sensitivity, skin adaptation capacity, and mechanical stability. Based on this, the authors implemented a self-powered gesture remote control system that can transmit the pulse signals from human fingers to the robot's palm, showing promise for application in the field of medical monitoring.

4. Applications of PENGs as Non-Invasive Sensors

PENGs have promoted the development of non-invasive flexible and wearable biosensors in recent years. Non-invasive flexible and wearable biosensors can accurately monitor variations in physiological characteristics to continuously track different health parameters in a patient-centric manner and provide valuable insights for healthcare applications.

4.1. PENG-Based Biofluid Sensors

Biosensors are widely used for the non-invasive chemical analysis of biological fluids, such as saliva, sweat, urine, tears, and interstitial fluid (ISF). Biofluids can be sampled non-invasively, which means that this approach will not damage the outermost protective layer of the skin and lead to contact with the blood, resulting in a minimal risk of injury to the patient.

Saliva

Saliva is a rich complex biological substances composed of a large number of intracellular and extracellular components that permeate through the blood [32][33][34]. Therefore, saliva is an excellent non-invasive sample for blood analysis aiming to monitor the health status of the patient.

For example, Yang and his team fabricated a sensing system for the real-time monitoring of the blood glucose concentration in human saliva [35]. It can be worn on various parts of the human body. The sensing mechanism is attributed to the coupling of the enzymatic reaction and the piezoelectric effect, where GOx on the ZnO nanowires reacts enzymatically with glucose upon contact with the glucose solution, producing gluconic acid and hydrogen peroxide. Furthermore, as H_2O_2 decomposes, H^+ can be adsorbed on the nanowire surface, and e^- is transferred to the Zno nanowire, increasing the surface carrier density. This approach extends the application scope of integrated sensing systems in disease medicine.

Selvarajan et al. developed a self-powered sensor based on BTO films for monitoring glucose in the saliva [36]. As expected, the 20% w/V BTo thin film sensor had a higher current response to the glucose concentrations ranging from 0 to 1 mM. Furthermore, 5 mM of glucose and 0.1 mM of interferent (galactose and uric acid) were used for the comparison, as shown by the I-T response curves, indicating that the current response of the galactose and uric acid was negligible compared to that of glucose. This suggests that the sensing device is sensitive and has a wide linear concentration range and low detection limits, providing a suitable method for other relevant clinical applications.

Sweat

Sweat is an ideal sample for non-invasive biosensors, as it is readily available and offers a wealth of physiological information about the health status [37]. For example, lactic acid in sweat is an important metabolite of anaerobic glycolysis and can be used to determine tissue viability and fitness levels. Meanwhile, uric acid in sweat is a major metabolite of purines and can be used to detect diseases related to gout and leukemia. The metabolism of glucose in sweat is related to blood sugar and can be used to detect diabetes, while Na^+ and K^+ are related to osmolality. As a result, sweat can be applied to monitor an individual’s physical health and diagnose diseases.

Lactate is a major component of sweat, and its concentration can be used to assess an athlete’s maximum performance during high-intensity activity and provides an advance warning. In 2020, Mao et al. designed a portable PENG-based biosensor that can be used for sweat analysis [38], and the structure of the sensor is presented. They adopted Kapton as a substrate for the device and modified the T-ZnO-nanostructured fabric with lactate oxidase (LOx) to achieve the real-time monitoring of the maximum lactate steady state (MLSS) of athletes in non-invasive conditions. lactic acid reacts with the enzyme to produce pyruvate and H_2O_2, followed by the decomposition of H_2O_2 into H^+, O_2, and e^-, and electrons are transferred to the T-ZnO nanowire array, increasing the surface carrier density. The magnitude of the output piezoelectric voltage is indicated by the colors of the rainbow, and the piezoelectric output is dependent on the mechanical energy provided by an external force.

Additionally, the continuous detection of the above-mentioned sweat components is essential. Instead of conventional sweat sensors, PENG-based sweat sensors can be composed of several different enzyme-modified unit devices, enabling the continuous detection of multiple molecules. Han et al. designed a piezoelectric electronic skin that can be used for sweat analysis [39]. As presented, the device can be attached to different parts of an athlete’s body to monitor their physiological status by analyzing the sweat composition. The device contains four piezoelectric biosensing units composed of ZnO nanowires modified by four enzymes, Lox (lactate oxidase), Gox (glucose oxidase), urease, and urease, which can monitor the glucose, lactate, urea, and uric acid concentrations in the sweat in real time.

Urine

The method of monitoring urine through non-invasive techniques has numerous advantages, such as the protection of patient privacy and simplification of the process of collecting and handling samples. Cysteine in urine is an essential amino acid in the body that contains a thiol group. Its abnormalities are associated with chronic diseases such as Alzheimer’s-like diseases, Parkinson’s disease, and rheumatoid arthritis. Therefore, urine detection can be used for the routine analysis of diseases [40].

In the presence of BT-NH, R-SH (thiol) loses an H^+ and transforms into a sulfate, and the sulfate side chain (R-S) in cysteine is a strong nucleophilic reagent that reacts with the NH groups on the BT NPs (electrophilic reagents). This results in the nucleophilic attack of $R\text{-}S^-$ on the NH group, resulting in the formation of an S-N bond. As a result, the cysteine binds to the film, increasing the surface’s negative charge. In addition, the sensor’s cysteine response is measured through the I-V technique, and the results indicate that the −4 V current increases with the increasing cysteine concentration (10 M–1 mM), and the increase in the current is linearly related to the cysteine concentration. Compared to conventional sensors, this method enables the real-time analysis of urine samples using non-invasive methods and exhibits a comparable or higher performance, including an excellent sensitivity, selectivity, reproducibility, and stability.

4.2. PENG-Based Respiratory Sensors

Breath plays an important role in human vital signs, and it can reflect changes in health conditions such as asthma, pneumonia, bronchitis, and other respiratory diseases [41][42]. In order to achieve the real-time monitoring and analysis of respiratory parameters, such as the molecules of some specific gases in exhaled air, respiratory mechanical signals, and temperature, various portable and miniaturized self-powered respiratory sensors have been developed.

Exhaled Gas Molecules

Previous research suggests that exhaled gas contains numerous organic and inorganic metabolites, some of which are closely related to human health and can serve as signals for certain diseases [43][44]. However, gas analysis instruments face numerous limitations, such as complex structures, high material costs, and unsustainable operation. Therefore, it is urgent to develop sensing devices that are portable, simple, and sustainable.

Fu et al. designed a non-invasive, self-powered breath analyzer [45]. The piezoelectric effect induced by the PVDF on the gas flow can provide power, and the gas-sensitive properties of the PANI electrode can be used for the detection of exhaled gas. The authors used sodium sulfate, sodium dodecyl benzene sulphonates, sodium oxalate, camphor sulphonic acid, and nitric acid as dopant sources of five polyaniline derivatives to form five gas-sensing units, which can diagnose respiratory diseases such as asthma, diabetes, cirrhosis, and inflammation via the detection of exhaled gases (acetone, ethanol, CO, NO_x, and CH_a) in the concentration range of 0 to 600 ppm, and the results show an excellent sensing performance. In addition, the device can analyze ethanol gas, thus simulating the diagnosis of fatty li.

Oximetry is a key indicator that is used to assess the presence of respiratory failure in patients with COVID-19 [46][47][48][49][50]. Lin et al. proposed a self-powered exhalation oxygen-sensing mouthpiece for the real-time monitoring of lung health information [51]. They used tetrapod ZnO (T-ZnO) hybridized with polyvinylidene fluoride (PVDF) attached to a flexible fabric. Owing to the coupling of the gas-sensitive properties with the piezoelectric effect, the T-ZnO/PVDF-based sensor converts the exhaled airflow energy into a piezoelectric signal, which not only serves as a power source but also increases with the increase in the exhaled oxygen concentration, thus monitoring the exhaled oxygen concentration in real time and reflecting the oxygen-filling capacity of the human lungs. This self-powered wearable sensing device can facilitate the non-invasive health monitoring of lung diseases.

Exhaled ammonia is one of the biomarkers of impaired renal function. Some studies indicate that an ammonia concentration of 1.1 ppm is considered relatively healthy, while ammonia above 1.6 ppm is unhealthy [52]. The testing of ammonia concentrations in patients' breath can be used to screen patients for potential kidney disease and provide effective treatment in advance. Zhang et al. created a PENG-based ammonia gas sensor [53]. The device consists of a flexible MoS_2 sheet PENG and an Au-$MoSe_2$-sensing membrane. The PENG attached to the human body can collect energy from various body movements to drive the ammonia sensor.

In conclusion, conventional gas-sensing devices have many limitations. The PENG-based self-powered respiratory sensor has attracted great interest from scholars in the field of medical sensing, and its electrical signal is closely related to the respiratory parameters, an aspect which has important clinical significance for the early diagnosis and treatment of numerous diseases.

Respiratory Temperature and Humidity

Except for exhaled gas molecules, human breathing involves heat and water. By analyzing the changes in the exhalation temperature and humidity, it is easy to distinguish four types of breathing: no breathing, weak breathing, normal breathing, and deep breathing. Furthermore, when a patient has symptoms of fever or respiratory inflammation, the exhaled gas temperature is always higher than that of a healthy patient. These characteristics enable electronic devices that can monitor breathing to have great potential for intelligent medical diagnostic applications.

Wang et al. developed an electronic skin textile that can precisely sense the breathing temperature [54]. The textile can be comfortably applied to human skin. It consists of a piezoelectric polyvinylidene fluoride nanofiber membrane doped with zinc oxide nanoparticles (PVDF/ZnO NFM) and flexible heat-resistant carbon nanofibers (CNFs). The temperature-sensing principle is depicte. The CNFs consist of disordered graphite structural layers, where each carbon atom is hybridized in the form of sp^2, and the lone electrons that are not involved in the hybridization overlap with each other to form off-domain π-bonds. These off-domain electrons move freely in the carbon atomic plane. As the temperature increases, the electrons originally bound by the atoms gain energy and become free electrons, resulting in a decrease in the resistance of the CNFs. To demonstrate the ability of the sensing textile to monitor temperature changes in physical objects, the textile is attached to a mask, and the results indicate that the resistance of the textile varies with the temperature, thus enabling the monitoring of the temperature of exhaled air under different breathing conditions. In addition, its temperature resolution is 0.381% /°C, and the temperature range is from 25 °C to 100 °C. This electronic skin textile has great promise for application in the diagnosis and monitoring of respiratory diseases.

The absorption of water molecules can significantly enhance the electrical conductivity of nanofibers (NFs) [55]. Gu et al. developed an active humidity sensor based on lead-free $NaNbO_3$ [56]. They synthesized a $NaNbO_3$ piezoelectric nanofiber with a monoclinic chalcogenide structure by the far-field electrostatic spinning method and transferred it to a polymer substrate in order to fabricate a flexible active humidity sensor. The device has an output voltage of up to 2 V and a negative correlation with ambient humidity in the range of 5%~80%. Its humidity-sensing mechanism originates from the proton hopping between H_3O^+ groups driven by the piezoelectric potential, which increases the leakage current inside the NFs.

Vivekananthan et al. designed a piezoelectric nanogenerator (PENG)-driven biopolymer humidity sensor [57]. They coated piezoelectric collagen on cotton fabric with an upright structure and piezoelectric properties, enabling its use as an energy harvester and humidity sensor. The PENG-based sensor exhibits an excellent linear response in the 50–90% humidity range. Its sensing mechanism is the chemisorption of water vapor on the collagen membrane surface or the replacement of oxygen on the membrane surface. Talth status, which can be applied for exercise monitoring and disease warning [58]. Several scholars have investigated the association of the respiratory rate with physical health status. For example, it may originate from anesthetic or sedation overdose and elevated intracranial pressure during surgery when the respiratory rate is lower than 0.2 Hz (12 bpm). Meanwhile, when the respiratory rate is greater than 0.4 Hz (24 bpm), it may derive from diseases such as anemia, fever, heart failure, and hyperthyroidism. Currently, it is necessary for people to develop self-powered electronic devices for monitoring the respiratory rate in order to monitor non-invasive diseases of the respiratory system, especially during the periods of outbreaks of COVID-19, aggravated air pollution, and frequent hazy weather [59].

Liu et al. proposed an active sensor based on PVDF piezoelectric nanogenerators for respiratory sensing and healthcare monitoring [60]. The output voltage and output current during respiration were as high as 1.5 V and 400 nA, respectively, which corresponded to the physiological signals, demonstrating the excellent accuracy and reliability of the device. Furthermore, the authors simulated several rapid respirations and compared them to the normal respiratory rate, and these respiratory profiles provided detailed information on the kinetics of the respiratory process and have great significance for the development of sensing devices for lung function assessment.

Wang et al. created a wearable, multifunctional piezoelectric MEMS (micro-electro-mechanical system) device [61]. The device measures less than 10 mm when placed on the finger and can be positioned in a mask to monitor movement states such as resting, running, and walking based on the breathing rate. The principle of the device is based on the voltage generated by the inverse piezoelectric effect of the PZT material to obtain the respiratory rate. When the mask is worn for a long time, an early lung health warning can be obtained based on an abnormally fast or slow breathing rate.

Researchers have developed a wealth of PENG-based non-invasive respiratory monitoring devices. They are positioned on the body, including the chest, abdomen, and throat, to collect mechanical signals. The direct contact of these areas with the skin ensures that PENG-based respiratory sensors can be driven by the physical motion caused by breathing and collect respiratory signals through this process. However, their operation has certain limitations and is vulnerable to environmental influences, such as humidity and electromagnetism. Other equipment, such as nasal airflow sensors, is also not reliable. In conclusion, PENG-based sensors offer a new way to monitor breat

Cardiovascular diseases, including heart and blood vessel diseases, have become one of the biggest threats to the health of the elderly [62][63]. Fortunately, with the advent of various advanced medical sensors, most diseases can be diagnosed in advance. The real-time and continuous monitoring of the body’s physiological signals, such as the radial pulse, heart rate, respiratory rate, and blood pressure, can provide medical information about many cardiovascular states and thus prevent some cardiovascular diseases.

Pulse

The radial artery pulse can be detected on the wrist. Its amplitude, frequency, and waveform are important cardiovascular parameters. Self-powered continuous arterial pulse monitoring systems can improve the quality of treatments for cardiovascular disease, thus extending the lives of patients. Traditional pulse monitoring sensors exhibit significant power consumption drawbacks that limit their continuous operation. To overcome this limitation, non-invasive sensors based on piezoelectric nanogenerators are used for the continuous monitoring of arterial pulses.

In 2022, Veeralingam et al. designed a Pb-free, sensitive, and flexible piezoelectric nanogenerator for measuring the human arterial pulse pressure [64]. They adopted a rotational coating technique to prepare polydimethylsiloxane/polypyrrole piezoelectrically active materials. Then, they deposited the PDMs/PPy composite polymer onto an ITO-coated PET substrate and coated an aluminum film onto the PET substrate as a counter electrode. When external pressure is present, nano-dipoles are formed inside the PDMS/PPy piezoelectric composite film due to the synergistic effect of the PDMS and αβ'-PPy polymers, generating piezoelectric potential. When the external pressure is released, the generated nano-dipoles are neutralized, and the piezoelectric potential disappears. This periodic compression and release of pressure to the PENG produce an AC-type response. Once the device is mounted on the wrist, the pressure response of the arterial pulse to the PENG can be observed. The high-intensity peak can be attributed to the systolic pressure peak of the pulse, while the low-intensity peak can be attributed to the diastolic pressure peak of the pulse. This PENG opens up new avenues for the development of biosensors for medical diagnostics.

Karan et al. developed spider-silk (SS)-based bio-piezoelectric nanogenerators (SSBPENG) [65]. Naturally, abundant spider silk exhibits a vertical piezoelectric coefficient of up to ~0.36 pm/V, excellent mechanical properties, an excellent biocompatibility, and biodegradability. The prepared SSBPENG devices show a high output performance, energy conversion efficiency (up to 66%), and sensitivity to arterial pulses (signals generated by tension). Furthermore, they can enable the health monitoring of throat movements during coughing, speaking, and drinking. Thus, these bio-piezoelectric materials can be used to fabricate PENGs for the future development of the medical field.

Heart Rate

The application of non-invasive sensors in the medical and healthcare fields can significantly improve the quality of life and living standards of patients and reduce healthcare costs. Medical sensors that measure the heart rate may be used for the detection of abnormal conditions, such as bradycardia or tachycardia.

Li and his team proposed a SnSe piezoelectric nanogenerator that can non-invasively monitor important health signs, such as the heart rate [66]. They adopted a mechanical stripping method to obtain a SnSe that exhibits a strong anisotropic piezoelectric response and piezoelectric output voltages reaching up to 760 mV. By integrating the SnSe nanogenerator and a single MoS-based sensor, they obtained a self-powered sensor unit (SPSU) without the need for a power supply. The device was installed on the wrist and chest as a pulse sensor, respectively, and the measurements of the heart rate (~90/min) were consistent, exhibiting an excellent sensing performance. Furthermore, the SnSe piezoelectric nanogenerator could successfully convert the mechanical energy generated by the heartbeat into electrical energy. Therefore, SnSe piezoelectric nanogenerators have great potential in the field of healthcare.

In addition, Li et al. developed a $MoSe_2$-based piezoelectric nanogenerator that can non-invasively monitor the human heart rate [67]. They synthesized a monolayer $MoSe_2$ sheet by chemical vapor deposition and achieved a 50% larger piezoelectric output signal than MoS_2 at a 0.6% strain, which indicates the excellent piezoelectricity of $MoSe_2$. By connecting the $MoSe_2$ nanogenerator to the tester's chest, the heart rate could be monitored by V-t curves. The piezoelectric signals associated with the heartbeat, such as the frequency and amplitude, were significantly increased by high-intensity exercise, indicating its high sensing performance.

Blood Pressure

Blood pressure measurement is an important method for diagnosing hypertension, and it is classified into two categories: invasive and non-invasive. Invasive measurements are required for critical conditions and complex cases. Traditional non-invasive measurement methods include cuff compressions, such as mercury sphygmomanometers used in hospitals and electronic sphygmomanometers used at home. The human blood pressure constantly fluctuates; therefore, the development of sensors that continuously measure blood pressure can provide doctors with a relatively accurate foundation for diagnosis and enable them to avoid misdiagnosis.

Tan et al. fabricated a PENG-based smart wristband that can be applied for the non-invasive monitoring of blood pressure [68]. The device consists of PENG-based sensor, rubber band, PLA housing, Bluetooth module, and battery. Moreover, the device can be used to acquire pulse wave signal signals with a noise ratio of 29.7 dB.The principle of the device is to combine pulse wave data collected by a deep learning model with a pre-built regression model to predict the blood pressure. Wearing this wristband enables the continuous monitoring of a patient's blood pressure, which opens up new ideas for the prevention and treatment of hypertension.

4.4. PENG-Based Motion Sensors

Foot and Hand Movement

The movement monitoring of both the upper and lower extremities is in high demand in a variety of application scenarios, ranging from patient rehabilitation to exercise training. Exercises such as finger flexion, arm swinging, clapping, running, and jumping can improve blood circulation to various organs of the body, thereby improving overall health.

Vivekananthan developed a Pb-free flexible PENG [69]. They adopted a solid-phase reaction method to prepare Pb-free (1−x) $KNaNbO_3$-x $BaTiO_3$ nanoparticles (x = 0.02, 0.04, 0.06, and 0.08). Then, these particles were impregnated into a polydimethylsiloxane (PDMS) matrix to fabricate composite films for the piezoelectric nanogenerators. The doping of BTO enhanced the piezoelectric properties of the KNN material (maximum electrical output of 58 V, 450 nA) without affecting the orthogonal phase of KNN. Furthermore, by attaching the PENG to the human hand and leg, it could be used as an active sensor to monitor human sleep and movement.

Choudhry et al. designed a shoe insole nanogenerator (SING) [70]. They dispersed four common piezoelectric materials, $BaTiO_3$ (BT), ZnO (ZO), soft pzt (P1), and hard pzt (P2), in silicon (Si) and then selectively added graphene nanopowder (GNP) to fabricate the SING and analyze its piezoelectric performance. In addition, to evaluate the sensing performance of the device, they conducted tests including foot stomping, walking, running and touching, in which the SING exhibited a high output performance (power density, 402 mW/m) in the case of real-time walking. The results suggest that this SING can be used as a self-powered biosensor for wearable devices, autonomous physiological monitoring, and tactile sensing.

Dutta et al. synthesized NiO@SiO_2/PVDF nanocomposites and exhibited the application of this material for the energy harvesting of human motion and tactile electronic skin sensing [71]. They coated silica onto NiO nanoparticles, thus hindering the agglomeration of the NiO nanoparticles in the PVDF matrix, and the uniform dispersion of the nanofillers enhanced the piezoelectric and dielectric properties of the composites. As a result, the PENG composed of this material exhibited a high output (power density, 685 W/m^3) and excellent conversion efficiency (13.86%), and it could light up to 85 LEDs when the PENG was gently touched by hand and charge a 2.2 μF capacitor to 22 V within 450 s. The device can not only power human-related electronic devices but also precisely detect an individual at rest or in motion. For example, the self-powered electronic skin sensor can be attached to a glove to distinguish between the movements of different fingers. This simple, sensitive, and portable piezoelectric nanogenerator opens up a new platform for the application of human-motion-based energy harvesters.

Kumar et al. proposed a piezoelectric nanogenerator based on a P(VDF-TrFE)/ZnO nanofiber membrane [72]. They dispersed ZnO in P(VDF-TrFE) solution at a concentration of 18% (*w/w*) and synthesized the P(VDF-TrFE)/ZnO nanocomposite by the electrostatic spinning method. The addition of the ZnO nanofiller significantly improved the phase fraction, roughness, viscosity, dynamic modulus, and loss modulus of the solution and reduced the damping coefficient of the solution. Moreover, they characterized the composite film, and the results showed that the addition of ZnO nanoparticles enhanced the β phase and improved the activity and sensitivity of the composite film. Moreover, the PENG could record the hand motions such as hand pressure, bending, and tapping with the voltage output. This PENG provides a simple self-powered pathway for many medical health-monitoring devices.

Muscle Stretching

Manjula et al. developed a flexible ZnO-nanosheet-based piezoelectric nanogenerator [73]. They prepared ZnO nanosheets by adopting a low-temperature, single-step hydrothermal method. Conductive aluminum foil was the substrate used for growing the ZnO nanosheets. Since the aluminum foil and ZnO nanosheets formed a layered double hydroxide (LDH) layer, the substrate provided excellent adhesion for the growth of the ZnO nanosheets, without any additional seed layer deposition. This PENG was tested under real-time mechanical forces such as muscle stretching, finger tapping, and foot pressure to verify the output of the nanogenerator and confirm the piezoelectric voltage Connecting this device in series with four 400 mV devices further enhanced the output voltage and confirmed the high stability and repeatability (400 mV) of the piezoelectric nanogenerator.

Eyelid Movement

Long-term work of the eyes and brain can cause eye strain. Eye fatigue may cause serious health problems if it is not detected and treated in a timely manner. Lü et al. developed an ultra-thin piezoelectric sensor that can monitor eye fatigue by collecting information about blinking, such as a high blink frequency, long eye closure time, weak gaze strength, and other abnormal conditions [74]. They adopted lead zirconium titanate (PZT) nanoribbons as the functional material for the sensor. Owing to the high piezoelectric coefficient of PZT, it can generate a high voltage signal when mechanically deformed by external forces. Moreover, the thickness of the sensor is only 10 μm, which allows for better contact with the eyelid skin during blinking.

4.5. Other Devices

In cases of poor wound healing, wound infection is a major concern. For example, it is not uncommon for a small wound to result in systemic infection or even amputation, especially in immunocompromised individuals. Even in healthy individuals, the appearance of a wound after trauma or surgery can be a major challenge. As a result, various wound dressing methods have been developed, such as electrical stimulation, which has been widely accepted. Due to its simplicity, portability, and biocompatibility, the PENG is an excellent candidate that can be used to assist in wound healing.

Liang et al. developed a ZnO-modified PVDF/sodium alginate (SA) piezoelectric hydrogel scaffold (ZPFSA) that can serve as a trauma dressing for skin repair [75]. The scaffold is prepared by 3D printing technology with a dual piezoelectric release model of vertical expansion and horizontal friction, exhibiting a stable piezoelectric response, favorable biocompatibility, and excellent antibacterial properties. In this device, SA acts as a support to drive the swelling and stretching of the PVDF in the absorption of the traumatic exudate. The ZnO-modified PVDF has stable hydrophilic polarization and shows good antimicrobial properties, and the ordered and regular pore structure of PVDF can rapidly absorb and remove exudate, thus generating a stable model and suitable piezoelectric current to stimulate cell proliferation, orderly collagen deposition, and trauma healing. Ultimately, in the study, it accelerated the healing rate of rat wounds and prevented scar formation.

Bhang et al. designed a ZnO-based piezoelectric skin patch (PZP) [76]. The fabricated patch consists mainly of PDMS and ZnO nanorods, which can generate pulsed potentials and EF after deformation under external force to promote skin recovery. The authors attached the PZP to the trauma sites of rats, and 54.8% and 95.2% of the ZnO-based patches produced 320 and 900 mV voltage outputs, respectively. The range of 0.150 to 1.2 V was found to be the ideal voltage for accelerating wound healing. In the authors' in vitro experiments, the curved patches created EF, which also encouraged dermal fibroblast migration and increased the generation and gene expression of fibroblast growth factors. Animal studies have revealed the significant effectiveness of zinc-oxide-based piezoelectric patches.

Du et al. created a biological patch (HPSP) composed of shellfish hydrogel (PDA-PAAm) and electro-spun polyvinylidene-fluoride (PVDF) nanofiber-based PENG that can be used to accelerate skin wound healing [77]. The patch mimics the action of the shellfish adhesion proteins and trauma endogenous electric field (EF), which can attach to the wound surface and generate a low-frequency pulsed voltage, thus facilitating the in vitro promotion of fibroblast proliferation and migration and even partial hair follicle regeneration. The test results showed that HPSP reduced the wound closure time of the skin defects by about 1/3, which is a significant advance in wound healing.

Although wound-monitoring sensing devices are promising, there are still some difficulties limiting their actual clinical use. First, the size of the PENG should be customized to match the size of the wound. Then, biocompatibility, elasticity, and durability are necessary for the PENG's ability to produce electrical stimulation. In addition, the effects of body fluids should be prevented. Wound exudate and body fluids can corrode PENG devices, and the question of how to maintain a high energy conversion efficiency and long-term stability in this environment is an issue that requires careful consideration. Finally, wound healing is a complex and dynamic process, and wounds of different sizes and depths require electrical stimulation of different intensities to promote wound healing.

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