•**Review**•

Flexible and wearable healthcare sensors for visual reality health-monitoring

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Abstract Visual reality (VR) health-monitoring by flexible electronics provides a new avenue to remote and wearable medicine. The combination of flexible electronics and VR could facilitate smart remote disease diagnosis by real-time monitoring of the physiological signals and remote interaction between patient and physician. The flexible healthcare sensor is the most crucial unit in the flexible and wearable health-monitoring system, which has attracted much attention in recent years. This paper briefly reviews the progress in flexible healthcare sensors and VR healthcare devices. The flexible healthcare sensor is introduced with basic flexible materials, manufacturing techniques, and their applications in health-monitoring (such as blood/sweat detection and heart-rate tracking). VR healthcare devices for telemedicine diagnosis are discussed, and the smart remote diagnosis system using flexible and wearable healthcare sensors, and a VR device, is addressed.

Keywords Flexible electronics; Flexible healthcare sensors; Visual reality; Telemedicine

1 Introduction

Today, our aging society requires considerable medical resources, which have caused an increasing amount of shortages. A limited amount of medical resources have been prioritized for patients who suffer from serious disease or have urgent needs. Current and traditional medical methods cannot meet the requirements of patient needs in a timely fashion. Flexible and wearable health-monitoring provides a revolutionary technology, which serves as an alternative to traditional diagnosis methods, putting health care on a path that is more remote, portable, and timely[1–4]. Flexible healthcare sensors are crucial units in wearable health-monitoring systems, which could transduce physiological signals of human body to electrical signals for quantitative analysis and evaluation of body condition. Physiological signals could be collected in real time by flexible healthcare sensors and transferred to a cloud database by wireless data transmission techniques. Then, these data can be used by a physician to evaluate body condition with an artificial intelligence (AI) deep-learning algorithm[5–7]. Visual reality (VR) is a computer simulation system in which a virtual world is created, providing an immersive interactive experience. Potential applications of VR in combination with modern medicine has been demonstrated, using computer graphics and computer vision to create a "VR + medical" system that has been used by physicians to conduct clinical trials[8–10]. As assumed in Figure 1, we believe that the combination of VR and flexible healthcare sensors will promote remote medicine, providing a paradigm for medicine that is smart, accurate, and reliable. The VR device could help physicians connect users in a virtual environment and obtain physiological signals of patients accurately and in a timely fashion. Then, the professional medical diagnosis results can be provided to patients through the Internet.

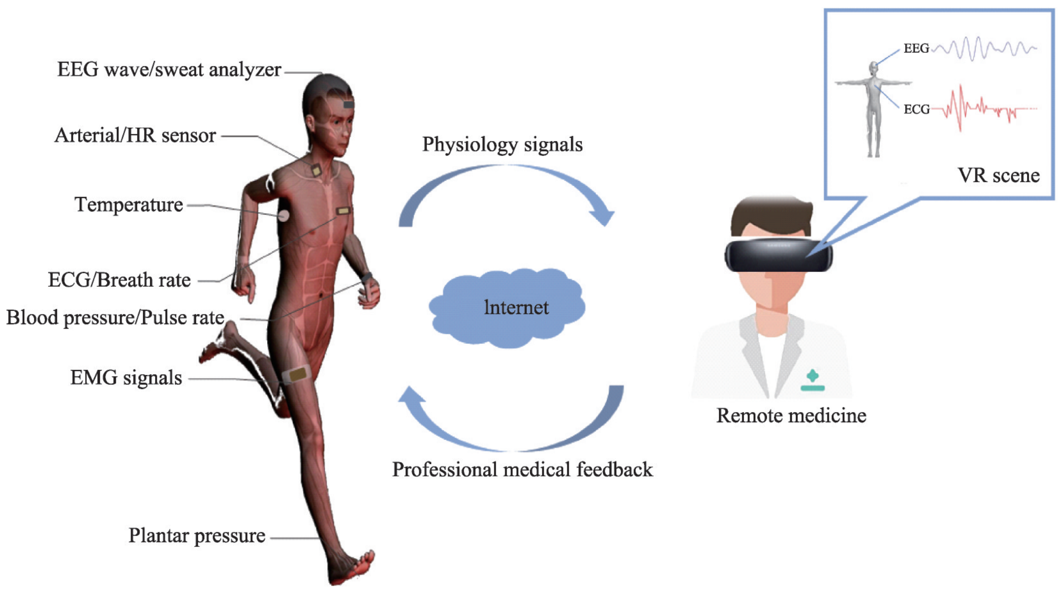

Figure 1 Compared to time-consuming medicine, convenient medicine could promote the sharing of medical resources, making it convenient for patients to access the physician anytime and anywhere and improving the quality and efficiency of diagnosis.

Several review papers have summarized the progress of flexible electronic devices and their applications in health-monitoring[11–16]. However, these papers lack discussion on the combination of flexible electronics with VR and AI. This review paper briefly summarizes the advancement in flexible healthcare sensors and VR healthcare devices. The flexible materials and manufacturing techniques for sensor fabrication, and their applications in health-monitoring (e. g., blood/sweat detection and heart-rate tracking) have been introduced. Finally, we briefly discuss the VR devices with flexible and wearable healthcare sensors for a smart telemedicine diagnosis system.

2 Flexible healthcare sensors

Currently, various flexible sensing electronics devices have been developed for healthcare applications, such as artificial bionic sensors and smart flexible sensors, which could be used in the monitoring of physiological signals. The key factors in flexible sensing electronics include materials, the manufacturing process, and device configurations, which refer to the interdisciplinary research that combines the fields of materials science, device physics, chemistry, electronics, and computer science. The characteristics of soft, stretchable, and flexible properties enabled those devices to attach to the skin, facilitating the wearability of these devices on any part of the body for healthcare application. Compared to conventional rigid and fragile sensors, flexible electronics make those health-monitoring applications more comfortable, biocompatible, energy-saving, and portable. In this section, we summarize the materials and manufacturing techniques for flexible electronics, and review several typical applications in health-monitoring.

2.1 Flexible materials for flexible healthcare sensors

Flexible materials are the basic building blocks of flexible healthcare devices. The intrinsic mechanically flexible and stretchable properties could be characterized from the polymers and rubbers that constitute these devices, owing to their specific molecular structures. Polymers such as polyimide (PI), polyethylene (PET), polyethylene (PEN), and polydimethylsiloxane (PDMS) have been demonstrated as promising materials that could serve as a substrate for flexible electronics[17-22]. Conducting polymers such as polyaniline (PANI) and poly(3-hexylthiophene) (P3HT) can be employed as channel materials and electrodes for flexible transistors and flexible sensors[23-25]. For example, Mannsfeld et al. reported patterned PDMS as dielectric layers of a capacitive sensing device and demonstrated a maximum sensitivity of $0.55kPa^{-1}$ and a relaxation time of 1ms[26]. Pan et al. described a type of conductive and elastic microstructure polymer consisting of hollow-sphere polypyrrole (PPy)[27]. This microstructure polymer has high sensitivity (~56.0−133.1kPa^{-1}at approximately 30Pa) and excellent stability of sensing features. The intrinsic mechanical properties of polymers make those materials better over traditional rigid inorganic materials in wearable applications because of their good attachable and biocompatible properties. In addition, these polymers could be easily used in device fabrication with low cost and large scale. However, the hysteresis of polymers results in devices with long response time, which casts a shadow on their applications in high-frequency vibration detection.

Rigid materials could be converted to flexible materials when their sizes are reduced to micro- and nano-scale, or are constructed with specific nanostructures. For example, bulk silicon wafer and glass slides are rigid and easily broken into pieces. If the thickness is reduced to less than 50μm, silicon wafer and glass slides could be bent and present mechanical flexibility[28]. Glass fibers with diameters at the microscale level have high tensile strength, which could be elongated to 3% without being broken[29]. Network structure composed by nanowires and nanotubes have been developed for flexible and transparent conducting films[30,31]. Most of the contact points in a network are physically stacked, such that they could be welded into a chemical bond[32]. Therefore, network structures shown electrical stability and reliability upon repeated bending and are promising as electrodes used in flexible electronics[33]. The chemically bonded contact points in networks decrease the contact resistance between the nanowires and reduce the power consumption in final devices. Low power consumption is one of the important advantages for wearable devices because it will extend working time and improve battery life.

Because of the requirement of electrical conductivity, sensing materials usually consist of inorganic and organic materials that possess metal and semiconducting properties. For example, carbon nanotubes and graphene are commonly used in flexible and wearable electronic sensors as electrodes owing to their tunable electrical conductivity[22]. Inorganic semiconductors with strong piezoelectricity, such as ZnO, have been demonstrated with high performance (high sensitivity and fast response) in flexible mechanical sensors and shown potential applications in wearable health-monitoring[34,35].

2.2 Micro-manufacturing for flexible healthcare sensor

The micro-manufacturing process is a fundamental step and important driving force for flexible electronics. This process could fabricate the circuit module on a flexible substrate and make the device miniaturized and highly integrated. Typically, there are two types of manufacturing processes: lithography and printing.

Lithography is a widely used technology for the fabrication of microelectronic devices because of its precise manufacturing with high resolution. The resolution of this process could reach the microscale and nanoscale level if electron beams and the UV light are used as exposure light. The principle of lithography is based on the photochemical properties of the photoresist in which the photoresist is modified and shows different dissolubility when exposed to UV light. Generally, lithography contains steps involving light exposure, developing, metal deposition, and lift-off. As shown in Figure 2, the photoresist was spin-coated (step 1) onto a flexible substrate for solid film, exposed (step 2) to UV light, and developed (step 3) to form a patterned photoresist. This was followed by metal film deposition (step 4) and lift-off (step 5). In this manner, conducting electrode patterns could be fabricated onto a target flexible substrate. In this lithography process, the sample was heated to the temperature of 100−150°C for solidification and immersed into a polar solvent, such as acetone, for lift-off. Therefore, the manufacturing on flexible substrate requires the substrate materials to be resistant to high temperature and polar solvent. PI, PEN, and PET were the suitable candidates for substrate materials to fabricate flexible electrode. Lithography on an elastic PDMS substrate is difficult because of the swelling effect of PDMS in acetone solvent and large coefficient of thermal expansion, which causes a large deviation in the patterning and alignment of the photoresist. Thermal expansion of PDMS could be decreased by changing the composition of the materials. There are few reports on PDMS-based flexible lithography devices. As the large value of thermal expansion sensitizes the material to temperature, the temperature-sensitive phenomenon was used to design a new type of flexible temperature sensors. Besides electrode fabrication, the lithography technology was also employed to fabricate semiconductors of channel materials with micro-patterns. For example, Sun and Rogers developed the "top-down" approach in which lithographic patterning and etching techniques create single-crystalline nano-/micro-structures of semiconductors (Figure 3a) [36]. However, some problems still exist in lithography technology for the fabrication of flexible electronics. The thermal expansion of flexible substrate makes resolution of alignment difficult to reach the nanoscale level. In the removal of the photoresist, the polar solvent damages the flexible organic electronic material, casting a shadow on their electrical properties and performance in final applications.

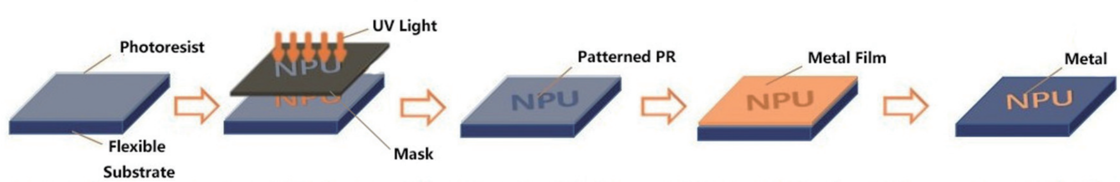

Figure 2 The schematic of lithography: 1) resist coating, 2) UV light exposure, 3) developing, 4) metal film deposition, and 5) lift-off.

Beyond lithography, printing technology is an effective, low cost, and large scale method for the fabrication of flexible electronic devices and large-area integrated circuits. Another important advantage of printing is that the use of polar solvent and a complex manufacturing process can be avoided. The technology could produce a dedicated function circuit by inputting patterned images that could be revised conveniently. Various and versatile printing inks (e. g., conducting ink, insulating polymer ink, and semiconducting ink) have been developed for printed electronics, such as FET devices and sensors[37−40]. Currently, there are several printing methods, including inkjet printing, screen printing, and aerosol-jet printing, that have been used to fabricate electronic devices. Because printing technology can print any ink-type material to an arbitrary target substrate, this technique and printed electronics are compatible and interlinked with flexible and stretchable electronics, such as organic electronics, plastic electronics, paper-based electronics, transparent electronics, and wearable electronics. Recent studies have demonstrated the solar cell, touch screen, and healthcare devices by printing[41−43]. For example, the surface gate electrode of the traditional crystalline silicon solar cell is prepared by screen-printing with conductive silver paste[44]. Organic and perovskite solar cells could be used in printing to reduce the cost of manufacturing[45]. With the recent development of conducting and sensing materials, printed flexible sensing electronics, especially healthcare sensors, have been reported with high sensitivity and multifunctionality. Yamamoto et al. have reported the use of printing technology to achieve multifunctional, disposable, and flexible medical sensors[46]. The low-cost printing process makes the sensor cheap and disposable, avoiding medical cross-infection. The multifunctionality of the device could be realized by its integration with modules monitoring ECG and body temperature. Recently, Guo et al. achieved a stretchable electronic circuit by the rolling and transfer printing of nickel eutectic gallium-indium alloy semi-liquid metal. The paper-based devices have stable electrical performance and high durability after repeated cycles of more than 1000, and the stretchable electrodes and strain sensor can sustain a strain of 100%[47]. Despite the wide use of lithography and printing technology in traditional micro-electronic circuits, the process parameters on flexible substrate should be further developed and improved. How to balance thermal expansion and resolution remains a challenging problem.

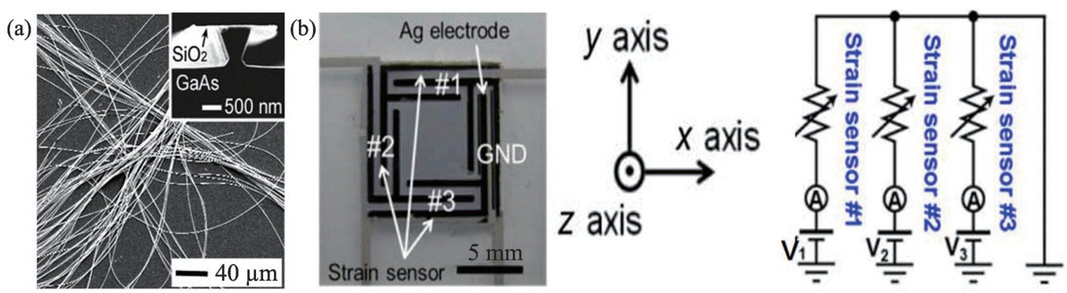

Figure 3 (a) SEM image of GaAs Nanowires[36]; (b) The printed acceleration sensor and circuit diagram[46].

2.3 Applications in monitoring health-related physiological signals

Wearable technology has developed rapidly and wearable products have remarkably emerged. Wearable devices with flexible healthcare sensors provide a novel and convenient way for health-monitoring and put traditional diagnosis methods toward the path of portability and remote use. With the development of novel flexible and soft materials, flexible healthcare devices perform multifunctionality that could monitor multiple physiological signals simultaneously. Flexible and wearable healthcare devices are more delicate, economical, comfortable, and durable. Figure 4 shows some typical applications of flexible electronics in monitoring health-related physiological signals.

2.3.1 Blood sensors

Oxygen saturation, pH value, and glucose concentration in blood are crucial physiological signals for indicating the physical condition of a body. Rapid analysis of these components in the blood plays an important role in clinical operation and evaluation of the state of health. However, conventional devices are cumbersome and uncomfortable. For example, monitoring oxygen saturation conventionally always involves using a finger clip, which limits physical movement. Detection of glucose concentration and pH value requires the destruction of skin to collect blood. In view of this situation, flexible blood sensors were developed to detect pH, glucose, and blood oxygen levels noninvasively. Khan et al. have invented a type of blood oxygen sensor that consists of organic electronics printed on flexible plastic and can be used attached to skin (Figure 5a)[48]. The sensor can monitor wound healing in real time. In contrast to traditional oximetry, this technology uses printed light-emitting diodes and photodetectors to alternately form an array

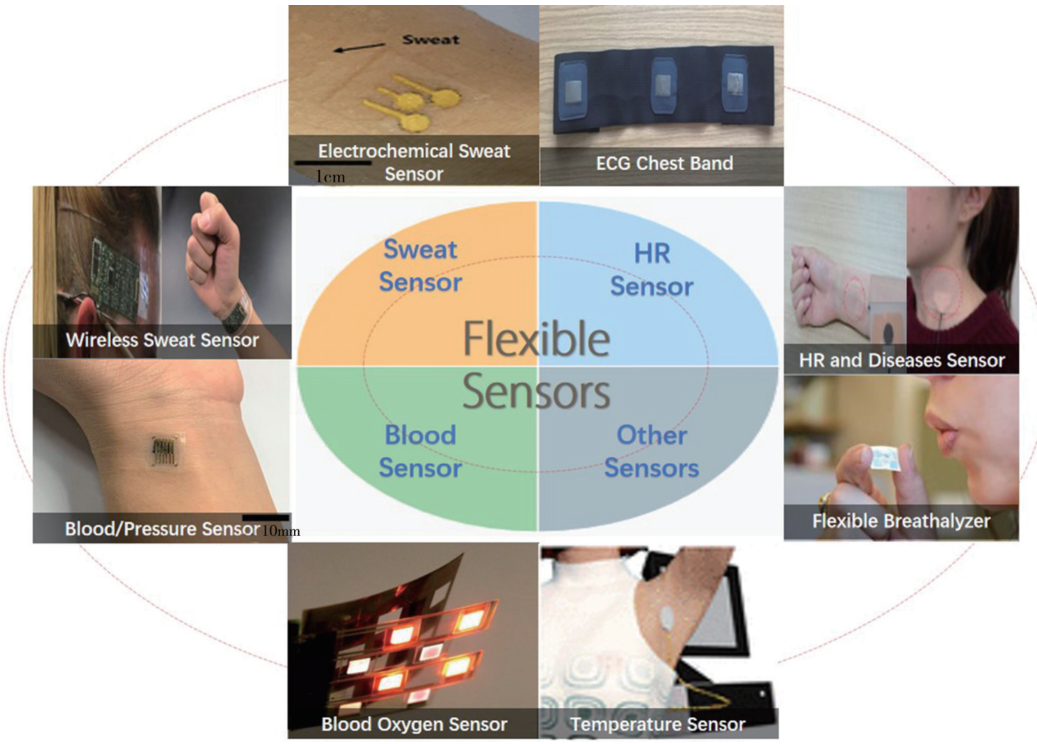

Figure 4 The collection of wearable flexible sensors for monitoring physiology signals. Blood oxygen sensor[48]. Wireless sweat sensor[49]; Blood and pressure sensor[50]; Temperature sensor[51]; Breathalyzer[52]; Electrochemical sweat sensor[53]; ECG chest band[54]; HR and diseases sensor[55].

of sensors that can detect blood oxygen levels at nine points simultaneously and can be placed anywhere on the skin. The sensor uses light reflection, rather than a transmitted pulse, to detect oxygen saturation because the traditional device is limited to specific tissues (e. g., earlobes and fingers) that cannot be transmitted by light. These flexible blood sensors can monitor the blood oxygen in real time in patients who suffer from diabetes and respiratory illness, and report the results in a timely manner. Monitoring the blood flow is essential to patients who are in recovery after reconstructive surgery. Implantable sensors for the detection of blood flow are commonly used in clinical practice; however, the process requires a medical staff to fix the device in a specifically designed position and brings the risk of infection. Boutry et al. developed a type of biocompatible and flexible pressure sensor that can measure arterial blood flow in contact and non-contact modes. The flexible device was fabricated by bio-degradable materials based on the configuration of the fringe-field capacitor (Figure 5b)[56]. The advantages of this flexible sensor are noninvasiveness, fast response, high stability, and good biocompatibility, which brings blood-monitoring toward a smart, safe, rapid, and comfortable age.

2.3.2 Sweat sensors

Body fluids, such as interstitial fluid and sweat, carry a great deal of vital information regarding the human body. Sweat is one of the most readily available body fluids and contains large amounts of inorganic salt (K^+, Na^+, Cl^-) from metabolism of the human body and is closely related to the state of body. It has been demonstrated that sodium ions in the blood can be used to detect dehydration, chloride ions to diagnose cystic fibrosis, and glucose to test diabetes. Different types of sensing units were integrated into a substrate based on the various components in sweat, and the device was attached to the surface of the human skin for physiological analysis. Various kinds of multi-component sweat analysis systems have been designed in

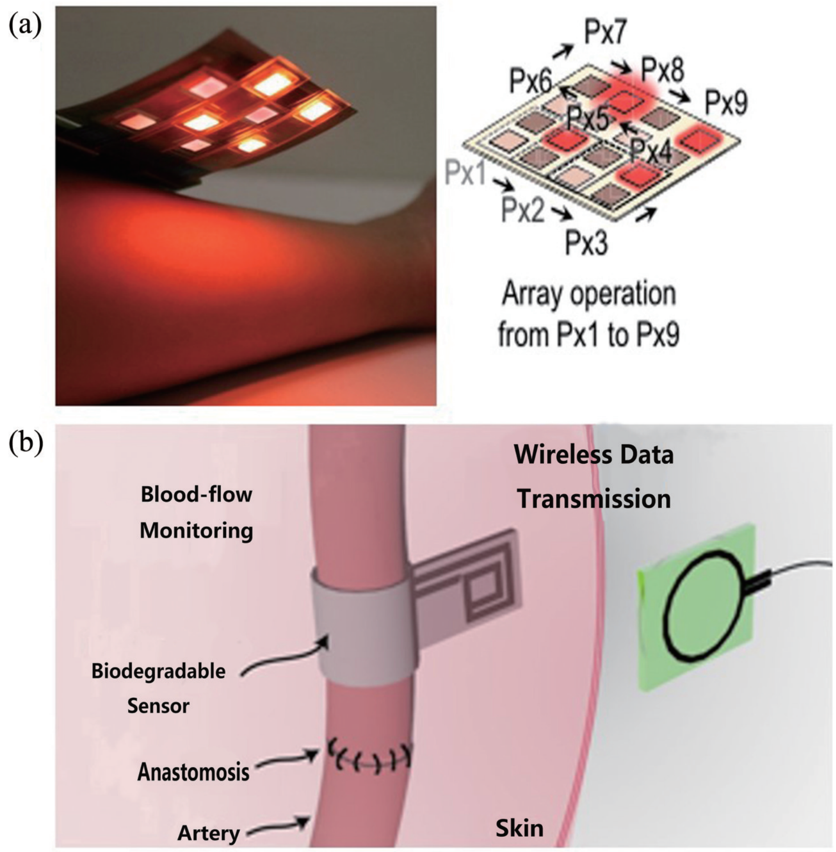

Figure 5 Blood sensors. (a) The new sensors, alternating arrays of printed light-emitting diodes and photodetectors, can detect blood oxygen levels in any part of the body. The sensor uses light-emitting diodes to emit red and near-infrared light, penetrating the skin and detecting the proportion of reflected light[48]; (b) The sensor made of biodegradable materials utilizes edge-field capacitance technology to monitor arterial blood and then transmits the data wirelessly[56].

recent years. For example, Bandodkar et al. developed a wireless electronic sensor with a biofuel cell for monitoring lactate, glucose, chloride, pH, and sweat rate (Figure 6a) [51]. This small and low-cost sensor could provide continuous monitoring of multiple components in sweat. The variation in sweat composition could be observed anywhere and at any time. Lei et al. reported stretchable, wearable, and modular multifunctional biosensors by MXene/Prussian blue (Ti_3C_2Tx/PB) composite (Figure 6b)[58]. The composite can be used for the durable and sensitive detection of biomarkers, such as glucose and lactate. In particular, they developed a unique modular design with three interfaces of solid, liquid, and gas that allow the sensor to measure multiple physicochemical signals with high sensitivity (35.3μA $mmol^{-1}cm^{-2}$ for glucose and 11.4μA $mmol^{-1}cm^{-2}$ for lactate), and great repeatability and stability. Smith et al. demonstrated a type of highly conductive and flexible cotton fiber sensor that is biocompatible and antibacterial[59]. The sensor shows high sensitivity and fast detection capability to the sweat pH in the range of 2.0 to 12.0. Recently, Yao et al. prepared an intelligent sweat analysis system, which is integrated with a micro-supercapacitor and self-powered module[60]. They demonstrated the system exhibiting the detection of accurate sweat signals and remote data sharing, through which the signals were sent to an individual mobile phone through wireless transmission technology. This method breaks the limitations of bio-enzyme sensors in measuring temperature and humidity. These devices will promote the concept of remote medicine for the pre-diagnosis of diseases, such as diabetes screening and kidney status detection.

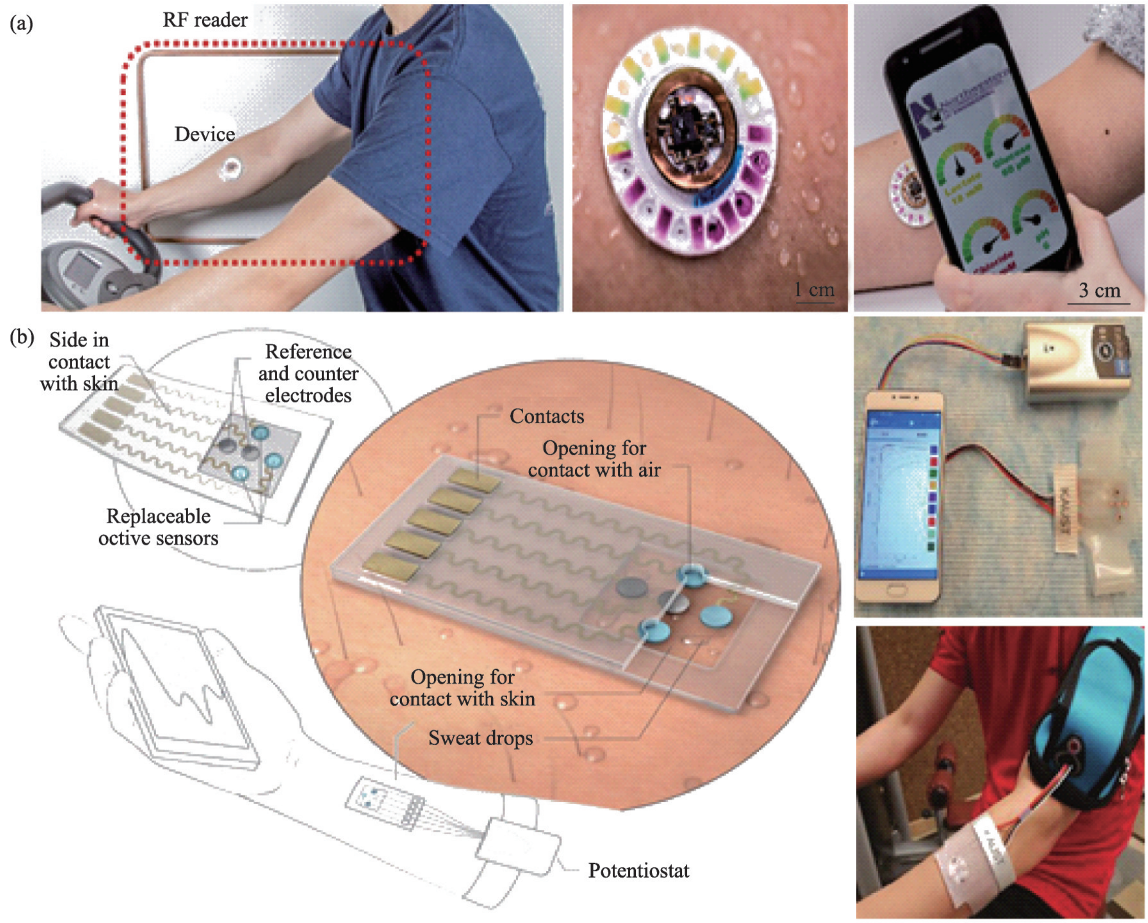

Figure 6 (a) The system of the wireless battery-free sweat sensor, the process of detecting during sweating, and the wireless transmission and analysis interface of sweat composition on the smart phone[57]; (b) Schematic diagram of the multi-functional sweat sensor. As shown in (b), the wearable monitoring film connects to an electrochemical analyzer and transmits data to smart phone through Bluetooth[58].

2.3.3 Respiratory and heart rate sensors

There are two ways to measure heart rate: photoplethysmography (PPG) photoelectric volume pulse wave and electrocardiogram (ECG) signal measurement. The method of PPG photoelectric volume wave uses pulsating changes in light transmittance in the blood to reflect heart rate. However, the accuracy of the method is affected by the influence of irregular exercise and sweat.

Measurement using the ECG signal patch requires several wired electrodes attached to the chest, ankle, and wrist for detection. It is a complex method and restricts physical movement. Conventional ECG signal collection cannot be conducted over a long working time; by contrast, flexible and wearable sensors show high sensitivity, fast response speed, great adhesion, optional stability, good portability, and comfort in heart-rate detection. Park et al. invented a self-powered ultra-flexible heart rate (HR) sensor by a patterned ultra-flexible organic solar cell, which can accurately monitor the heart rate with high signal-to-noise ratio in real-time (Figure 7a)[61]. The OPV and OECTs were integrated on the top of ultrathin polymer substrate. In the manufacturing of OPV, the nanopattern of ZnO maximizes the efficiency of OPV and weakens the reflection of incident light, such that the performance of sensor is not affected by the light angle. Meanwhile, it also exhibited excellent mechanical stability and durability. Wang et al. designed a stretchable optical HR sensing patch system with promising performance (Figure 7b)[62]. The device has been used in close contact with skin, displaying significant HR fluctuation frequency during intensive exercise. However, the resolution of the collected original waveform still needs improvement.

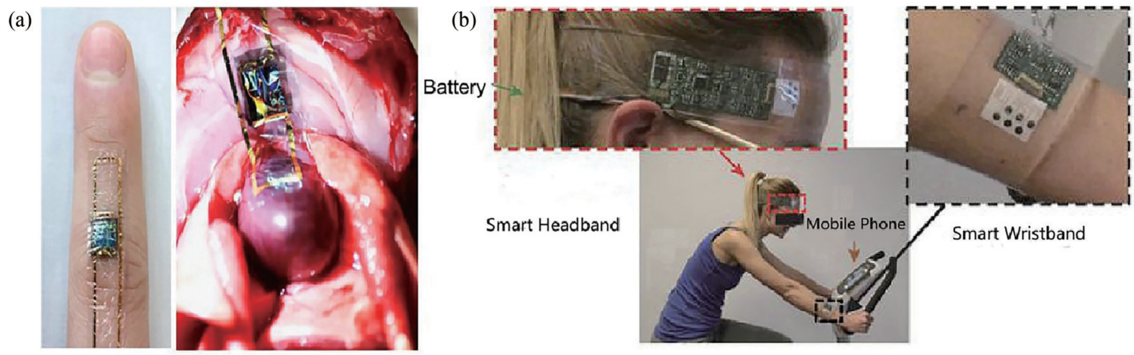

Figure 7 (a) The size of the self-powered wearable electronic sensor and the photography of this sensor attached to the heart of a rat for monitoring heart rate[61]; (b) The smart analysis system of real-time flexible sensor for monitoring physiological signals during exercise, including, and data collecting from the sensor[49].

Skin-inspired flexible sensors, such as electronic skin, are designed to mimic the human skin for pressure, strain, stretch, and temperature sensing. Real-time monitoring of the wrist pulse provides a convenient way for HR detection. Several research groups have fabricated electronic skins by organic semiconductors, inorganic nanowires, carbon nanotubes, graphene, metal nanowires, and microstructure conducting polymers[62–66]. Electronic skin could be attached to the wrist to detect the wrist pulse because of its high accuracy, sensitivity, and resolution in detecting tiny pressure. In our previous studies, we developed ultra-sensitive pressure sensors by micropatterned PDMS with carbon nanotube films[3]. The device presented high sensitivity and accuracy to the wrist pulse and demonstrated capability to distinguish the wrist pulse from persons with different body conditions.

3 VR technology for health-monitoring

The most prominent feature of VR is that it can provide users a sense of immersion. VR combines new applications with multi-field technologies, changing the service model of the industry and expanding the perceptual boundary. Currently, VR shows potential applications in the fields of computers, medicine, military, education, aerospace, and entertainment. For example, miniature VR goggles, ear-wearing equipment for panoramic sound, lightweight tactile feedback gloves, and digital smell interface have been studied and are likely to serve humanity in the near future[67]. According to the user experience, there are mainly three types of VR hardware equipment: (1) PC head-mounted device with high immersion. The drawbacks of this device are the limited portability and high system configuration, which make it more suitable for the enterprise user. (2) Portable and mobile VR, such as Google Cardboard. The advantage of this type of VR includes rich VR resources and low cost. (3) Hybrid and integrated VR system. This system integrates the processor and screen together for the function of display and calculation.

As shown in Figure 8, new VR applications for healthcare have been designed based on the rapid development of VR technology. The main themes for VR in the area of medicine are remote disease surveillance, rehabilitation training, and physical and mental monitoring.

3.1 VR for physiological monitoring

VR can be used in monitoring health signals by physiological sensors and immersive virtual scenes. A VR health-monitoring system contains a sensor unit for the detection of individual physiological signals, VR

Figure 8 The collection of VR devices for healthcare. Head-mounted VR[68]. Tactile VR devices[69]. VR surgery for newborns[70]. VR laparoscopy simulator[71]. VR ICU treatment for reducing patient pain[72]. VR-based treadmill for rehabilitation of patients with Parkinson's disease[73].

equipment for the visual interaction interface, and a software program. Physiological signals vary under different scenes. For example, heart rate and respiratory rate could be increased by exercise. Different states of body condition may be reflected by indicators of electrophysiological signals. EEG with different virtual scenes can reflect the concentration, relaxation, and mood of the participant[74]. If the user is equipped with a VR headset and EEG monitor to carry out activities, the system integrated software program records the effects of brain waves in real time. The user could freely adjust posture, and the physician could obtain a wide variety of EEG samples. VR enhances the communication between patient and physician, and enables a comprehensive understanding of patient information. VR devices provide a way to monitor health signals in different scenarios at anytime and anywhere.

3.2 VR for teletherapy

VR equipment is used for the remote diagnosis of disease or rehabilitation by vision therapy VR. Telemedicine surveillance with VR visual scene allows physicians to immerse themselves to practice clinic diagnosis and operation. Rasool et al. proposed to use 3D simulation and tactile sense interaction to compensate for a lack of cases. The virtual lesion modeling scene was used to simulate minimally invasive surgery[75]. De Mauro et al. have achieved an immersive surgery experience by the combination of tactile force simulator with VR neurosurgical microscopes. Similarly, Xia et al. presented a novel and low-cost approach for image-based virtual haptic venipuncture simulation, which used 2D actual photos with tactile feedback and real-time interaction between force feedback and a 3D operation screen (Figure 9)[76].

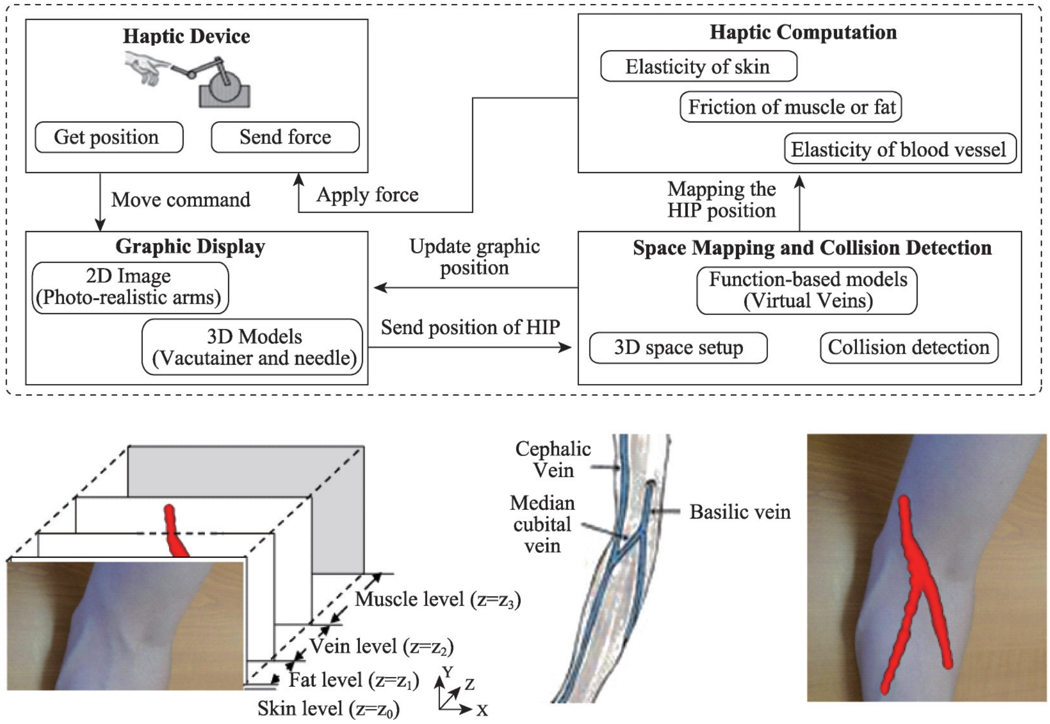

Figure 9 The haptics-based Virtual Reality training system for Venepuncture[77].

VR technology also has been used for the treatment of mental illness, such as anxiety disorders, traumatic and stress-related disorders (PTSD), obsessive-compulsive and related disorders (OCD), and schizophrenia spectrum and other psychiatric disorders. During treatment, the system makes use of computer graphics, physiological signal sensors, and visual imaging technology, which enable patients to immerse themselves in a scene provided by VR equipment to obtain perceptual experience and emotional response.

3.3 Rehabilitation training

VR could help rehabilitating patients in areas such as stress management, autism relief, and stroke treatment. For example, Powell et al. demonstrated the potential of VR to ameliorate pain and improve rehabilitation by building a system of gait rehabilitation[77]. The VR screen can adjust the patient step signal and then adjust the frequency of the scene switching and audio rhythm to alleviate the pain in the rehabilitation process. Moreover, VR can be integrated with multiple kinds of sensors for remote medicine. Marasco et al. put forward a system of motor control for prosthetic hands by VR[78]. In particular, this study combined the kinesthetic sense, intent, and vision to improve body movement control. These systems help physicians and patients to achieve fast remote detection. In brief, they have demonstrated the potential of disease cure and healthcare monitoring. Presently, an increasing number of VR products have been used in healthcare services. With the development of VR technology and flexible electronics, the medical industry will take on a new look in the near future.

4 Conclusions and outlook

We presented a comprehensive review on the recent advances of technologies and applications in the field of flexible healthcare sensors and VR healthcare devices. Several flexible functional materials and typical micro-manufacturing technology have been described. Besides sensor units, the flexible and wearable healthcare system also includes the power supply unit, integrated circuit for signal processing, and wireless communication units for data transfer. Therefore, the key will be investigating novel materials (e.g., flexible energy materials and soft semiconductors) and advanced manufacturing and integration techniques, not only for sensor units but also for all functional units of the flexible healthcare system.

Flexible healthcare sensor and VR technologies are considered to be revolutionary techniques for healthcare, enabling services such as remote disease diagnosis. The techniques will promote not only the revolution of the next medical instruments toward portability, wearability, remote use, and timeliness, but also the change in the diagnosis method in clinical practice. Recently, wearable health-monitoring was demonstrated by flexible healthcare sensors for telemedicine applications. Health-related physiological signals could be collected by flexible sensors and transmitted to a hospital and database for analysis. The role of the physician role is still crucial and irreplaceable, as patients need professional medical advice that can be generated by analyzing physiological signals and referring to the results of an algorithm. Typically, physiological signals vary widely from different parts of human body. Patients will obtain various physiological signals when the flexible healthcare sensors are worn on different parts of the body, which will make diagnosis difficult. VR technology provides an effective way to connect physicians with patients. Physicians could use this technology to ask patients to correct the placed position for flexible and wearable healthcare sensors. VR technology could be used to improve the accuracy of diagnosis by integrating the sensing system established via the flexible and wearable healthcare devices. Therefore, the combination of flexible and wearable healthcare sensor and VR technology will be a potential disruptive technology for healthcare.

References

1 Kim D H, Lu N, Ma R, Kim Y S, Kim R H, Wang S, Wu J, Won S M, Tao H, Islam A, Yu K J, Kim T I, Chowdhury R, Ying M, Xu L, Li M, Chung H J, Keum H, McCormick M, Liu P, Zhang Y W, Omenetto F G, Huang Y, Coleman T, Rogers J A. Epidermal electronics. Science, 2011, 333(6044): 838‒843
DOI:10.1126/science.1206157

2 Gao W, Emaminejad S, Nyein H Y Y, Challa S, Chen K, Peck A, Fahad H M, Ota H, Shiraki H, Kiriya D, Lien D H, Brooks G A, Davis R W, Javey A. Fully integrated wearable sensor arrays for multiplexed *in situ* perspiration analysis. Nature, 2016, 529(7587): 509‒514
DOI:10.1038/nature16521

3 Wang X W, Gu Y, Xiong Z P, Cui Z, Zhang T. Electronic skin: silk-molded flexible, ultrasensitive, and highly stable electronic skin for monitoring human physiological signals (adv. mater. 9/2014). Advanced Materials, 2014, 26(9): 1309
DOI:10.1002/adma.201470054

4 Sheridan C. Apple moves on health, drug developers shift into smart gear. Nature Biotechnology, 2014, 32(10): 965‒966
DOI:10.1038/nbt1014-965a

5 Zang Y P, Zhang F J, Di C A, Zhu D B. Advances of flexible pressure sensors toward artificial intelligence and health care applications. Materials Horizons, 2015, 2(2): 140‒156
DOI:10.1039/c4mh00147h

6 Zhao W X, Bhushan A, Santamaria A, Simon M, Davis C. Machine learning: A crucial tool for sensor design. Algorithms, 2008, 1(2): 130‒152
DOI:10.3390/a1020130

7 Vu C, Kim J. Human motion recognition by textile sensors based on machine learning algorithms. Sensors, 2018, 18(9): 3109
DOI:10.3390/s18093109

8 Shortliffe E H. The adolescence of AI in Medicine: Will the field come of age in the '90s? Artificial Intelligence in Medicine, 1993, 5(2): 93‒106

DOI:10.1016/0933-3657(93)90011-q

9 Horn W. AI in medicine on its way from knowledge-intensive to data-intensive systems. Artificial Intelligence in Medicine, 2001, 23(1): 5−12
DOI:10.1016/s0933-3657(01)00072-0

10 Mintz Y, Brodie R. Introduction to artificial intelligence in medicine. Minimally Invasive Therapy & Allied Technologies, 2019, 28(2): 73−81
DOI:10.1080/13645706.2019.1575882

11 Takei K, Honda W, Harada S, Arie T, Akita S. Toward flexible and wearable human-interactive health-monitoring devices. Advanced Healthcare Materials, 2015, 4(4): 487−500
DOI:10.1002/adhm.201400546

12 Zang Y P, Zhang F J, Di C A, Zhu D B. Advances of flexible pressure sensors toward artificial intelligence and health care applications. Materials Horizons, 2015, 2(2): 140−156
DOI:10.1039/c4mh00147h

13 Lou Z, Wang L L, Shen G Z. Recent advances in smart wearable sensing systems. Advanced Materials Technologies, 2018, 3(12): 1800444
DOI:10.1002/admt.201800444

14 Khan Y, Ostfeld A E, Lochner C M, Pierre A, A C. Monitoring of Vital Signs with Flexible and Wearable Medical Devices. Advanced Materials, 2016, 28(22): 4373-4395
DOI:10.1002/adma.201504366

15 Zhang T, Bai Y Y, Sun F Q. Recent advances in flexible self-healing materials and sensors. Scientia Sinica Informationis, 2018, 48(6): 650−669
DOI:10.1360/n112018-00117

16 Li T, Li Y, Zhang T. Materials, structures, and functions for flexible and stretchable biomimetic sensors. Accounts of Chemical Research, 2019, 52(2): 288−296
DOI:10.1021/acs.accounts.8b00497

17 Wang X W, Liu Z, Zhang T. Flexible sensing electronics for wearable/attachable health monitoring. Small, 2017, 13 (25): 1602790
DOI:10.1002/smll.201602790

18 Zeng K, Guo Q, Gao S, Wu D M, Fan H J, Yang G. Studies on organosoluble polyimides based on a series of new asymmetric and symmetric dianhydrides: Structure/solubility and thermal property relationships. Macromolecular Research, 2012, 20(1): 10−20
DOI:10.1007/s13233-012-0007-4

19 Sekitani T, Zschieschang U, Klauk H, Someya T. Flexible organic transistors and circuits with extreme bending stability. Nature Materials, 2010, 9(12): 1015−1022
DOI:10.1038/nmat2896

20 Nomura K, Ohta H, Takagi A, Kamiya T, Hirano M, Hosono H. Room-temperature fabrication of transparent flexible thin-film transistors using amorphous oxide semiconductors. Nature, 2004, 432(7016): 488−492
DOI:10.1038/nature03090

21 Kaltenbrunner M, Sekitani T, Reeder J, Yokota T, Kuribara K, Tokuhara T, Drack M, Schwödiauer R, Graz I, Bauer-Gogonea S, Bauer S, Someya T. An ultra-lightweight design for imperceptible plastic electronics. Nature, 2013, 499 (7459): 458−463
DOI:10.1038/nature12314

22 Lipomi D J, Vosgueritchian M, Tee B C K, Hellstrom S L, Lee J A, Fox C H, Bao Z N. Skin-like pressure and strain sensors based on transparent elastic films of carbon nanotubes. Nature Nanotechnology, 2011, 6(12): 788−792
DOI:10.1038/nnano.2011.184

23 Laukhina E, Pfattner R, Ferreras L R, Galli S, Mas-Torrent M, Masciocchi N, Laukhin V, Rovira C, Veciana J. Ultrasensitive piezoresistive all-organic flexible thin films. Advanced Materials, 2010, 22(9): 977−981
DOI:10.1002/adma.200902639

24 Gburek B, Wagner V. Influence of the semiconductor thickness on the charge carrier mobility in P3HT organic field-

effect transistors in top-gate architecture on flexible substrates. Organic Electronics, 2010, 11(5): 814–819
DOI:10.1016/j.orgel.2010.01.023

25 Harada S, Kanao K, Yamamoto Y, Arie T, Akita S, Takei K. Fully printed flexible fingerprint-like three-axis tactile and slip force and temperature sensors for artificial skin. ACS Nano, 2014, 8(12): 12851–12857
DOI:10.1021/nn506293y

26 Mannsfeld S C B, Tee B C K, Stoltenberg R M, Chen C V H H, Barman S, Muir B V O, Sokolov A N, Reese C, Bao Z N. Highly sensitive flexible pressure sensors with microstructured rubber dielectric layers. Nature Materials, 2010, 9 (10): 859–864
DOI:10.1038/nmat2834

27 Pan L J, Chortos A, Yu G H, Wang Y Q, Isaacson S, Allen R, Shi Y, Dauskardt R, Bao Z N. An ultra-sensitive resistive pressure sensor based on hollow-sphere microstructure induced elasticity in conducting polymer film. Nature Communications, 2014, 5: 3002
DOI:10.1038/ncomms4002

28 Wang S, Weil B D, Li Y B, Wang K X, Garnett E, Fan S H, Cui Y. Large-area free-standing ultrathin single-crystal silicon as processable materials. Nano Letters, 2013, 13(9): 4393–4398
DOI:10.1021/nl402230v

29 Wang D P, Wang Q Z, Wang Z M, Jiang H Y, Zhang Z, Liu P, Xu C, Gao L Y. Study on the long-term behaviour of glass fibre in the tensile stress field. Ceramics International, 2019, 45(9): 11578–11583
DOI:10.1016/j.ceramint.2019.03.028

30 Rathmell A R, Bergin S M, Hua Y L, Li Z Y, Wiley B J. The growth mechanism of copper nanowires and their properties in flexible, transparent conducting films. Advanced Materials, 2010, 22(32): 3558–3563
DOI:10.1002/adma.201000775

31 Baughman R H. Carbon nanotubes: the route toward applications. Science, 2002, 297(5582): 787–792
DOI:10.1126/science.1060928

32 Chung W H, Kim S H, Kim H S. Welding of silver nanowire networks via flash white light and UV-C irradiation for highly conductive and reliable transparent electrodes. Scientific Reports, 2016, 6: 32086
DOI:10.1038/srep32086

33 Wu H, Kong D S, Ruan Z C, Hsu P C, Wang S, Yu Z F, Carney T J, Hu L B, Fan S H, Cui Y. A transparent electrode based on a metal nanotrough network. Nature Nanotechnology, 2013, 8(6): 421–425
DOI:10.1038/nnano.2013.84

34 Gullapalli H, Vemuru V S M, Kumar A, Botello-Mendez A, Vajtai R, Terrones M, Nagarajaiah S, Ajayan P M. Flexible piezoelectric ZnO-paper nanocomposite strain sensor. Small, 2010, 6(15): 1641–1646
DOI:10.1002/smll.201000254

35 Xiao X, Yuan L Y, Zhong J W, Ding T P, Liu Y, Cai Z X, Rong Y G, Han H W, Zhou J, Wang Z L. High-strain sensors based on ZnO nanowire/polystyrene hybridized flexible films. Advanced Materials, 2011, 23(45): 5440–5444
DOI:10.1002/adma.201103406

36 Sun Y, Rogers J . Inorganic semiconductors for flexible electronics. Advanced Materials, 2007, 19(15): 1897–1916
DOI:10.1002/adma.200602223

37 Pajor-Świerzy A, Socha R, Pawłowski R, Warszyński P, Szczepanowicz K. Application of metallic inks based on nickel-silver core–shell nanoparticles for fabrication of conductive films. Nanotechnology, 2019, 30(22): 225301
DOI:10.1088/1361-6528/ab0467

38 Joseph A M, Nagendra B, Bhoje Gowd E, Surendran K P. Screen-printable electronic ink of ultrathin boron nitride nanosheets. ACS Omega, 2016, 1(6): 1220–1228
DOI:10.1021/acsomega.6b00242

39 Kwon Y J, Park Y, Lee W. Inkjet-printed organic transistors based on organic semiconductor/insulating polymer blends. Materials, 2016, 9(8): 650
DOI:10.3390/ma9080650

40 Zhang F, Tuck C, Hague R, He Y F, Saleh E, Li Y, Sturgess C, Wildman R. Inkjet printing of polyimide insulators for the 3D printing of dielectric materials for microelectronic applications. Journal of Applied Polymer Science, 2016, 133

(18): 11
DOI:10.1002/app.43361

41 Kim Y Y, Yang T Y, Suhonen R, Välimäki M, Maaninen T, Kemppainen A, Jeon N J, Seo J. Photovoltaic devices: gravure-printed flexible perovskite solar cells: toward roll-to-roll manufacturing (adv. sci. 7/2019). Advanced Science, 2019, 6(7): 1970044
DOI:10.1002/advs.201970044

42 Ferri J, Perez Fuster C, Llinares Llopis R, Moreno J, Garcia-Breijo E. Integration of a 2D touch sensor with an electroluminescent display by using a screen-printing technology on textile substrate. Sensors, 2018, 18(10): 3313
DOI:10.3390/s18103313

43 Khan S, Ali S, Bermak A. Recent developments in printing flexible and wearable sensing electronics for healthcare applications. Sensors, 2019, 19(5): 1230
DOI:10.3390/s19051230

44 Jeffries A M, Mamidanna A, Ding L, Hildreth O J, Bertoni M I. Low-temperature drop-on-demand reactive silver inks for solar cell front-grid metallization. IEEE Journal of Photovoltaics, 2017, 7(1): 37−43
DOI:10.1109/jphotov.2016.2621351

45 Uzum A, Kanda H, Ito S. Perovskite/crystalline silicon tandem solar cells fabricated by non-vacuum-process. In: 2015 IEEE 42nd Photovoltaic Specialist Conference (PVSC). New Orleans, LA, New York, USA, IEEE, 2015
DOI:10.1109/pvsc.2015.7355659

46 Yamamoto Y, Harada S, Yamamoto D, Honda W, Arie T, Akita S, Takei K. Printed multifunctional flexible device with an integrated motion sensor for health care monitoring. Science Advances, 2016, 2(11): e1601473
DOI:10.1126/sciadv.1601473

47 Guo R, Yao S Y, Sun X Y, Liu J. Semi-liquid metal and adhesion-selection enabled rolling and transfer (SMART) printing: A general method towards fast fabrication of flexible electronics. Science China Materials, 2019, 62(7): 982−994
DOI:10.1007/s40843-018-9400-2

48 Khan Y, Han D, Pierre A, Ting J, Wang X C, Lochner C M, Bovo G, Yaacobi-Gross N, Newsome C, Wilson R, Arias A C. A flexible organic reflectance oximeter array. Proceedings of the National Academy of Sciences, 2018, 115(47): E11015−E11024
DOI:10.1073/pnas.1813053115

49 Gao W, Emaminejad S, Nyein H Y Y, Challa S, Chen K, Peck A, Fahad H M, Ota H, Shiraki H, Kiriya D, Lien D H, Brooks G A, Davis R W, Javey A. Fully integrated wearable sensor arrays for multiplexed *in situ* perspiration analysis. Nature, 2016, 529(7587): 509−514
DOI:10.1038/nature16521

50 Huang K H, Tan F, Wang T D, Yang Y J. A highly sensitive pressure-sensing array for blood pressure estimation assisted by machine-learning techniques. Sensors, 2019, 19(4): 848
DOI:10.3390/s19040848

51 Tao X L, Liao S L, Wang S Q, Wu D, Wang Y P. Body compatible thermometer based on green electrolytes. ACS Sensors, 2018, 3(7): 1338−1346
DOI:10.1021/acssensors.8b00249

52 Bihar E, Deng Y X, Miyake T, Saadaoui M, Malliaras G G, Rolandi M. A Disposable paper Breathalyzer with an alcohol sensing organic electrochemical transistor. Scientific Reports, 2016, 6: 27582
DOI:10.1038/srep27582

53 Oh S Y, Hong S Y, Jeong Y R, Yun J, Park H, Jin S W, Lee G, Oh J H, Lee H, Lee S S, Ha J S. Skin-attachable, stretchable electrochemical sweat sensor for glucose and ph detection. ACS Applied Materials & Interfaces, 2018, 10 (16): 13729−13740
DOI:10.1021/acsami.8b03342

54 An X, Stylios G. A hybrid textile electrode for electrocardiogram (ECG) measurement and motion tracking. Materials 2018, 11(10): 1887
DOI:10.3390/ma11101887

55 Sekine T, Sugano R, Tashiro T, Sato J, Takeda Y, Matsui H, Kumaki D, Domingues dos Santos F, Miyabo A, Tokito S. Author correction: fully printed wearable vital sensor for human pulse rate monitoring using ferroelectric polymer. Scientific Reports, 2018, 8: 6359
DOI:10.1038/s41598-018-22746-3
56 Boutry C M, Beker L, Kaizawa Y, Vassos C, Tran H, Hinckley A C, Pfattner R, Niu S M, Li J H, Claverie J, Wang Z, Chang J, Fox P M, Bao Z N. Biodegradable and flexible arterial-pulse sensor for the wireless monitoring of blood flow. Nature Biomedical Engineering, 2019, 3(1): 47‒57
DOI:10.1038/s41551-018-0336-5
57 Bandodkar A J, Gutruf P, Choi J, Lee K, Sekine Y, Reeder J T, Jeang W J, Aranyosi A J, Lee S P, Model J B, Ghaffari R, Su C J, Leshock J P, Ray T, Verrillo A, Thomas K, Krishnamurthi V, Han S, Kim J, Krishnan S, Hang T, Rogers J A. Battery-free, skin-interfaced microfluidic/electronic systems for simultaneous electrochemical, colorimetric, and volumetric analysis of sweat. Science Advances, 2019, 5(1): eaav3294
DOI:10.1126/sciadv.aav3294
58 Lei Y J, Zhao W L, Zhang Y Z, Jiang Q, He J H, Baeumner A J, Wolfbeis O S, Wang Z L, Salama K N, Alshareef H N. A MXene-based wearable biosensor system for high-performance *in vitro* perspiration analysis. Small, 2019, 15(19): 1901190
DOI:10.1002/smll.201901190
59 Smith R E, Totti S, Velliou E, Campagnolo P, Hingley-Wilson S M, Ward N I, Varcoe J R, Crean C. Development of a novel highly conductive and flexible cotton yarn for wearable pH sensor technology. Sensors and Actuators B: Chemical, 2019, 287: 338‒345
DOI:10.1016/j.snb.2019.01.088
60 Lu Y, Jiang K, Chen D, Shen G Z. Wearable sweat monitoring system with integrated micro-supercapacitors. Nano Energy, 2019, 58: 624‒632
DOI:10.1016/j.nanoen.2019.01.084
61 Park S, Heo S W, Lee W, Inoue D, Jiang Z, Yu K, Jinno H, Hashizume D, Sekino M, Yokota T, Fukuda K, Tajima K, Someya T. Self-powered ultra-flexible electronics via nano-grating-patterned organic photovoltaics. Nature, 2018, 561 (7724): 516‒521
DOI:10.1038/s41586-018-0536-x
62 Wang N X, Yang A N, Fu Y, Li Y Z, Yan F. Functionalized organic thin film transistors for biosensing. Accounts of Chemical Research, 2019, 52(2): 277‒287
DOI:10.1021/acs.accounts.8b00448
63 Liu Z, Xu J, Chen D, Shen G Z. Flexible electronics based on inorganic nanowires. Chemical Society Reviews, 2015, 44 (1): 161‒192
DOI:10.1039/c4cs00116h
64 An R, Zhang B M, Han L L, Wang X D, Zhang Y L, Shi L Y, Ran R. Strain-sensitivity conductive MWCNTs composite hydrogel for wearable device and near-infrared photosensor. Journal of Materials Science, 2019, 54(11): 8515‒8530
DOI:10.1007/s10853-019-03438-3
65 Xu M X, Li F, Zhang Z Y, Shen T, Zhang Q, Qi J J. Stretchable and multifunctional strain sensors based on 3D graphene foams for active and adaptive tactile imaging. Science China Materials, 2019, 62(4): 555‒565
DOI:10.1007/s40843-018-9348-8
66 Park S H, Park J, Park H N, Park H M, Song J Y. Flexible galvanic skin response sensor based on vertically aligned silver nanowires. Sensors and Actuators B: Chemical, 2018, 273: 804‒808
DOI:10.1016/j.snb.2018.06.125
67 Cao F. Overview of research and development of VR technology at home and abroad. science and technology information, 2019, 5 (in Chinese)
DOI: 10.3969/j.issn.1001-8972.2019.05.010
68 Benham S, Kang M, Grampurohit N. Immersive virtual reality for the management of pain in community-dwelling older adults. OTJR: Occupation, Participation and Health, 2019, 39(2): 90‒96
DOI:10.1177/1539449218817291

69 Gugenheimer J, Dobbelstein D, Winkler C, Haas G, Rukzio E. FaceTouch. In: Proceedings of the 2016 CHI Conference Extended Abstracts on Human Factors in Computing Systems. Santa Clara, California, USA, ACM Press, 2016 DOI:10.1145/2851581.2890242

70 Vega-Medina L, Perez-Gutierrez B, Tibamoso G, Uribe-Quevedo A, Jaimes N. VR central venous access simulation system for newborns. In: 2014 IEEE Virtual Reality (VR). Minneapolis, MN, USA, IEEE, 2014 DOI:10.1109/vr.2014.6802081

71 Wang F, Burdet E, Vuillemin R, Bleuler H. Knot-tying with visual and force feedback for VR laparoscopic training. In: 2005 IEEE Engineering in Medicine and Biology 27th Annual Conference. Shanghai, China, IEEE, 2005 DOI:10.1109/iembs.2005.1615801

72 Gerber S M, Jeitziner M M, Wyss P, Chesham A, Urwyler P, Müri R M, Jakob S M, Nef T. Visuo-acoustic stimulation that helps you to relax: A virtual reality setup for patients in the intensive care unit. Scientific Reports, 2017, 7: 13228 DOI:10.1038/s41598-017-13153-1

73 Park H S, Yoon J W, Kim J, Iseki K, Hallett M. Development of a VR-based treadmill control interface for gait assessment of patients with Parkinson's disease. In: 2011 IEEE International Conference on Rehabilitation Robotics. Zurich, New York, USA, IEEE, 2011 DOI:10.1109/icorr.2011.5975463

74 Yang X Z, Ren Y Q. Development of virtual reality and EEG linkage system and exploration of its educational research function. Distance Education Journal, 2019, 37(1): 45−52 (in Chinese)

75 Rasool S, Sourin A, Xia P, Weng B, Kagda F. Towards hand-eye coordination training in virtual knee arthroscopy. 2013 DOI:10.1145/2503713.2503715.

76 Xia P, Sourin A. Design and implementation of a haptics-based virtual venepuncture simulation and training system. 2012

77 Powell W, Powell V, Simmonds M. Virtual reality for gait rehabilitation-promises, proofs and preferences. In: Proceedings of the 7th International Conference on PErvasive Technologies Related to Assistive Environments. Rhodes, Greece, ACM Press, 2014 DOI:10.1145/2674396.2674450

78 Paul D M, Jacqueline S H, Jon W S, Courtney E S, Beth M O. Illusory movement perception improves motor control for prosthetic hands. Science Translational Medicine, 2018, 10(432): eaao6990