Nano Materials Science 6 (2024) 263–283

Contents lists available at ScienceDirect

Nano Materials Science

journal homepage: www.keaipublishing.com/cn/journals/nano-materials-science/

Nanomaterial-assisted wearable glucose biosensors for noninvasive real-time monitoring: Pioneering point-of-care and beyond

Moein Safarkhani [a,1], Abdullah Aldhaher [b,1], Golnaz Heidari [c], Ehsan Nazarzadeh Zare [d], Majid Ebrahimi Warkiani [e,*], Omid Akhavan [f], YunSuk Huh [a,**], Navid Rabiee [f,g,h,***]

[a] NanoBio High-Tech Materials Research Center, Department of Biological Sciences and Bioengineering, Inha University, Incheon, 22212, Republic of Korea
[b] Department of Chemistry, Sharif University of Technology, Tehran, Iran
[c] School of Natural Sciences, Massey University, Private Bag 11 222, Palmerston North, 4410, New Zealand
[d] School of Chemistry, Damghan University, Damghan, 36716-45667, Iran
[e] School of Biomedical Engineering, University of Technology Sydney, Sydney, NSW, 2007, Australia
[f] Department of Physics, Sharif University of Technology, P.O. Box 11155-9161, Tehran, Iran
[g] Centre for Molecular Medicine and Innovative Therapeutics, Murdoch University, Perth, WA 6150, Australia
[h] School of Engineering, Macquarie University, Sydney, New South Wales, 2109, Australia

ARTICLE INFO

Keywords:
Glucose sensor
Biosensor
Wearable devices
Noninvasive
Real-time monitoring

ABSTRACT

This review explores glucose monitoring and management strategies, emphasizing the need for reliable and user-friendly wearable sensors that are the next generation of sensors for continuous glucose detection. In addition, examines key strategies for designing glucose sensors that are multi-functional, reliable, and cost-effective in a variety of contexts. The unique features of effective diabetes management technology are highlighted, with a focus on using nano/biosensor devices that can quickly and accurately detect glucose levels in the blood, improving patient treatment and control of potential diabetes-related infections. The potential of next-generation wearable and touch-sensitive nano biomedical sensor engineering designs for providing full control in assessing implantable, continuous glucose monitoring is also explored. The challenges of standardizing drug or insulin delivery doses, low-cost, real-time detection of increased blood sugar levels in diabetics, and early digital health awareness controls for the adverse effects of injectable medication are identified as unmet needs. Also, the market for biosensors is expected to expand significantly due to the rising need for portable diagnostic equipment and an ever-increasing diabetic population. The paper concludes by emphasizing the need for further research and development of glucose biosensors to meet the stringent requirements for sensitivity and specificity imposed by clinical diagnostics while being cost-effective, stable, and durable.

1. Introduction

Diabetes is a chronic illness that is growing more common, especially in poorer countries is a prevalent issue that has an impact on a sizable section of the world's population [1,2]. It is distinguished by abnormal blood glucose levels, which may result in side effects including heart attack, blindness, nerve damage, and renal failure [3]. Serious health problems and, eventually, death, can result from diabetes. The main cause of diabetes is high blood sugar levels, which issues with insulin production or use in the body can cause. Diabetes can be classified into two basic categories: type 1, a condition where the body does not generate enough insulin, and type 2, where the body develops a resistance to the effects of insulin. Both types can cause problems with the way the body processes carbohydrates, fats, and proteins and can affect the effectiveness of insulin in the body's tissues. The prevalence of diabetes is a significant concern, with approximately 382 million people currently affected. The World Health Organization and International Diabetes Federation predict that during the next 25 years, will rise to 592 million [4,5]. To address the significant impact of diabetes on individuals, society, and the economy, it is important to develop early

* Corresponding author.
** Corresponding author.
*** Corresponding author. School of Engineering, Macquarie University, Sydney, New South Wales, 2109, Australia.
E-mail addresses: majid.warkiani@uts.edu.au (M.E. Warkiani), yunsuk.huh@inha.ac.kr (Y. Huh), nrabiee94@gmail.com (N. Rabiee).
[1] These authors contributed equally to this article.

https://doi.org/10.1016/j.nanoms.2023.11.009
Received 22 September 2023; Accepted 23 November 2023
Available online 15 December 2023

detection devices that are both effective and well-tolerated. Technology such as nanosensor devices which can automatically take and analyze samples and have defined signaling readouts, which may help to reduce the mortality and disability rates associated with diabetes. These advanced devices may be particularly useful in detecting diabetes early on and enabling timely interventions to manage the condition [4].

Diabetes and its complications are complex conditions influenced by genetic and environmental factors. In the past, researchers observed that some people with diabetes were more likely to develop complications than others, even if they seemed similar regarding their clinical features and glucose control. Further investigations of families with and without diabetes revealed that the latter were more likely to experience microvascular and macrovascular problems than the former. These studies provide evidence that genetics has a role in diabetes and the issues that accompany it. However, the inability of linkage analysis to identify loci with large effects, the tendency of candidate gene studies to produce false positives, and the lack of large enough sample sizes in early genome-wide association studies to detect modest genetic effects that are common in complex traits all contributed to the difficulty of identifying specific genetic factors in early genetic studies. Additionally, the process of identifying genetic factors was further complicated by the fact that studying complications of diabetes, which have multiple risk factors and unclear disease progression, is challenging [6–8].

2. Biosensing of glucose

Managing diabetes, a chronic condition affecting a huge percentage of the world's population, requires constant monitoring of blood glucose levels and prompt diagnosis of any abnormalities. Researchers have developed various approaches to create glucose nano/biosensors that can accurately signal and quickly monitor blood glucose levels through the use of different transducers such as optical fluorescence, chemiluminescence, frequency, and electrical signals. Many different glucose testing techniques have been created because of how important it is to detect glucose in body fluids while dealing with diabetes. Developing detecting tests for the timely identification of blood glucose levels is crucial for lowering death rates and learning more about the factors that lead to diabetes. Much emphasis in the study is being placed on the development of glucose nano-biosensors that are both efficient and affordable for use in the earlier detection and mitigation of diabetes [9].

The most recent glucose sensor is based on Michael addition and Schiff base reactions to generate a coating of tannic acid-3-aminopropyltriethoxysilane (TA-APTES) on activated carbon cloth (aCC). To create AuNPs/TA-APTES/aCC electrodes, *in situ* reductions of gold nanoparticles (AuNPs) were additionally employed. The sensor is formed by immobilizing glucose oxidases (GOx) on the surface of the AuNPs (Fig. 1A). The resultant GOx AuNPs/TA-APTES/aCC sensor offers several advantages over traditional glucose sensors. Its unique design, combined with the use of nanomaterials, enhances sensitivity, leading to quicker responses and lowered limits for detection. Some of the sensor's exceptional applicability is shown in Fig. 1B–E and reported data disclosed that the performance has been maintained even in complex biofluids, such as sweat. For instance, they assessed the cyclic voltammetry response of prepared sensors in the presence of 1 mM glucose with various scan rates and under different atmospheres. Prepared sensors' flexibility makes it ideal for skin-mounted applications, which could significantly improve glucose level monitoring in patients with diabetes or other chronic conditions that require continuous monitoring. This research introduces a promising new glucose-sensing approach that could ultimately result in more accurate and convenient monitoring for patients [10]. Another research describes the creation of a new type of nanofiber (NFs) that can be adjusted in size, made from copper oxide (CuO) and nickel oxide (NiO), using a method called coaxial electrospinning and calcination. The resulting NFs have a high surface area, making them suitable for catalytic applications. Additionally, the interface between CuO and NiO improves their electrocatalytic performance. These NFs show promising electrocatalytic characteristics for glucose oxidation, with a high sensitivity of 1324.17 μA mM^{-1} cm^{-2} and a wide linear range from 1 to 10,000 μM whenever the ratio of CuO to NiO is 0.4. It was shown that these NFs were successful in monitoring glucose levels in actual blood samples, which makes them perceived as competent for use in biomedical purposes [11]. Therefore, by changing the nanomaterial substrate and changing the detection method, it would be possible to adjust the detection mechanisms and also possible interferences.

2.1. Glucose monitoring by piezoelectric devices

Piezoelectric sensors are a type of device that uses targeted biomolecules and a piezoelectric component, like quartz, to detect changes in resonance frequency. These changes occur due to the interaction between the oscillating crystal and the biomolecules under specific conditions. Piezoelectricity, which refers to a material's capacity to produce a current when it is exposed to mechanical stress, is what is used in the manufacturing process of these sensors. They can be made using both surface and bulk acoustic waves. By monitoring mass variations in response to fluctuations in the crystal's oscillation frequency, biomolecules that have been absorbed or bonded to the sensor might well be identified [12,13]. Piezoelectric devices are commonly fabricated by polymers like polylactic acids and polyvinylidene fluoride and anisotropic crystals such as zinc oxide, aluminum nitride, aluminum phosphate (berlinite), and quartz. Due to the high importance of compounds biocompatibility for designing biosensors, especially glucose, lots of researchers are trying to design bio-friendly and lead-free sensors. Piezoelectric Immunosensors are devices that use antigens or antibodies as biorecognition moiety. The binding of the analyte to these elements on the surface of the piezoelectric compounds leads to measurable oscillation frequency change. MIP-based (Molecularly Imprinted Polymer) Piezoelectric Sensors have an ability of high sensitivity and selectivity towards target molecules (glucose) because these synthetic polymers can be equipped with special recognition sites. The promising features of nanomaterials made them prime candidates for the design and development of non-invasive, biocompatible, biodegradable, cost-effective, and sensitive monitoring devices. The piezoelectric responses can be enhanced by incorporating the nanomaterials in the piezoelectric biosensors [14,15].

A unique sort of glucose-monitoring wearable gadget has been developed by researchers, it is fully flexible and powered by the user's own glucose, meaning it does not require an external power source. The device integrates two diverse types of flexible electronics: a biofuel cell and a circuit-board decal made from biocompatible microbial nanocellulose. Together, the LED indication the glucose sensor, and the enzymatic glucose fuel cell could make up a proof-of-concept device. It is thin and lightweight, measuring only a few square centimeters and weighing less than 40 mg. The device continuously lights up an LED when the glucose level is present, it is a promising option for low-cost applications that need clear path detection of glucose, and it could identify glucose at a broad range of concentrations in various industries such as medicine, agriculture, husbandry, and food and beverage [16].

A unique wearable sensor that could continually monitor sweat pH concentrations was recently disclosed in a research study. The device comprises a flexible microbalance with piezoelectric membranes made of Aluminum Nitride and equipped with hydrogels that are pH sensitive. The researchers created various samples with different membrane radiuses and tested them using laser Doppler vibrometer in different buffer solutions. The team chose the smallest sample, which had a radius of 300 μm since it showed the highest pH sensitivity with a responsivity of 12 kHz/pH. They subjected this sample to further testing in artificial sweat solutions, where it proved capable of detecting pH changes in sweat. This marks a new type of pH sensor that can be worn on the body and is useful in identifying pathological or physiological changes in the body by monitoring sweat pH levels. This sensor is flexible, gravimetric, and

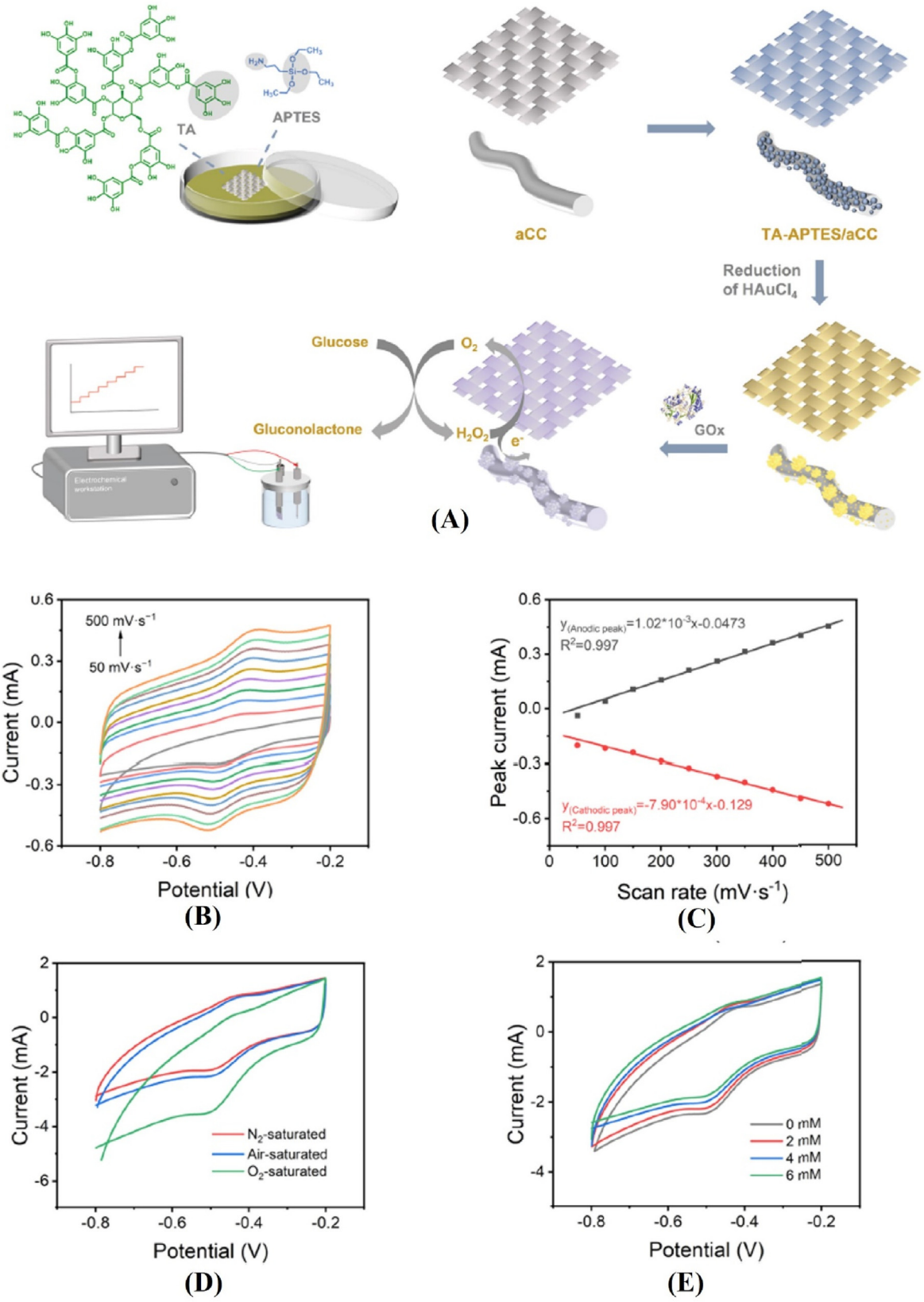

Fig. 1. **(A)** The steps involved in making a GOx/AuNPs/TA-APTES/aCC biosensor. **(B)** Sensor's CV response curves in the presence of 1 mM glucose, with a variety of scan rates (50–500 $mV{\cdot}s^{-1}$), **(C)** Scanning rate vs anodic/cathodic peak plots, **(D)** The constructed sensor's CV response curves in 1 mM glucose-containing PBS solution under nitrogen, air, and oxygen saturation. **(E)** Sensor's CV response curves to varying glucose concentrations in air-saturated PBS. Reproduced (reprinted) with permission from Ref. [10].

compliant, indicating its potential application in the biological and material sciences beyond the wearable device domain [17,18]. A novel closed-loop system that detects and adjusts blood glucose levels in real time without the need for blood analysis or insulin injection has been developed. This self-powered system is powered by the body's own motion and provides immediate treatment for metabolic diseases. It comprises a brain stimulator, a micro-control unit, an energy harvester, and an active blood glucose sensor. As the body moves, the glucose sensor, which is composed of ZnO nanowire arrays and enzymes, creates piezoelectric voltage. This voltage acts as a glucose detection signal. The body's mechanical energy is converted into electricity by the energy harvester, which is a piezoelectric ceramic device. This electricity is then used to energize the entire system. In the event that inappropriate blood glucose levels are identified, the micro-control device will send brain stimulation pulses to the dorsomedial region of the ventromedial hypothalamus (VMHdm). These pulses will cause a rise in blood glucose levels. The brain stimulator was able to raise blood glucose levels by 39 % within 10 min in mouse samples. Brain-machine interfaces for metabolic illness precision medicine are advanced by this self-powered closed-loop device, which also makes physiological findings more accessible [19]. A novel approach has been developed to detect glucose oxidase (GOD) activity in *Aspergillus n*iger (*A. niger*) spores using a piezoelectric sensor (PIS). As this process makes it possible to produce gluconic acid utilizing *A niger* spores as biocatalysts, it has generated considerable excitement in the food business. The PIS method involves detecting GOD activity by measuring real-time frequency shift changes recorded by the device resulting from the catalysis of β-D-glucose to gluconic acid by GOD. The method provides kinetic parameters, recoveries, and optimal GOD activity in *A. niger* spores under different conditions. This PIS methodology is more accurate, quicker, and more convenient than the conventional approaches, and it does not call for any extra chemicals to be used. The discovery of new GOD biocatalysts is one of the many potential applications of this method [20].

By utilizing the piezo-enzymatic-reaction pairing effect of GOx@ZnO nanowires, the device generates a piezoelectric signal that carries information about glucose levels. The nanowires in the ZnO nanowire arrays are evenly dispersed across the substrate and have an average diameter of 160 nm, as shown by scanning electron microscopy. No external electrical source is required for this system, as the piezoelectric voltage serves as both the power source and the biosensing signal. That has been implanted in mice to detect blood glucose levels, demonstrating its potential for diabetes prevention and treatment. These findings present a new approach to diabetes management [21].

2.2. Glucose monitoring by electrochemical devices

Electrochemical biosensors are devices that use an electrode surface to detect changes in the concentration of specific substances, like glucose, through the production of electrical current during a reduction-oxidation (redox) reaction. The strength and type of electrical signal generated by these sensors are dependent on their electrochemical properties, such as conductivity, current, impedance, and potential [22].

In 1962, a report by Clark and Lyons introduced electrochemical biosensors, which used an enzyme-based electrode to detect glucose. On an oxygen electrode, the glucose oxidase enzyme was confined behind a semipermeable dialysis membrane. In 1970, Clark was granted a patent for his invention, which was a method of transforming electroactive substrates into electroactive compounds that made use of enzymes. This system had not one but two distinct electrode configurations. In the existence of contaminating chemicals, the substrate was converted into an electroactive material by enzymes housed in a thin capillary layer across the membrane and the electrode. The secondary electrode system was particularly susceptible to contaminants in the samples. By deducting the current recorded by the initial electrode system from the observational studies by the secondary electrode system, Clark's technology was able to accurately detect glucose levels. This innovative method marked a significant advancement in the biosensor technology [23]. During the 1970s, the Yellow Springs Instrument Company was the first to develop a commercial glucose analyzer utilizing electrochemical technology, known as the YSI 23 A biosensor. The system used glucose and glucose oxidase in entire blood samples to create hydrogen peroxide, which was then detected by amperometric method. Hydrogen peroxide production was linearly related to glucose concentration. To ensure accurate glucose level measurement, the YSI 23 A biosensor employed a two-membrane system, allowing glucose molecules to penetrate and reach the enzyme layer while blocking out larger substances such as enzymes and proteins to reduce interference and improve device accuracy. Finally, amperometry was used to identify the hydrogen peroxide created throughout the reaction on the platinum electrode surface. This was the very first commercial use of biosensor technology for glucose monitoring.

The introduction of electrochemical glucose biosensors has brought about a sea change in the way diabetes is managed by making it possible to check one's blood glucose levels in a method that is less time-consuming and more discreet. The first commercially available glucose biosensor, the 23 A sensor probe, was introduced in 1975 but was costly and susceptible to interference due to its platinum electrode and high voltage. Electrochemical biosensors evolved as an area to solve these issues, with the goals of enhanced performance, smaller devices, and lower costs. The second generation of electrochemical glucose biosensors integrated various technologies such as surface chemistry, screen-printing, and semiconductor integration. This facilitated rapid electron transport from the enzyme to the electrode, using synthetic electron acceptors like redox couples or mediators, leading to decreased interference and greater sensitivity to glucose. In 1984, scientists announced the development of the earliest mediated amperometric biosensor detecting glucose, and screen-printing was used to create disposable and miniaturized electrodes for amperometric biosensors. These innovations led to the launch of the first home-use blood glucose biosensor, ExacTech by MediSense, in 1987. Amperometric biosensors and consumer items for personal use have come a long way since the introduction of mediators and screen-printed electrodes [24–26].

Researchers have made great strides in developing third-generation glucose biosensors in an effort to address the shortcomings of mediator-based devices. One promising approach to achieving direct communication between the electrode and enzyme is the use of long, flexible polymers with a high density of linked osmium-complex electron relays, such as poly (4-vinylpyridine) or poly (vinylimidazole). These polymers can form a 3D network with the enzyme, bringing the enzyme closer to the polymer matrix's redox centers. Another technique involves modifying the enzyme itself through carbodiimide chemistry, such as by attaching ferrocenecarboxylic acid to the glucose oxidase, to improve the electrical communication between the enzyme's redox center and the electrodes. Additionally, modifying the redox center of glucose oxidase, flavin adenine dinucleotide (FAD), with ferrocene and reconstructing the apo-enzyme with the ferrocene-modified FAD is another method that has been employed. These recent advancements in glucose biosensor technology hold great promise for the development of more effective and efficient methods for monitoring blood glucose levels [27–29].

2.2.1. Nickel-based nanoarchitectures

The use of transition metal elements such as nickel in chemical reactions in recent years has become increasingly popular due to their ability to promote the oxidation of organic compounds. In particular, nickel nanoparticles have shown promise in the catalysis of glucose by directly oxidizing the molecule under alkaline conditions. In spite of nickel's notoriety as a transition metal with a long history of use in catalytic chemistry, the metal has its limits when it comes to glucose catalysis. They include weak mechanical strength and electrical conductivity as well as a propensity to clump together over time and vulnerability to environmental factors. However, despite these challenges, Ni-based materials have been widely employed in glucose catalysis. Previous studies have shown that nickel nanoparticles can be used to

catalyze the direct oxidation of glucose under alkaline conditions. Various types of Ni-based materials have been utilized, including Ni, NiO, $Ni(OH)_2$, Ni_3N, Ni_2P, $Ni_3(PO_4)_2$, Ni-MOF, and Ni alloys, Ni may partly electrooxidize organic materials in alkaline circumstances, as shown by Fleishman et al. Regardless of the material's initial state, an electron transfer happens between the Ni^{3+}/Ni^{2+} redox pair on the surface of Ni-based materials when glucose is electrooxidized. This happens during the electrooxidation process. These results may pave the way for the creation of more efficient catalysts for the oxidation of glucose [30,31].

The treatment of diabetes relies heavily on regular glucose monitoring, and scientists have been striving to develop novel technologies to improve the convenience and accuracy of glucose monitoring. One promising technology is a core-shell hierarchical three-dimensional, structure based on nickel-copper-layered double hydroxide (Ni–Cu LDH) that has been developed for non-invasive glucose detection. Ni–Cu LDH shells with $Cu(OH)_2$ nanowire backbones are grown on a Cu foam substrate (Ni–Cu LDH@$Cu(OH)_2$ NWs/CuF), forming a morchella-like structure. By varying the mole ratio of Ni and Cu, an electrode with a fast response/recovery time, good anti-interference and reproducibility properties, and resistance to bending has been optimized (Ni:Cu = 4:2). This optimized electrode has been utilized to develop a sensitive device by integrating it with counter and reference electrodes in a micro-cavity made of polydimethylsiloxane (PDMS). The device boasts a low detection limit of 1.3 μM, a broad linear range of 0.006–1.6 μM, and a high sensitivity of 7.08 μA/cm^2. Additionally, it is reliable and has been put to application in the accurate measurement of glucose concentrations in human serum. Due to its great stability, selectivity, and sensitivity, the Morchella-shaped Ni–Cu LDH hierarchical structure has been shown to be a viable material for enzymeless glucose detection. Constant glucose measurement with this sort of sensor may provide a less time-consuming and more reliable option for diabetics [32].

Because of their capacity to catalyze glucose oxidation, nickel-based

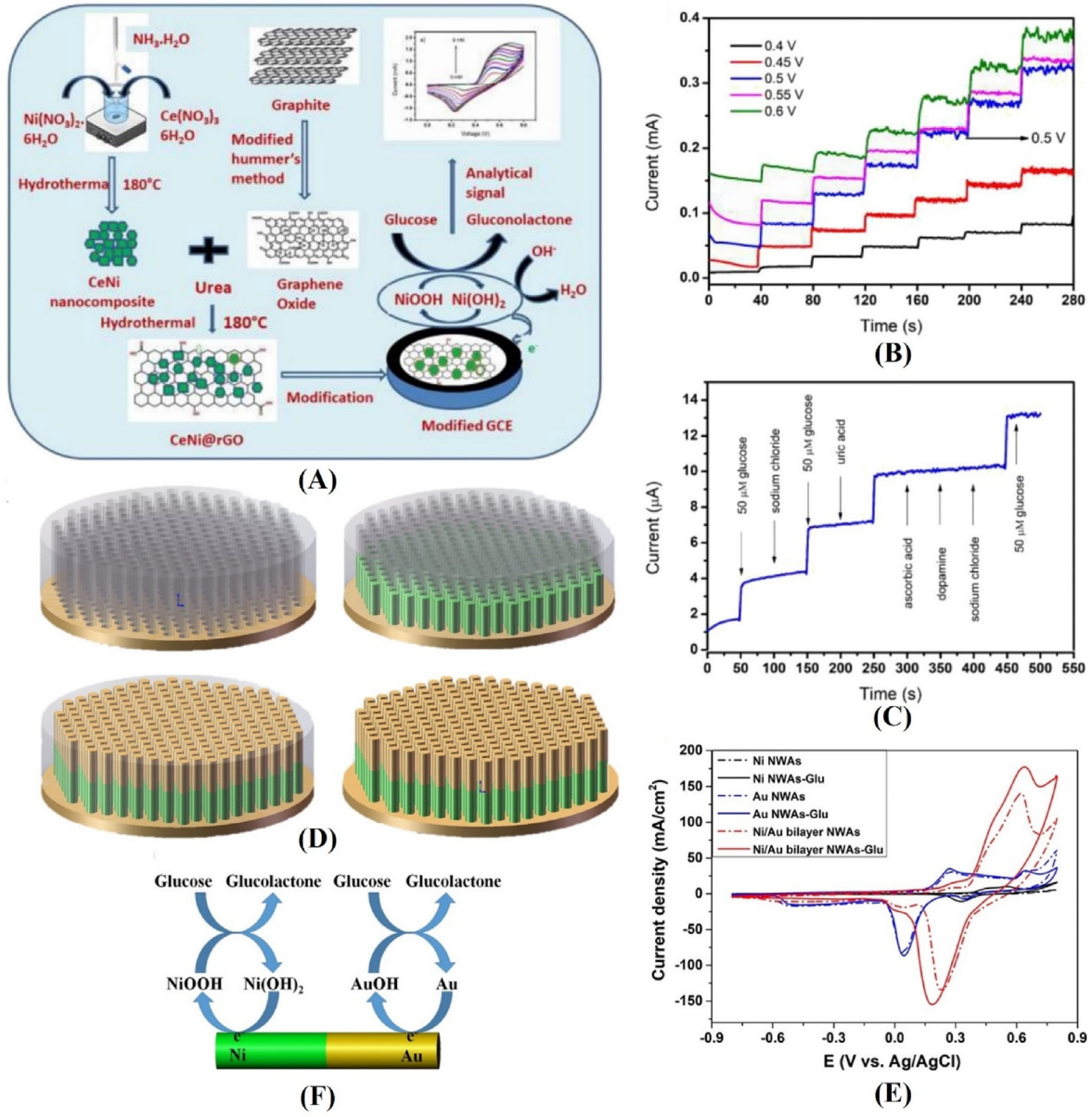

Fig. 2. **(A)** Schematic illustration of electrode modifying for sensing the glucose. **(B)** the CeNi@rGO-GCE amperometric responses at various working potentials and the addition of 50 μM glucose. **(C)** CeNi@rGO-GCE selectivity test with interfering of various compounds [37]. **(D)** Ni/Au biNWAs fabrication illustration. **(E)** Ni NWAs– Ni/Au, Au NWAs-, and biNWAs-modified electrodes cyclic voltammograms in the presence and absence of 1 mM glucose. **(F)** redox reaction mechanism. Reproduced with permission from Ref. [38].

substances have been extensively employed in the creation of electrochemical glucose sensors. For instance, commercial Ni foam (NF) has been utilized as a working electrode in a simple electrochemical glucose sensor having a detection limit of 2.2 μM and a linear range of 0.05–7.35 mM. Nevertheless, Ni nanoparticles often require support such as graphene or a silica nanochannel membrane to catalyze the electrochemical process of glucose detection effectively. NiO has also been employed as a support on NF, which resulted in an electrochemical glucose sensor with a detection limit of 0.46 μM and a linear range of 0.005 mM–5.5 mM, because of higher stability and lower toxicity than nickel. Carbon nanosheets and nanotubes are among the materials that have been applied as supports for NiO in electrochemical sensors, and $Ni(OH)_2$-based sensors have shown performance comparable to NiO-based sensors. Additionally, corrosion-resistant and electron transfer-effective materials like nickel nitrides and phosphides have been applied in the development of electrochemical glucose sensors. Furthermore, porous materials, such as Ni-MOF, have been explored as potential detecting materials because of their exceptional adsorption properties for glucose [33–36].

Researchers have discovered a novel material, a three-dimensional core-shell hierarchical structure composed of nickel-copper layered double hydroxide (Ni–Cu LDH), that has been used to develop a highly accurate and sensitive glucose sensor and the modification procedure is shown in Fig. 2A. They assessed the amperometric response after the addition of 50 μM glucose in various working potentials (Fig. 2B). The Ni–Cu LDH structure has a rapid response time of 1.5 s and a recovery time of 3.5 s when detecting 200 μM glucose concentrations. It has excellent anti-interference and reproducibility properties, as well as the ability to resist bending. It is very resistant to bending and interference, and it also produces accurate results. The optimized sensor, based on this structure, has a sensitivity of 7.08 μA per micromolar per square centimeter, a detection limit of 1.3 μM, and a linear range of 0.006–1.6 μM. The sensor has been evaluated for stability and tested with human serum, demonstrating an accurate detection limit of 13 μM for glucose levels (Fig. 2C). In summary, the use of the three-dimensional core-shell hierarchical structure based on Ni–Cu LDH has flashed promise as an enzymeless glucose sensor for clinical and medical applications [37].

Electrochemical nanosensors have been exploited using various hierarchical molecular arrangements and 3D structures at different locations on the surface of nanoelectrodes, including the center, top, and edge. NiO nanostructures, particularly NiO nanospheres with a hierarchical microstructure, have demonstrated great potential for improving glucose detection sensitivity. Recent studies have utilized 3D Ni/NiO nanoelectrode hierarchies and NiO nanospheres modified with carbon-nitrogen dots to create glucose nanosensors with dendritic NiO@carbon-nitrogen architecture, it allows for the precise and selective measurement of glucose in bodily fluids. NiO nanoflower sensors, with their significant surface flaws, big segments, active catalytic sites, and huge surface area could explain the sensors' exceptional efficiency. Additionally, hierarchical nanosensors based on NiO nanostrand morphologies have been created, that provide selective glucose sensing by using Ni foam platform electrodes with 3D modifications to their micro-, meso-, and macropore sizes. Electrocatalytically active, low-resistance, mass-transport efficient, and electrically robust nanoelectrode surfaces are all easily fabricated thanks to the nanostrand shape. These sensors have shown good reproducibility, fast response, high stability, selectivity, and sensitivity in glucose detection in biological samples. Compared to nanosheet-based sensor systems, the use of nanostrand-designed electrodes has been shown to be particularly effective in detecting a wide range of glucose concentrations with high sensitivity and a low detection limit [39–41].

Glucose detection using nanosensors with a 3D molecular structure and a hierarchical molecular organization has been shown to be reliable, even in the existence of confounding compounds. These sensors utilize different hierarchical NiO structures, like hollow spheres, flowers, nanoflakes, and hedgehog-like shapes. Hexagonal β-$Ni(OH)_2$ and cubic NiO nanophases have been employed in these sensors to achieve high selectivity in detecting glucose in human blood samples. The use of these sensors allows for sensitive and specific detection of glucose in biological samples [42,43].

Nanocomposite-based electrodes have been found to be effective in sensing glucose samples. Nonenzymatic glucose sensors based on CoNi nanowires have been shown to be sensitive enough to detect amounts of glucose from 0.1 to 1.0 $\times$ 10^{-3} m. Furthermore, ZnO–NiO composite nanosheets that were thermally annealed onto 3D macroscopic porous carbon were utilized to develop a nonenzymatic glucose sensor that boasts a fast response time of less than 3 s, a wide detection ranges from 13 $\times$ 10^{-6} m to 4.86 $\times$ 10^{-3} m, a low limit of detection of 4.12 $\times$ 10^{-6} m, and high sensitivity of 448.6 μA mm-1 cm^{-2}. Another example is the use of NiO-NP-modified multiwalled carbon nanotube nanocomposites immobilized onto a carbon paste electrode for glucose sensing with a limit of detection of 11.04 $\times$ 10^{-9} m and a detection range spanning from 1 $\times$ 10^{-6} m to 0.5 $\times$ 10^{-3} m to 9.0 $\times$ 10^{-3} m [44–46].

An innovative approach to synthesizing Ni/Au bilayer nanowire arrays (Ni/Au biNWAs) has led to the development of a highly sensitive and non-invasive glucose sensor and its fabrication procedure is shown in Fig. 2D. The researchers utilized a template-assisted electrodeposition process to manufacture the Ni/Au biNWAs, which had a length of 16 μm and a diameter of 200 nm. The sensor demonstrated exceptional electrocatalytic activity for glucose oxidation, with an ultrahigh sensitivity of 5154.84 μA per millimolar per square centimeter in the range of 50 to 10,000 μM, and an incredibly low detection limit of 10.69 μM. In addition, in the presence and absence of 1 mM glucose, they evaluated the cyclic voltammograms (Fig. 2E) and the sensor showed rapid response times of 2.5 s and high selectivity, without any interference from other components found in human blood. The accuracy and precision of the sensor were also tested in detecting glucose levels in human blood serum, with a relative standard deviation of 0.67–2.68 %. The mechanism of redox reaction is demonstrated in Fig. 2F. This sensor has significant potential for monitoring glucose levels non-invasively in the body [38].

Enzyme-free nanosensors have been designed to detect glucose by using a combination of Ni nanoparticles and TiO_2 nanowires on the electrode surface and its structure is illustrated in Fig. 3A. The glucose detection was highly accurate with a sensitivity of 50.97 μA mm^{-1} cm^{-2} and a detection range of 1 $\times$ 10^{-6} m to 7 $\times$ 10^{-3} m, while the limit of detection was low at 0.18 $\times$ 10^{-6} m. The Ni nanoparticles were arranged in an ordered, rhizobia-like formation on the surface of axial Ti-tubular foils to enhance surface activity, and diffusivity and lower the resistivity. Jung and colleagues have created a flexible field-effect transistor-based nonenzymatic glucose sensor using NiO quantum dot-modified ZnO nanorods and the fabrication procedure is demonstrated in Fig. 3B. The prepared sensor revealed excellent selectivity and high sensitivity (interfering species concentration: 0.1–0.5 mM) in detecting glucose concentrations between 0.001 and 50 $\times$ 10^{-3} m under physiological conditions (Fig. 3C). Also, they assessed the applicability of prepared sensors on real samples like whole blood and serum (Fig. 3D) [47]. A separate study used Cu_2O nanoarchitects to modify a helical TiO_2 nanotube electrode, developing a nonenzymatic glucose sensor with a limit of detection of 62 $\times$ 10^{-6} m and the ability to detect concentrations between 3.0 and 9.0 $\times$ 10^{-3} m [48–50]. Recently, the glucose sensing chip has been developed by Li et al. They designed $PtNi_{(1:3)}$ dual gel-based non-enzymatic wearable sweat glucose biosensor that revealed excellent flexibility, selectivity, and sensitivity. The stability analysis result of their dual-structural Pt–Ni hydrogel was outstanding, and they claimed that designed dual-structural metallic hydrogel where applicable even after 2 months. The interconnection networks between $Ni(OH)_2$ nanosheets and PtNi nanowires have led to conspicuous stability and electrocatalytic activity in oxidation of glucose in neutral circumstances [51].

Metal-organic frameworks (MOFs) are a kind of porous material with unusual qualities including a huge surface area, high porosity, and the capacity to be chemically tuned. These features are what make MOFs so

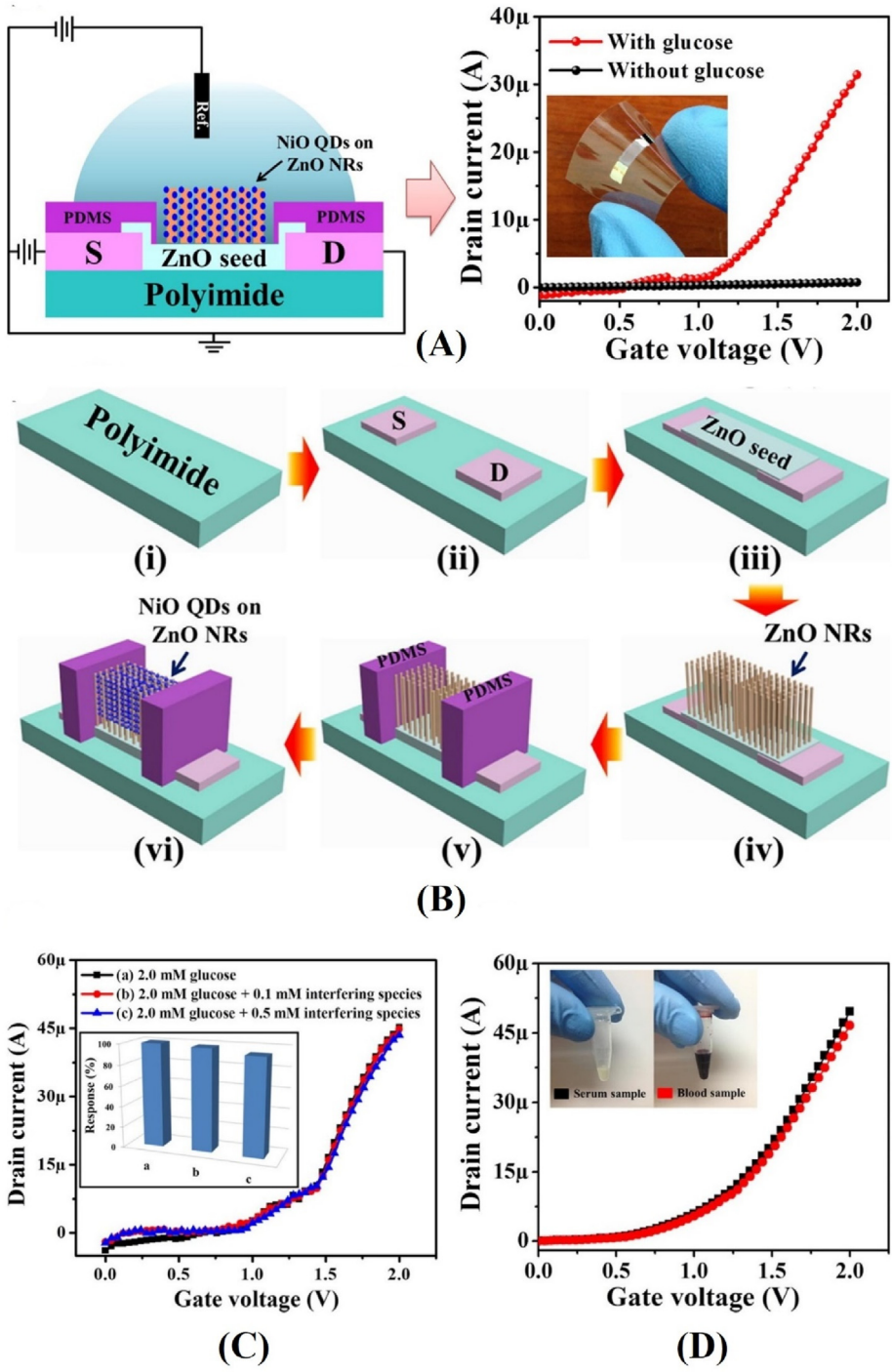

Fig. 3. **(A)** The nonenzymatic f-FET glucose sensor schematic and its I_d-V_g response in the presence/absence of 0.10 mM glucose at pH 7.4 and PBS buffer (0.10 M). **(B)** nonenzymatic f-FET glucose sensor fabrication procedure scheme. **(C)** interference analysis of fabricated sensor I_d-V_g. **(D)** I_d-V_g responses of the fabricated sensor on real samples (whole blood and serum). Reproduced with permission from Ref. [47].

promising for use in sensor technologies. Additionally, MOFs can be designed to have excellent electrochemical properties, making them useful in the electrochemistry [52,53]. The 3D nickel (II)-terephthalic acid (Ni(TPA))/metal-organic framework (MOF) flower was fabricated using solvothermal synthesis and its preparation mechanism is shown in Fig. 4A. In this study, to improve the MOF's electrochemical activity and stability, single-walled carbon nanotubes (SWCNTs) were sonicated with Ni(TPA) MOF. A Ni(TPA)-SWCNT-modified carbon electrode was developed to test the viability of this nanocomposite in a non-enzymatic electrochemical sensor for glucose measurement. They evaluated the amperometric responses of the prepared sensor after the addition of various concentrations of glucose. According to the findings, the nanocomposite exhibited a more potent electrochemical response to the oxidation of glucose. The Ni(TPA)-SWCNT modified electrode exhibited exceptional performance with an LOD of 4.6 Mm for glucose detection, as shown in Fig. 4B and C [54].

Research from a variety of fields has shown that Ni-MOF is an excellent electrocatalytic material, with remarkable electrochemical activity in the oxidation of glucose. The electrochemical properties of UiO-67@Ni-MOF made them suitable for glucose detection, with a rapid

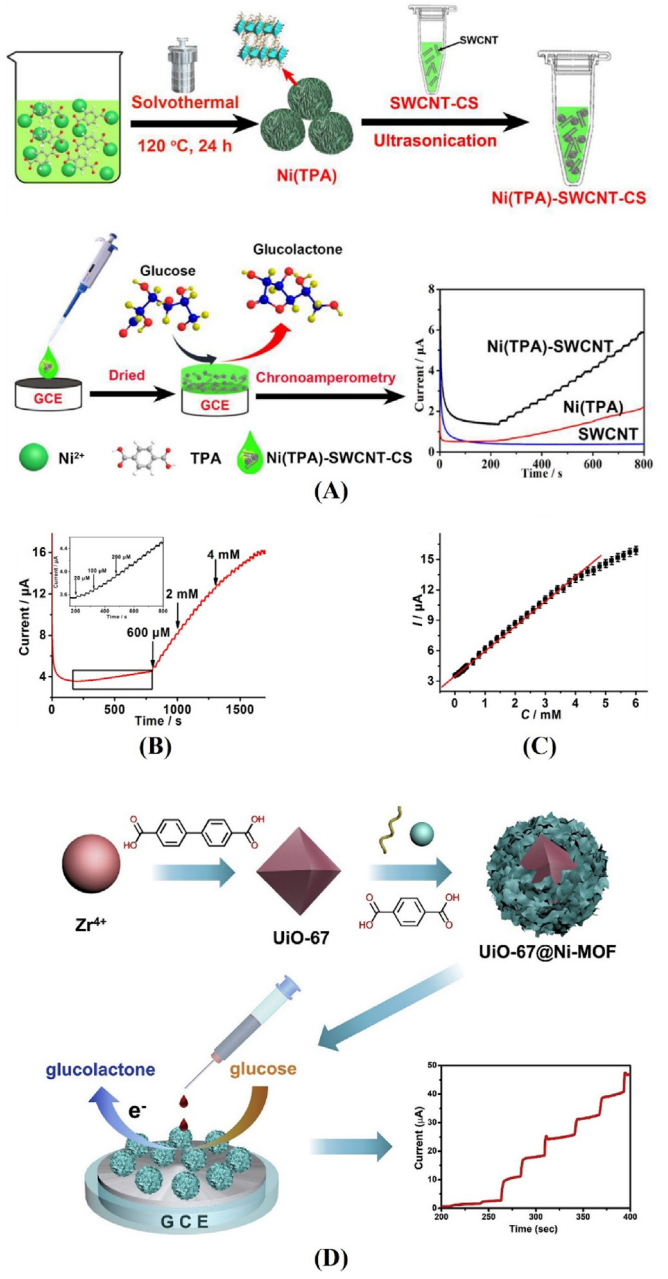

Fig. 4. **(A)** Graphical depiction of the Ni(TPA)-SWCNT composite's production process and its use in sensing glucose. **(B)** The addition of 0.02 mM glucose elicited amperometric responses in Ni(TPA)-SWCNT-CS/GCE. **(C)** The plot of electrocatalytic current of glucose versus concentrations of glucose. Reproduced with permission from Ref. [54]. **(D)** synthesis Scheme of the core-shell UiO-67@Ni-MOF composites through internal growth under polyvinylpyrrolidone regulation and non-enzymatic sensing of glucose. Reproduced with permission from Ref. [55].

response time of fewer than 5 s and a low limit of detection (LOD) of 0.98 μM. The UiO-67 served as the core for the Ni-MOF shell's growth, as shown in Fig. 4D. Moreover, the sensor displayed long-term stability, repeatability, and efficient reproducibility. This study suggests that the sensor has promising prospects for sensing non-enzymatic glucose, with a high potential for rapid diabetes diagnosis and daily blood glucose monitoring [55].

2.2.2. Cobalt-based nonenzymatic nanoarchitectures

Producing a nanostructure made of cobalt oxide (Co_3O_4) that is capable of selectively detecting glucose levels in human blood serum was accomplished via the use of a technology that was both efficient and economical. The nanostructure in the form of a flower had a thickness of between 200 and 300 nm, and it boosted the signaling response of glucose while also increasing its selectivity. Fan and colleagues used an eggshell membrane to create a 3D hierarchical meso/macroporous Co_3O_4 film for glucose sensing, which proved to be a low-cost and environmentally friendly method. Additionally, the Electrodeposition of CoOx NPs was performed on electrochemically reduced graphene, which was then supported on a glassy carbon electrode with a diameter of less than 100 nm. This allowed for the production of CoOx NPs. The end result was a rapid-response, glucose-sensing electrode that was both selective and sensitive. Another study involved the development of a nonenzymatic glucose nanosensor using 3D Co_3O_4 on a porous Ni substrate. High electrochemical activity and sensitivity with a detection limit of 1×10^{-6} m (S/N = 3) were shown by a nanosensor electrode made of 50 nm Co_3O_4 cluster nanofibers grown layer-by-layer onto a 3D Ni substrate. In the existence of competing compounds in human blood serum, including D-fructose, cysteine, dopamine, sodium chloride, uric acid, and ascorbic acid, it nevertheless showed high selectivity [56,57].

Materials based on the metal cobalt are being researched for potential application in glucose sensors, including cobalt alloy, Co_3O_4, $Co(OH)_2$, and CoOOH. To enhance conductivity, these materials are often combined with other substances like graphene. Co_3O_4, which is a semiconducting material and has poor conductivity on its own, has been used to create a glucose sensor that can detect glucose with a detection limit of 26 μM in the linear range of 0.088–7 mM. Researchers have also synthesized Co(OH)F nanoflowers using a microplasma method and loaded them onto carbon cloth to create an overly sensitive sensor with a detection limit of 0.75 μM and a sensitivity of 1806 μA mM^{-1} cm^{-2}. Cobalt-based materials, such as CoP and Co_3N, are also being investigated for their possible application in glucose sensors due to their outstanding conductive qualities as transition metal nitride and phosphide, respectively. Sensors using these materials have detection limits of 1 μM and 0.5 μM and sensitivities of 3325.6 μA mM^{-1} cm^{-2} and 5168.6 μA mM^{-1} cm^{-2}, respectively [58–60].

Glucose sensors are being developed using a wide range of nanostructures based on cobalt-based materials such as cobalt alloy, CoOOH, $Co(OH)_2$, and Co_3O_4. These materials are often combined with other substances, like graphene, to enhance conductivity in cobalt-based catalysts. Co_3O_4 is a biologically compatible semiconducting material that is not very conductive on its own, but when loaded onto 3D-KSCs, it creates a sensor with a detection limit of 26 μM and a linear range of 0.088–7 mM. Co(OH)F nanoflowers were also loaded onto carbon cloth using a microplasma-based synthesis method, resulting in a sensor with a sensitivity of 1806 μA mM^{-1} cm^{-2} and a detection limit of 0.75 μM. New cobalt-based materials, such as Co_3N and CoP, have also been synthesized and show improved performance as glucose sensors due to the excellent conductive properties of transition metal nitride and phosphide. These materials are used to create sensors with detection limits of 1 μM and 0.5 mM and sensitivities of 3325.6 μA mM^{-1} cm^{-2} and 5168.6 μA mM^{-1} cm^{-2}, respectively [58,61,62].

2.2.3. Copper-based nonenzymatic nanoarchitectures

Inexpensive semiconductors based on CuO nanostructures have been developed, highly catalytic nonenzymatic glucose sensors. These nanostructures include nanosheets, nanowires, and nanoparticles, which were coated onto carbon clothes to create effective glucose sensors. The CuO nanosheets were found to be particularly sensitive, selective, and rapid responding. High efficiency for glucose detection was also shown using CuO nanoparticles inkjet printer onto an Ag electrode, even in the vicinity of large quantities of interference substances. Good electrochemical characteristics, quick reaction, high selectivity, and sensitivity were all achieved by the regulated production of CuO nanospheres for glucose detection. Using a modified electrode fabricated from fluorine-doped tin oxide and the controlled vertical development of ZnO nanorods coated

with CuO nanoparticles is another interesting idea for a sensor system. This design demonstrated excellent reproducibility and workability, high sensitivity, a low limit of detection, and excellent electrocatalytic performance for speedy glucose testing. Overall, these sensor designs highlight the effectiveness of CuO nanostructured geometries in achieving high accuracy in the glucose sensing [63–65]. A promising electrochemical biosensor based on CuO/ZnO-DSDSHNM has been developed, which offers a large surface area that enhances the electrochemical reactivity of glucose oxidation. The biosensor was fabricated for the detection of glucose on a glassy carbon electrode (GCE) by applying CuO/ZnO-DSDSHNM (Fig. 5A). The sensor has a limit of detection of 357.5 nM, a sensitivity of 1536 nA mM^{-1} cm^{-2}, and a broad dynamic range that extends from 500 nM all the way up to 100 mM. Furthermore, the sensor exhibits excellent applicability, high selectivity, stability, and long-term reproducibility for glucose recognition. Biosensor's amperometric response has been assessed after the addition of various concentrations of glucose at 0.60 V (Fig. 5B). The results show that the Nafion/CuO–ZnO-DSDSHNM/GCE-based Nafion/CuO-DSDSHNM material production and sensor fabrication techniques have significant promise for future research on high-performance glucose sensing [66].

Various materials, like metallic copper and different copper compounds, can come in different shapes like nanowires (with diameters of around 10 nm and lengths of up to several micrometers), nanoflakes (with thicknesses of around 20 nm), nanorods (with diameters ranging from 20 to 50 nm), nanoflowers (with petal sizes of around 100 nm), and nanocubes (with edge lengths of around 50 nm). Copper nanowires, which have a high aspect ratio (typically around 10:1), are frequently utilized in sensors that measure glucose in body fluids. Researchers have been able to improve the detection limit and sensitivity of these sensors by using different methods to produce copper nanowires. For instance, using a hydrothermal technique, scientists were able to lower the detection limit to 1 nM, with a response time of around 5 s. Additionally, adding a carbon coating (with a thickness of around 5 nm) on copper cubes helped to prevent oxidation and improve sensor performance, achieving a detection limit of 21.35 μM, a linear range of 40 μM to 40 mM, and a sensitivity of 2565 μA mM^{-1} cm^{-2}. CuO has been widely researched, and its method of catalyzing glucose is similar to that of nickel, which is based on the conversion of Cu^{3+}/Cu^{2+} under alkaline conditions (with a pH range of around 9–12) [67–69].

A non-enzyme-based sensor for highly accurate glucose detection was developed by using CuO nanostructures that were shaped like petals. At a detection limit of 0.259×10^{-6} m for glucose, this electrode demonstrated both good specificity and sensitivity. Another non-enzyme glucose sensor was created by combining gold nanoparticles, a special type of organic-metal structure, and a unique 3D electrode. This sensor has an extremely low limit of detection and could measure glucose concentrations as low as 14.77×10^{-6} mM despite being able to measure a wide range of values [70,71].

A non-enzyme-based glucose sensor was created by employing a composite material comprised of carbon and copper and its fabrication procedure is illustrated in Fig. 5C. This composite material was then enhanced by putting a MOF on a copper foam electrode. Finally, the

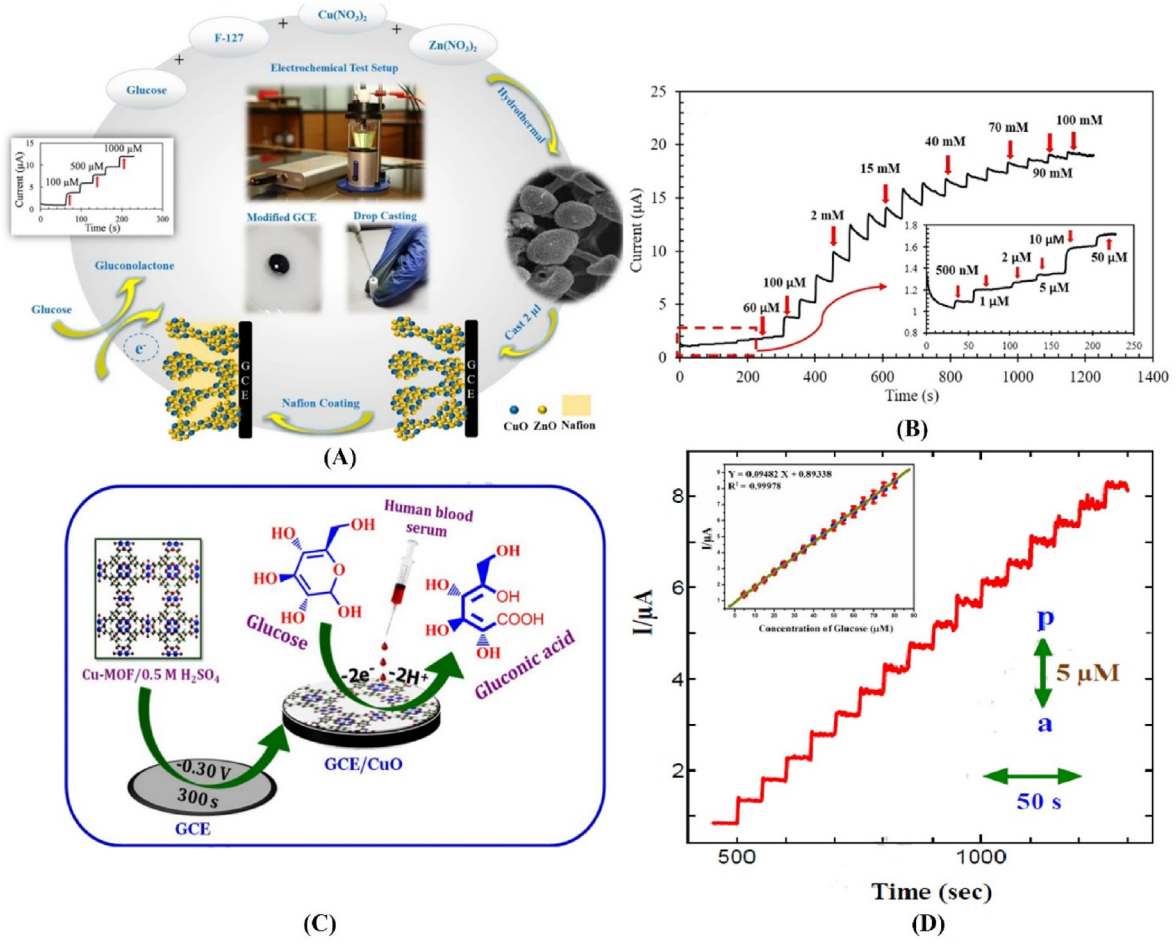

Fig. 5. **(A)** Schematic of the CuO/ZnO-DSDSHNM biosensor for glucose detection in human blood samples. **(B)** The effect of glucose concentrations ranging from 500 nM to 100 mM on the amperometric response of a biosensor operating at 0.60 V has been assessed. Reproduced with permission from Ref. [66]. **(C)** Electrochemical deposition of CuO onto a glassy carbon electrode for glucose detection in human blood serum. **(D)** Glucose detection on a GC/CuO electrode in 0.1 M NaOH as shown by an amperometric curve. At 50-s intervals, the glucose concentration is increased by 5 mM with each additament. Reproduced with permission from Ref. [72].

sensor was tested for its ability to detect glucose. The developed electrode had a rapid glucose detection time, having an exceptionally low limit of detection (LOD) of 0.6×10^{-6} m, a high sensitivity of 10.1 mA cm^{-2} mm^{-1}, and a response time of around 2 s. They monitored the glucose sensing through their detector with specific time intervals. The amperometric curve with the addition of 5 mM glucose with each additament is demonstrated in (Fig. 5D). To further improve the sensor's performance, a specific type of copper oxide-MOF was electrodeposited onto a glassy carbon electrode, resulting in a sensor that had a wide detection range of 500×10^{-9} m to 5×10^{-3} m and a LOD of 70×10^{-9} m (when the signal-to-noise ratio was 3) [72,73].

CuO nanostructures are a promising material for use in non-enzyme glucose sensors because of their high electrical conductivity and catalytic activity. However, the selectivity and sensitivity of sensors based on CuO alone can be limited. Scientists have been adding things like silver nanoparticles (AgNPs) to CuO nanostructures to make these sensors more effective. Glucose sensors have been demonstrated to benefit from the incorporation of AgNPs into CuO nanostructures in order to increase their selectivity and sensitivity. The non-enzymatic glucose sensor created by Zheng et al. makes use of CuO nanostructures modified with AgNPs. CuO nanofibers (NFs) modified with AgNPs were used on an indium tin oxide (ITO) electrode in this study. The resulting sensor showed a LOD of 51.7×10^{-9} m, a detection range of $0.5–500 \times 10^{-6}$ m, and a sensitivity of 1347 μA cm^{-2} mm^{-1}. Research reveals that the incorporation of AgNPs into CuO nanostructures greatly expands the detection range and sensitivity of glucose sensors. Another example is the non-enzyme glucose sensor developed by Shamsipur et al. A nonenzymatic glucose sensor was developed using a Cu-supported mesoporous template, SBA-15-Cu (II), on a glassy carbon electrode (GCE) upgraded with Nafion. The resultant sensor detected glucose in the range of 0.5×10^{-6} m to 2×10^{-3} m with a LOD of 0.075×10^{-6} m in human blood and showed great selectivity and sensitivity in the existence of competing species like dopamine, ascorbic acid, and urea. By using the modified CuO-MOF and glassy carbon electrode, the sensor showed improved performance and increased selectivity. Overall, the addition of AgNPs to CuO nanostructures and the application of MOFs and other modifications have been shown to significantly enhance the sensitivity, selectivity, and detection range of non-enzyme glucose sensors, making them a promising technology for the accurate and reliable measurement of glucose in various samples [74–76].

2.2.4. Noble metal-based nonenzymatic nanoarchitectures

Employing AuNP and CuO nanostructures composite material, a highly sensitive and stable glucose sensor was created, which was synthesized to take advantage of the strong electrocatalytic properties of the AuNP–CuO nanocomposites. The sensor had a low limit of detection of 1.4×10^{-6} m, a wide detection range of $5–650 \times 10^{-6}$ m, high sensitivity of 3126.76 μA mm^{-1} cm^{-2}, a quick response time of 3 s, and required a low applied voltage of +0.6 V, when tested on biological samples like human urine and serum. In electrochemical sensors, it is standard practice to utilize metal nanoparticles (NPs), namely Pd, Pt, Ag, and Au, because of the many benefits associated with their usage. They have low biocompatibility and toxicity, high electrocatalytic activity, and fast charge transfer. These features make them suitable for use in sensors and other analytical devices, as they can identify very diluted samples of their intended analytes and are also relatively safe to use in biological systems [77,78].

Palladium nanoparticles (Pd NPs) embedded on ionic liquid-formed fibrillated mesocage carbon (Pd NPs@IFMC) were used to develop a novel non-enzymatic glucose sensor. The increased electrochemical activity of the sensors may be attributed to the architecture, which has a high density of uniformly dispersed palladium nanoparticles on a mesoporous carbon substrate. This allowed for improved glucose molecules diffusion and binding to the sensor surface which resulted in enhanced sensitivity and selectivity in glucose sensing. With a limit of detection of 0.2×10^{-3} M and a detection range of $1–55 \times 10^{-3}$ M, the Pd NPs@IFMC sensors demonstrated outstanding electrocatalytic capabilities for oxidation of glucose while operating at a potential of +0.4 against Ag|AgCl|KCl. Additionally, the sensors had good stability, and recyclability, and were selective even when other potentially interfering molecules were present [79].

Synthesizing Ag@ZIF-67 nanostructures that demonstrated good stability allowed for the development of a glucose sensor that was very selective and sensitive. The Ag@ZIF-67 nanostructures were used as a sensor on a glassy carbon electrode and displayed good electrocatalytic activity for detecting glucose with a low limit of detection of 0.66×10^{-6} M (S/N = 3) within a wide concentration range of $2–1000 \times 10^{-6}$ M, and consistent results over a long period of time. In addition, by depositing Pt/Au nanoparticles onto a boron-doped diamond electrode, another type of glucose sensor was made that showed a low limit of detection of 0.0077×10^{-3} M, the wide linear range of $0.01–7.5 \times 10^{-3}$ M and was selective even in the existence of other interfering substances like acetaminophen, UA, DP, and AA. These sensors made with noble metal electrodes have the potential to be used in medical analysis due to their high-performance [80,81].

2.2.5. Carbon-based nonenzymatic nanoarchitectures

Because of their extensive surface area and their capacity to increase electron transport and bioactivity of receptors, carbonaceous nanostructured materials including carbon nanotubes (CNTs), graphene, and fullerene have attracted substantial interest for application in electrochemical sensing. Pd NPs were used to modify CNTs to create a nanosensor for glucose detection through a redox reaction. Even in the vicinity of additional compounds that may cause interference, such as AA, UA, and p-acetamidophenol, these Pd NP/CNT nanosensors were able to detect glucose levels with an extremely high degree of selectivity. In addition to this, they demonstrated strong repeatability, high sensitivity, and linear dependency across a broad range of glucose concentrations in urine samples, which ranged from 0 to 46×10^{-3} m. Additionally, the electrodeposition of NiO NPs/Pt on an ER-GO/GCE platform resulted in a selective and highly catalytically active electrode for non-enzymatic glucose sensing, with a detection range from 2×10^{-6} m to 5.66×10^{-3} m and a LOD of 0.2×10^{-3} m. 1D nanostructure arrays of Pt/Ni nanowires have been reported by other researchers to be a sensitive and effective electrode for the detection of glucose in alkaline solutions, with a LOD of 1.5×10^{-3} m and a detection range from 2×10^{-6} m to 2×10^{-3} m [82–85].

Ultrathin films of alizarin and aminophenylboronic acid (ARS-PBA) were deposited, layer by layer, over double-layered hydroxide nanosheets on an ITO electrode to create a unique glucose-detecting sensor. These sensors showed selective electrochemical activity towards glucose, with a low LOD of 4.0 nmol L^{-1}, a wide detection range of 0–1.00 μmol L^{-1}, and a fast response time. For electrochemical glucose detection, another way comprised utilizing chitosan-CNT core-shell composites with varying ratios on ITO electrodes. Glucose was detected directly, without a mediator, using a GOD-chitosan-CNT/ITO electrode that was stabilized via coupling strategy. The rapid electron-transfer constant of these electrodes was 8.2 s^{-1}. To further improve the selectivity and sensitivity of glucose sensing, SnS_2 nanoplates were also used to change the surfaces of multiwall CNT-GOD electrodes. Additionally, non-enzymatic glucose nanosensors were fabricated using simple MoS_2 microflowers and 3D MoS_2/graphene electrodes, which demonstrated low LOD, a wide detection range, and a fast response time as shown in Fig. 6A. The amperometric behavior of the prepared sensor has been assessed under changing the glucose level condition (Fig. 6B). Moreover, Ni-doped MoS_2/rGO nanocomposites were also found to exhibit high sensitivity and selectivity towards glucose molecules with a wide detection range and fast response time [86–89].

Combining MoS_2, CNT, and NiNPs can result in synergistic effects on electrical conductivity, allowing for rapid electron transport on the electrode surface and improving the sensor's sensitivity for glucose detection. This biosensor exhibited a low LOD of 0.19 μM and a high

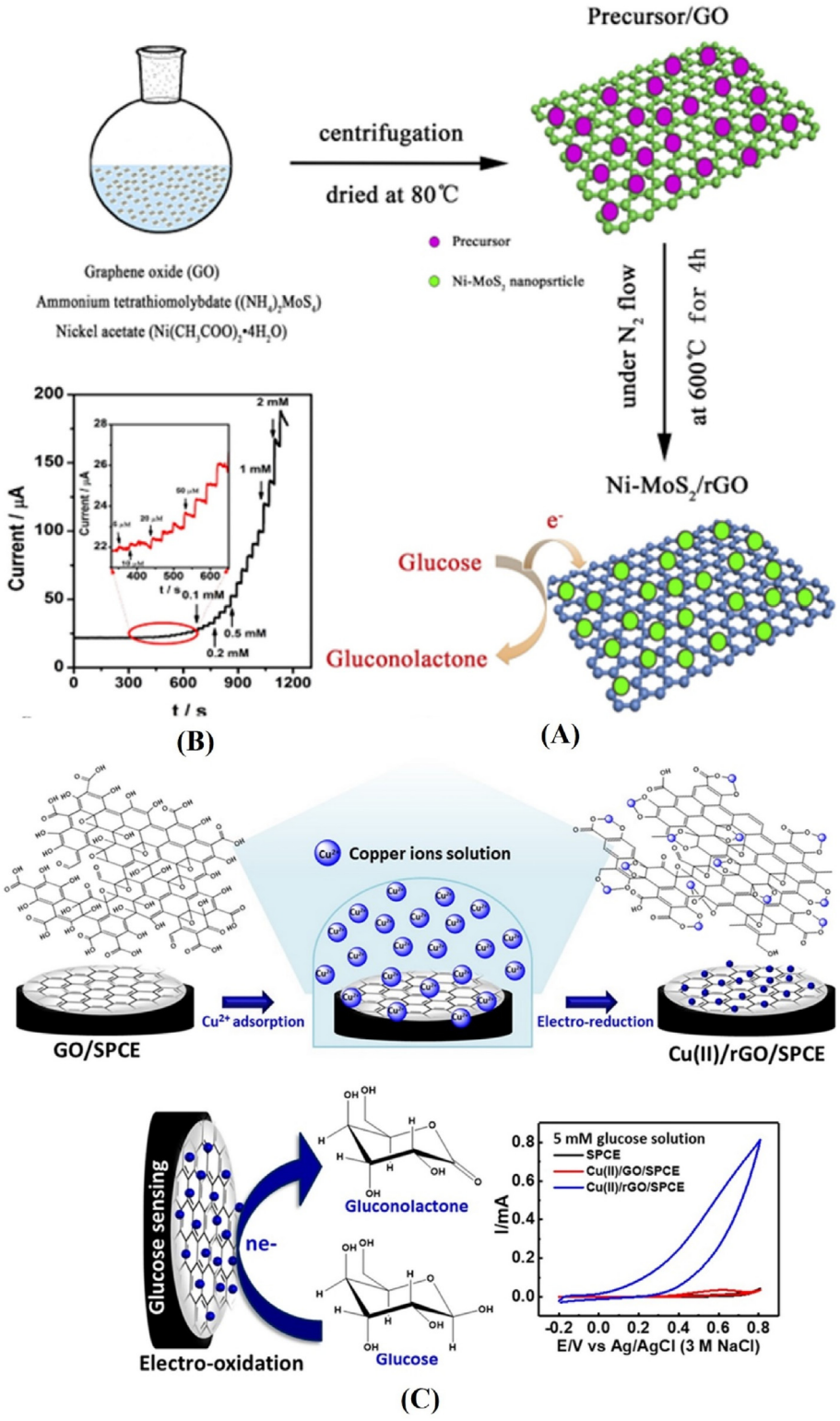

Fig. 6. **(A)** The fabrication of Ni–MoS_2/rGO composites is shown in a simplified scheme. **(B)** The effect of glucose level on the amperometric behavior of Ni–MoS2-3/rGO/NF/GCE. Reproduced with permission from Ref. [86]. **(C)** The Cu(II)/rGO nanocomplex-modified SPCE was used to fabricate a non-enzymatic glucose sensor. Reproduced with permission from Ref. [91].

sensitivity of 1212 μA mM^{-1} cm^{-2} with a fast response time of 3 s. It is a viable contender for glucose-sensing systems due to its extraordinary catalytic performance and low-cost [90]. A highly conductive rGO has been found to enhance glucose oxidation on the electrocatalyst Cu(II), leading to high sensitivity in glucose detection and the synthesis process is demonstrated in Fig. 6C. In addition, Serum glucose may be measured using the Cu(II)/rGO nanocomplex-modified electrode due to its anti-interference characteristics, high repeatability, and great stability. The sensor has a low detection limit of 65 μM. and high electrocatalytic efficiency for the oxidation of glucose. This copper (II)/rGO-based sensor

with excellent performance has great potential for accurately quantifying glucose levels in real samples [91].

The development of highly selective, stable, and sensitive glucose sensors has spurred a rise in the study of nanostructured materials and their composites in this application. Several methods of manufacturing have been investigated to boost the sensors' functionality, including modifying surface properties and immobilizing enzymes or nanoparticles onto the sensors. As a result of these efforts, glucose sensors that have a broad range of detection capabilities and low detection thresholds have been developed. The use of distinct types of nanostructured materials, like metal-organic frameworks, metal nanoparticles, carbon nanotubes, and graphene have been explored for glucose sensing. Each type of material offers unique properties that can be leveraged for glucose sensing. For example, graphene and carbon nanotubes have large surface areas and excellent electrical conductivity, making them suitable for electrochemical sensing. Metal nanoparticles like Au, Ag, Pt, and Pd have high electrocatalytic activity, fast charge transfer, and low toxicity, which are also beneficial for electrochemical sensing. MOFs have a high surface area, good chemical stability, and tunable pore size that can be used to immobilize enzymes or nanoparticles for glucose sensing. In addition to these materials, many fabrication techniques have been employed to improve sensor performance, such as layering ultrathin films, growing

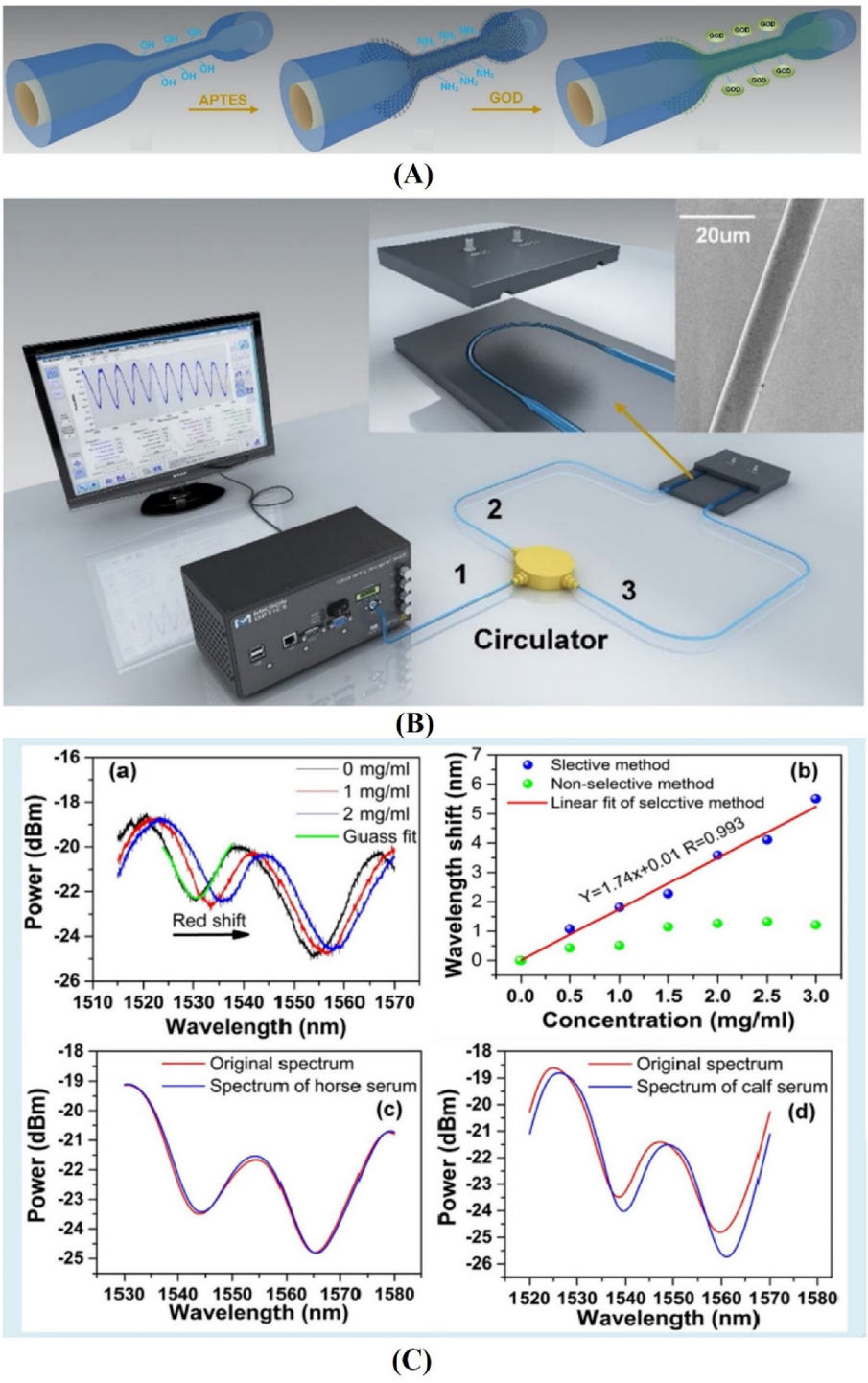

Fig. 7. **(A)** An instance of the immobilization of GOD onto microfiber in diagrammatic design. (a) Hydroxyl-groups activated microfiber, (b) APTES-modified microfiber, and (c) GOD-immobilized microfiber. **(B)** Arrangement of the experiments to determine the refractive index and identify glucose. After being shaped into the shape of a probe using the improved multimode microfiber, it was then inserted into the U-shaped groove. **(C)** Spectra of solutions at varying amounts of glucose. (a) Concentration-dependent spectral profiles of glucose solutions. (b) Concentration-wavelength-resonance relationship. (c) detected spectrum of horse serum and (d) calf serum. Reproduced with permission from Ref. [95].

metal-organic frameworks on a surface, electrodeposition, and immobilizing enzymes or nanoparticles. These techniques allow researchers to tune the properties of the sensors, like surface area, electronic properties, and chemical properties. Glucose sensing in a wide range of samples, including urine, blood, and other biological fluids, may be made more practical and inexpensive if these methodologies were successful in creating glucose sensors with high selectivity, stability, and sensitivity. There is potential for many uses for these sensors, which include monitoring glucose levels in diabetes patients, performing glucose assays in clinical settings and research, and even developing wearable or implantable devices for continuous glucose monitoring. Optimizing the fabrication and design of these nanostructured glucose-based sensors also opens new possibilities for developing other biosensors. The same principles and techniques used to improve glucose sensors' sensitivity, stability, and selectivity can be applied to developing other types of biosensors for detecting other molecules, such as lactate, urea, or glucose oxidase. Moreover, these nanostructured-based glucose sensors can be used in developing countries and rural areas where medical equipment and facilities are scarce. This technology could be more accessible and less expensive than traditional glucose sensors, making it more feasible for use in those areas. Overall, developing nanostructured-based glucose sensors has provided a favorable solution for cost-effective and efficient glucose sensing and has opened new opportunities for biosensing.

2.3. Optical and visual diabetes biosensors

Advances in many different areas, including medical surveillance, environmental monitoring, and food safety have been made possible through the use of optical biosensors. These biosensors utilize techniques such as SERS, absorptiometry, reflectometry, fluorescence, and SPR-based biomolecular sensing to achieve high accuracy and sensitivity in detecting blood glucose levels. They have the potential for daily monitoring and early warning [92–94].

Li et al. have proposed an alternative to the costly and non-biocompatible fiber-surface plasmon resonance biosensor, in the form of a fiber-optic microprobe modified with GOD for selective and sensitive detection of glucose. The biosensor was created in three steps, involving surface activation with H_2SO_4/H_2O_2 solution, amination-surface modification with 3-aminopropyl-triethoxysilane, and silanization of the modified GOD-covered fiber surfaces with organo-functional alkoxysilane molecules and the GOD immobilization procedure is shown in Fig. 7A. They identified the glucose and determined the refractive index after shaping the multimode microfiber (Fig. 7B). Assorted studies have been done by Li and coworkers to prove the applicability of their developed sensor. As can be seen in Fig. 7C they assessed the concentration-dependent profiles, the relationship among concentration-wavelength-resonance, and glucose in calf serum and horse serum. All in all, optical fiber sensors are a potentially useful tool for the quick monitoring of glucose levels in a variety of human body contexts, with desirable features including low maintenance, low cost, long-distance sensing, immunity to electromagnetic interference, remote detection, compact size, fast response, reliability, and high sensitivity [95].

The scientists utilized both multiphoton lasers scanning microscopy and scanning electron microscopy (SEM) to verify the surface characteristics of the biosensor components that had undergone different modification steps. The SEM was useful in identifying the structural design of the biosensor, while the multiphoton laser scanning microscopy managed to identify the presence of GOD through its fluorescent properties. The fiber optic sensor was shown to exhibit a clear shift in the resonant wavelength when exposed to various glucose concentrations, indicating a linear relationship with a broad range of glucose concentrations (0–3.0 mg/mL) and a response coefficient of 1.74 mg/mL. It was determined that evaluating the sensor in animal serum was the best way to validate its accuracy. The study also highlighted how important it is to use GOD to adapt optical fibers for glucose detection and sensing since it was another focus of the study. In summary, sensors that are based on optical fibers provide a dependable platform for the detection of glucose in a variety of situations [96–99].

Fluorescence-based biosensors, which use various methods such as surface-enhanced infrared absorbance, surface-enhanced fluorescence, and chemiluminescence (CL), are a popular choice in various fields, particularly in pharmaceuticals and clinical analysis. They are incredibly useful for detecting glucose in different samples, as they are simple to use, low cost, and highly sensitive. These sensors can detect glucose indirectly by recognizing the H_2O_2 produced from the enzymatic reactions catalyzed by glucose. H_2O_2 is a significant agent of reactive oxygen species, and thus it can be used in various signaling transduction methods. In addition, Fluorescence-based sensors have the added advantage of noninvasiveness and protection of the host system [100–102].

2.3.1. Chemiluminescence-based biosensors

CL biosensors are a type of technology that uses light emission resulting from chemical reactions to detect biomolecules with a wide range of detection, rapid response, and high sensitivity. They are frequently used in several domains like dietary testing, the pharmaceutical industry, and clinical analysis. The success of CL-based glucose sensors heavily depends on the immobilization process, the probe, and the platform design [103,104].

2.3.2. SPR-based biosensor

Biosensors based on SPR (Surface Plasmon Resonance) can detect and measure glucose levels by sensing changes in the refractive index. These biosensors use a bioreaction between glucose and immobilized biomolecule receptors on the surface. Many different industries have made use of them, including medical analysis, drug development, environmental and agricultural pollution monitoring, and pathogen detection. A novel glucose sensor using an organic-inorganic hybrid material was developed, providing high sensitivity, selectivity, and detection range for glucose. The sensor could accurately detect glucose levels in different physiological fluids like blood and tears in approximately 5 and 0.4×10^{-3} m, respectively. This sensor was created by immobilizing Ag nanoparticles of around 5–10 nm into a glucose-imprinted boronate-derived gel system called poly (N-isopropylacrylamide-co-acrylamide-co-4-vinylphenylboronic acid) to monitor glucose concentration within a range of $0–20 \times 10^{-3}$ m [105,106].

Researchers developed an SPR-based hyaluronate−AuNPs/glucose oxidase (HA−AuNP/GOx) complex and invented a wireless patch-type glucose sensor for noninvasive real-time glucose monitoring in sweat. The fabrication method and final sensor's scheme is shown in Fig. 8A. High enzyme stability, faster enzyme response, a large surface area, and good dispersibility may be imparted upon AuNPs and HA. The HAAuNP/GOx complex was generated when thiolated HA was conjugated to AuNPs and GOx was bound to the resulting HAAuNP/GOx complex. The wireless glucose sensor which is illustrated in Fig. 8B showed LOD of 0.5 mg/dL, fast response (5 s), and slow water evaporation (0.11 μL/min). Here, the wireless patch-type glucose sensor was shown to correlate well with commonly produced blood glucometers for measuring glucose level [107].

2.3.3. SERS-based sensor

Raman signal analysis is the basis of the Surface Enhanced Raman Scattering (SERS) technique, which could be used to determine the concentration of glucose in both aqueous and blood samples. This method is highly sensitive; it can detect even small levels of glucose (hyperglycemia). Researchers have demonstrated that when glucose is deposited onto objects made of silicon and modified with AgNPs it enhances the intensity of the SERS signal. Sensors patterned this way were able to detect extremely low levels of glucose, up to 0.05 mg/mL, with a detection limit compared to the normal levels found in real blood samples using SERS. Additionally, 2-thienylboronic acid was incorporated onto metal surfaces to enable noninvasive sensing of glucose in a range of

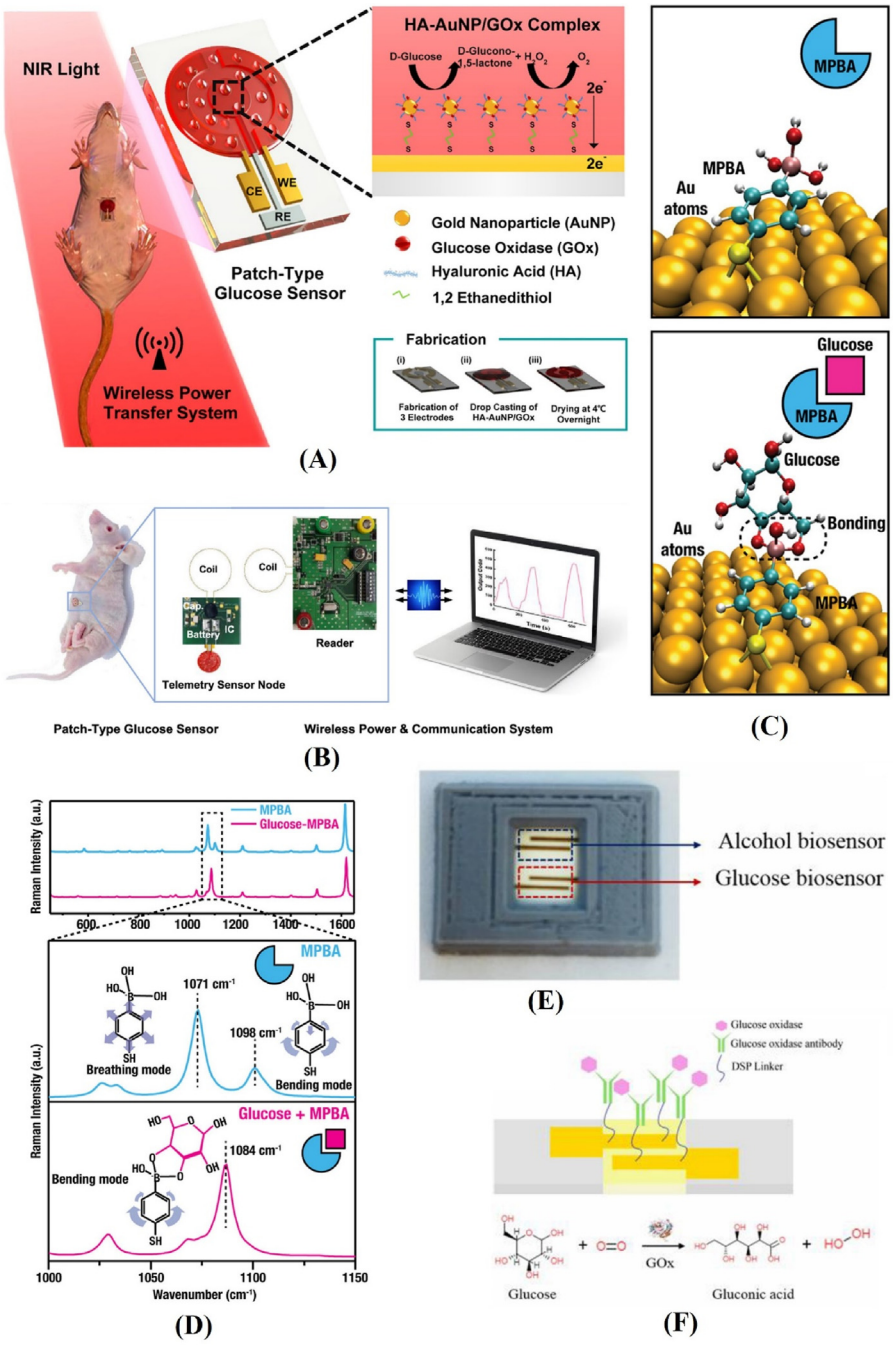

Fig. 8. (A) Diagram of HA− AuNP/glucose oxidase (GOx) wireless patch-type glucose sensor for noninvasive sweat glucose monitoring. **(B)** The HA−AuNP/GOx complex patch-type glucose sensor's wireless power transmission systems. Reproduced with permission from Ref. [107]. **(C)** Reviewing (OH−) DFT-simulation geometries -MPBA's Raman-peak-shifting mechanism before and after glucose binding **(D)** SERS spectra of MPBA presenting the C−Stretching-coupled C-ring-breathing mode at 1071 cm^{-1}. Reproduced with permission from Ref. [113]. **(E)** Combinatorial biosensor diagram. **(F)** Diagram of improved immunoassays for synthesized sweat alcohol and glucose detection. Reproduced with permission from Ref. [114].

1–500 × 10^{-6} m. Other researchers have used Au nanostar@SiO_2 core-shell with GOD as a SERS sensor for detecting glucose with a detection limit of 16 × 10^{-6} m. in the range of 0.025–25 × 10^{-3} m. Other chemical compounds such as 4-cyanophenylboronic acid, 4-mercaptophenylboronic acid, and phenylboronic acid were also used for detecting glucose with detection limits of 0.01 × 10^{-6} m, 0.01 × 10^{-6} m, and 16 × 10^{-6} m, respectively. These sensors have high selectivity and sensitivity due to their unique nanostructure and the specific chemical compounds they incorporate [108–112].

By following the glucose-stimulated shift in the SERS emission of mercapto phenylboronic acid (MPBA), researchers showed fast glucose sensing in the range from 0.1 to 30 mM. Here, under the binding of glucose to MPBA (Fig. 8C), the peak changes from 1071 to 1084 cm^{-1}. Also, due to the fact that the link between MPBA and glucose may be broken, constant measurement of the surrounding glucose levels, which can enable long-term glucose control, is now possible. This conventional glucose sensor was used to monitor intraocular glucose in rabbit eyes to an accuracy of 0.5 mM using miniature Raman-mode SERS implants. The SERS spectra of MPBA were simulated in the vicinity of bonded glucose and are shown in Fig. 8D. The thiol group of MPBA binds to the Au substrate, and the hydroxyl group of glucose reacts with the hydroxyl group of MPBA to form a covalent link [113].

3. Remote, online, real-time, and wearable biosensor devices for glucose self (*in situ*)-Monitoring

The treatment for diabetes relies heavily on accurate glucose monitoring, but traditional methods like insulin injections and frequent blood collection can be painful, stressful, and carry additional health risks. As a result of this, there is an ever-increasing need for glucose monitoring

tools that do not require the use of needles but are nevertheless simple, portable, and user-friendly. Wearable devices like headbands or wristbands that provide comfortable, non-invasive monitoring can greatly improve diabetes management. Such devices should also include specific features and functions to facilitate their use in managing diabetes. For instance, the first challenge in the way of wearable biosensors can be the electrode surface. Although the whole electrode's composition is so influential, the importance of the outer layer is much more significant. The porous surfaces such as nanoporous gold, graphitic nanocarbon structures, and nanoporous graphene can be incorporated into the transducer to enhance the sensitivity of the sensor and its signals by increasing the bioreceptor loading capability and electron transfer area. Biomolecules or biomarkers cannot be continuously monitored through wearable sensors owing to some limitations, the most important one is biofouling. Biofouling occurs by covering the sensor surface with unwanted biological components such as lipids and proteins. In most cases, this accumulated surface loses its readability, selectivity, and sensitivity which leads to inaccurate results. Different attempts for addressing this issue have been developed, one of which is antifouling biosensor construction that prevents adhesion of unwanted biomolecules on the sensor's surface. Coating the sensor surface with different Anti-biofouling protective polymers and hydrogels like serum albumin, Nafion, polyvinyl chlorides, and chitosan for prevention of gradual surface passivation are vastly studied but all biomarkers need their own optimized coating agents. Another concern can be system-level considerations that are momentous for ensuring the analyte monitoring (on-body) by wearable systems. Sustainable powering, wireless communication, data collection, and curation, and *in situ* sensing should be carefully considered during the wearable sensor design [115–117].

There is a demand for devices that can continuously and accurately measure glucose levels in the body. Conventional methods of glucose monitoring, like injection and blood collection, can be painful and carries some risks. Wearable nanosensors have the potential to provide continuous and detailed data on the state of health of a patient, including data on the molecular level. However, wearable sensors provide limited data on complex physiological processes. A prototype model that combines a wireless printed circuit board with multiple sensors could be used to monitor various circumstances of a physiological aspect, including skin temperature and salt content of perspiration. Researchers are also developing noninvasive sensors that can monitor biomolecule levels by analyzing skin, tears, and sweat [118–120]. The development of wearable and touchable glucose sensors requires interdisciplinary collaboration from fields such as chemistry, electronics, physics, medicine, materials science, and engineering to provide actionable and useful information for diabetic individuals [121–124].

Sweat is becoming an interesting alternative for glucose detection due to traditional blood glucose testing difficulties [125]. However, collecting and analyzing sweat also presents its own challenges, such as lactic acid presence, temperature changes, and enzyme damage from skin friction and deformation. Researchers have developed wearable patch devices as the solution; these devices use soft bioelectronics to accurately detect ultra-trace amounts of glucose in sweat in real-time. The patches also offer the added advantage of delivering drugs through microneedles. The patch designs focus on creating a robust multilayer structure and minimizing functional components in the sensor layout. The active glucose oxidase enzyme is immobilized on a porous gold fabric electrode using a simple drop-casting method. The patch uses electrochemical signals to continuously monitor and detect sweat glucose in a real-time [126]. A wearable sensor patch that can stretch with the body's movement is being developed to collect sweat directly from the skin surface effectively. The compact, disposable strip design makes it easy to wear and measures sweat glucose. Multi-functional devices capable of monitoring glucose levels and delivering insulin through microneedles are an area of increasing interest. These devices take precise glucose measurements in sweat to deliver a precisely calibrated insulin dose through microneedles attached to the adhesive patch.

Researchers have been exploring ways to use low-cost, small IoT platforms for personalizing health and diabetes monitoring. The research field of non-invasive glucose sensor wearable devices is one example. One proposed method uses a thin zinc oxide layer on a flexible substrate as a non-invasive glucose sensor. This device can continuously measure glucose levels between 0.01 and 50 mg/dL with high accuracy in a both synthetic and real sweat. Another approach is an electrochemical sensor made of flexible stainless steel modified with platinum nanoparticles for continuous glucose detection. This device uses an electrochemical analysis circuit, microcontroller, and wireless connection to achieve non-enzymatic, continuous glucose sensing. It allows remote monitoring for managing chronic disease and promoting wellness via controlling glucose levels in real-time (Fig. 8E and F) [114,127].

Small, skin-like wearable devices with the capability of precise glucose monitoring are already commercially accessible. One example is the GlucoWatch biographer, a miniaturized device that non-invasively measures glucose levels through the skin, utilizing a reverse ionic spray and a sensor that uses an amperometric method. This device can be worn for up to 12 h and effectively manages severe and long-term diabetes. Though, newer wearable devices have been developed that incorporate nanoscale sensory systems that can be activated with a simple finger touch to improve the configuration and management of diabetes postponing the development of problems without raising the risk of hypoglycemic episodes [128].

3.1. *Transdermal glucose monitoring*

Researchers have developed a wrist-mounted sensor that can detect and measure glucose levels in sweat by creating a thin, stretchable, and waterproof film sensor. The sensor uses graphene-doped gold nanoparticles and is modified with a Nafion fluoropolymer patch, resulting in a highly sensitive electrochemical signal when detecting glucose. This non-invasive wearable patch provides a strong electrical signal indicating glucose levels, allowing for effective blood sugar management in the body. Additionally, this patch can perform a dual function, determining glucose concentrations in sweat samples and providing accurate insulin delivery for diabetes management through a touchable skin patch [129].

Researchers have developed wearable sensors to accurately detect glucose levels in sweat. These compact patches have pH and temperature sensors. These may be used to monitor glucose levels optically and are constructed of a combination of gold-doped graphene and a serpentine gold mesh. Daily glucose levels may be monitored thanks to the device's Bluetooth connectivity with other devices. Another emerging patch utilizes layers of 1 mm tall polymer-shaped microneedle-coated tridecanoic acid to release the appropriate dosage of diabetes medication through the skin. Regarding daily glucose monitoring, these patches may send analytical findings to mobile devices like smartphones. Moreover, a wearable wireless sensing device that can selectively and concurrently assess sweat glucose and electrolytes has been created through electrochemical means, providing real-time analysis and precise information on sweat glucose levels during indoor and outdoor physical activities [129].

Using perspiration as a non-invasive way for measuring glucose levels is one method, it is widely available and easily accessible throughout the body, and the glucose levels in sweat closely reflect those in the blood. Because of this, several different types of wearable glucose monitors have been created. These include colorimetric sensors, widely used for basic monitoring of glucose levels and work by measuring changes in color that occur when glucose is present. Additionally, more advanced electrochemical sensors have been developed, such as "tattoo-like" devices or smart wristbands designed for fast and quantitative glucose measurement through changes in electrical signals at different concentrations. These sensors work by using an electrode to detect the electrical current produced by glucose in sweat, which results in a signal that can be easily read and analyzed by an electronic device [121,130–133]. Lipani et al. introduced a pathway-selective (various glucose pathways are illustrated in Fig. 9A), a transdermal, and non-invasive graphene-based platform for

monitoring the glucose level (the correlation among array pixel and follicles number is shown in Fig. 9B). They found that the preferential pathway is the follicular path and their developed system illustrated quantized Glucose level detection. In addition, they clearly demonstrated the non-follicular and follicular glucose extraction fluxes quantification. Also, they assessed healthy human blood sugar (interstitial fluid-borne glucose) continuously with pixel array (Fig. 9C and D) [134].

A study led by Lipani et al. has discovered a non-invasive way to measure glucose levels by utilizing a miniaturized sensor array. The sensor works by sensing glucose through the pathways found in the skin,

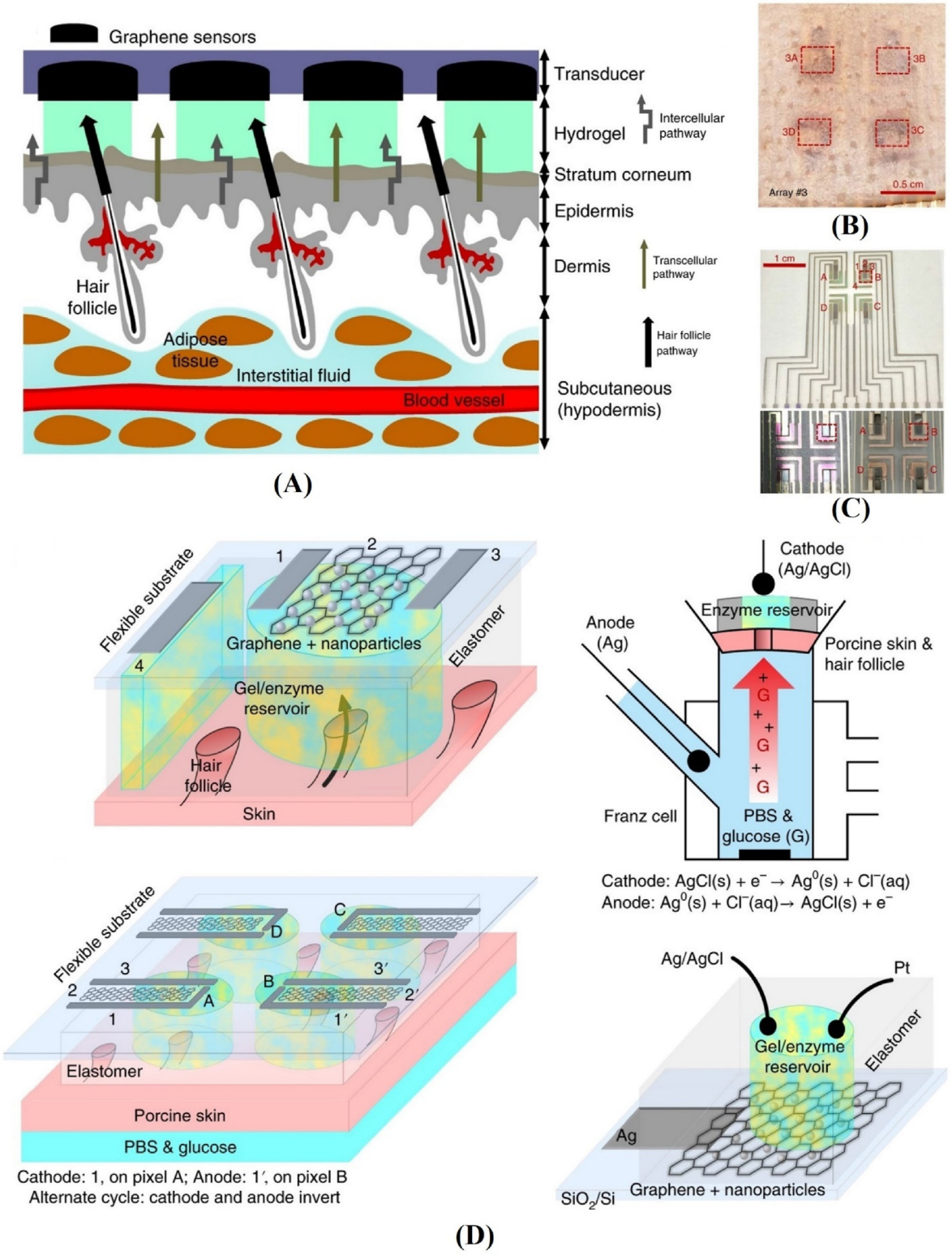

Fig. 9. **(A)** Various glucose pathways. **(B)** Visual correlation among each array pixel and follicle number. **(C)** The complete layout for array realization. **(D)** Generic individual miniature pixel and Deconstructed, 3D pixel configuration and *ex vivo* 2 × 2 Planar array with flexible substrate. Reproduced with permission from Ref. [134].

ex vivo in mammals, and it can measure a broad variety of glucose levels in humans. The sensor relies on optoelectronic systems, enabling it to function without electrical power or wired connections. This makes it convenient for use at home and in a clinical setting. The research also suggested the possibility of using the sensor alongside microneedle-based drug delivery, providing a less invasive way to monitor glucose and manage diabetes [135,136].

A team of researchers developed a new type of flexible, skin-like biosensor that uses a paper battery to detect glucose levels in intravascular hemolysis. Glucose is brought to the skin's surface by reverse iontophoresis after hyaluronic acid has been absorbed into the interstitial fluid via the device. The device works by raising the osmotic pressure in the interstitial fluid, allowing intravascular glucose and excess glucose samples to be refiltered from the vessel onto the skin surface and detected by the biosensor. The biosensor consists of multiple layers, including a 1 mm immobilization layer of glucose oxidase, a 51.8 nm electrochemical nanoscale transducer layer, polymethyl methacrylate, polyimide, and a 100 nm thin layer of gold, mimicking the properties of skin for more accurate glucose detection [137].

The levels of glucose in the blood can now be tracked using a newly designed gadget, and deliver insulin in a single, cost-effective, user-friendly device. This catheter-based system, developed by Matsumoto and the team, uses a synthetic gel-based polymer that responds to sugar by releasing insulin when the polymer detects glucose levels. This device was tested on healthy and diabetic mice implanted under the skin. It showed promising glucose monitoring and insulin delivery results for cases of insulin resistance or deficiency [138].

3.2. Noninvasive human tear glucose wearable biosensors

The use of tears as a non-invasive method for monitoring glucose levels in the body is gaining popularity due to its ease of collection and close correlation with blood glucose levels. Tear collection can be happened by various techniques but the most promising one is utilizing a sensor in a place that always be in direct contact with tears. In this regard, researchers have developed smart contact lenses with built-in sensors that can detect glucose levels using amperometric analysis with the enzyme glucose oxidase. The sensor is housed within a flexible, permeable membrane to provide a comfortable and discreet means of monitoring glucose levels in real time. An early version of this technology was tested in rabbits, which were very sensitive to glucose while blocking out other compounds in the tear fluid. In addition, the sensors have been equipped with wireless communication chips, allowing the data to be transmitted to external devices for continuous monitoring and management of diabetes [139–142]. Although smart contact lenses can detect the level of glucose from tear fluid that is closely correlated with blood, it demonstrated a 20-min delay. Scientists have classified smart contact lenses into three subcategories **1:** electrochemical contact lenses which utilize electrochemical sensors for the detection of glucose levels. The optimized design of these sensors is integrating the sensors on the outer part of lenses which any change in the level of the glucose leads to a change in the electrical current and this data can be wirelessly sent to the installed software on the smart watches, cell phones, and computers. **2:** Light-diffractive smart contact lenses that use photonic crystals (2D or 3D) which can detect the level of glucose. The various levels of glucose can lead to changes in the photonic crystals' structures followed by shifting in diffracted wavelengths. If the shift were large enough, it would be vivid and can be seen by the naked eye, otherwise, the data should be analyzed by software on smart devices. **3:** Last but not least can be fluorescent-based smart contact lenses which are equipped with fluorescent glucose sensors. These types of smart contact lenses like some other types have the ability of continuous detection utilizing tear fluid. The change in glucose level will lead to fluorescence color change and it needs smart devices to detect the exact level. The development of smart glucose-sensing eye drops can be the most promising technology. These types of sensors do not need any expensive hardware- and software for the detection of the level of glucose. The development of ratio-metric eye drops which can be responsive to trace amounts of glucose changing are a hot topic. A wide range of color changes which can demonstrate various levels of glucose level in daylight and fluorescent at night can save the patient's life by fast detection of high blood sugar levels.

Jeon et al., 2021 developed a nanoparticle-embedded smart contact lens for tear glucose level optical assessment which is illustrated in Fig. 10A. Their engineered camera-based optical monitoring system could detect the glucose level without any special electronic component. The sensing mechanism is schematically illustrated in Fig. 10B. Another plus point of their study would be proposing the algorithm for image processing which had the ability to optimize the accuracy of the measurements in various situations. They also successfully assessed the *in vivo* tear samples which illustrated the high correlation between measured glucose levels through various techniques and proved their designed sensor's quantitative efficacy (Fig. 10C) [143].

4. Advanced point-of-care glucose-level control

The field of glucose monitoring is continually evolving, focusing on creating low-cost, portable devices that can provide continuous monitoring. To achieve this goal, researchers have explored various approaches, such as using building blocks to improve sensor function, reliability, and cost-effectiveness, and nanoscale and biosensor technologies for simultaneous, noninvasive observing of glucose concentrations in different physiological fluids. These advancements in sensor design, including miniaturization, improved accuracy, and integration into wearable devices, provide hope for a significant improvement in diabetic care. Additionally, Improving the evaluation and therapy of diabetes may be aided by the creation of skin-like, flexible, and low-power nanosensors that can identify glucose in diverse samples.

Various strategies have been presented for adapting a PGM (glucose measuring system) for use in alternative lab procedures. Most of these methods involve using a glucose-loaded nanocarrier or glucose-generating enzyme released upon binding to a target. However, other sensing mechanisms have also been explored. Employing synthetic substrates eaten by a target enzyme is one such approach; this may either lead to the release of glucose or the creation of intermediates that are subsequently transformed into glucose by a second enzyme. This method has been used to detect enzymes like α-mannosidase, alkaline phosphatase, b-D-galactosidase, galactose-1-phosphate uridyltransferase, and α-amylase. Additionally, As shown with *E. coli* and influenza virus H1N1, one may deduce the concentration of the pathogen based on the function of the targeted enzyme, which must be found on the outer layer of the pathogen for this to be possible. Additionally, some researchers have expanded the range of substrates used in these assays, exploring the response of PGMs to other substances like galactose, catechol, acetaminophen, and NADH [144–148]. Another method for detecting pathogens using PGMs is based on monitoring glucose consumption by bacterial metabolism. The rate at which glucose decreases as time passes may be used as a proxy for bacterial concentration or as an indicator of the effectiveness of disinfectants or other contaminants in water samples. Additionally, some researchers have combined nucleic acid amplification techniques with PGMs to detect DNA, mercury ions, and the enzyme telomerase. These systems typically involve an initial step of nucleic acid amplification, followed by detecting the amplified nucleic acid through enzymatic transduction, using either a competitive or sandwich assay. Incredibly low detection limits are possible with this technology, although it often necessitates longer response times [149–152].

5. Conclusion

Wearable smart monitoring technologies for healthcare provide several potential and problems despite tremendous progress in the sector. One major challenge is the need for more advanced material preparation methods and techniques to create and design sensors, electrodes, and

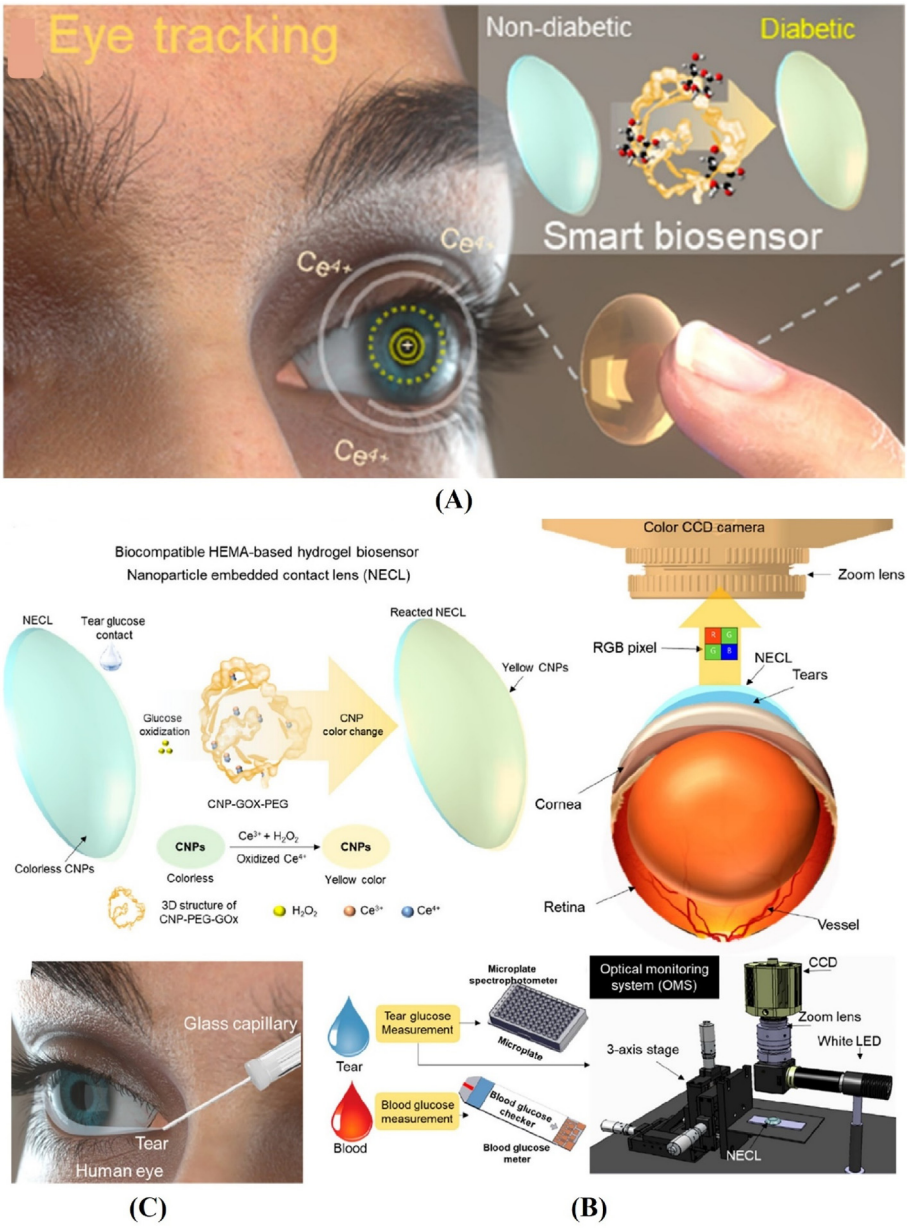

Fig. 10. **(A)** Nanoparticles assisted smart biosensor illustration. **(B)** Schematic illustration of optical monitoring system and colorimetric nanoparticle embedded contact lens. **(C)** human blood and tear glucose level analysis for healthy patients by microplate spectrophotometers, blood glucose meter, and optical monitoring system. Reprinted with permission from Ref. [143]. copyright 2021. American Chemical Society.

substrates for integrated monitoring systems that are high-performance attributable to their custom architectures and multi-functional components. For example, Elemental doping, polarization, and other methods can be used to boost the ferroelectric property of piezoelectric sensors; electrode conductivity can be increased through structure tailoring (including wrinkle structure and crystal modification); and porous substrates can be crafted to make supporting materials more flexible and air permeable. Another challenge in developing wearable smart monitoring devices is the need for subtle sensing mechanisms that can detect different physiological signals. This is very necessary for the prompt identification of illnesses. To this end, researchers are exploring and utilizing sensor materials with multiple functions. For example, using materials that exhibit both piezoelectric and pyroelectric effects can provide simultaneous information on pressure and temperature, allowing for multi-mode health monitoring. Another important aspect of developing wearable smart monitoring devices is the integration of health sensors into a single intelligent wireless system. This system should include storage, calculation, data collection, and display components, with a clear and easy-to-read output signal. This would make it possible for continuous, real-time health assessment. Additionally, Future advancements in the area of health-tracking devices are anticipated to focus on introducing self-powered and self-healing qualities into the measuring device in accordance with the present environmental development plan. Lastly, designing implantable physiological monitors that are comfortable, fashionable and can be integrated into clothes or worn as wristbands or smartwatches is a crucial development direction for health monitors. The devices should have excellent flexibility, durability, breathability, and water-resistance properties to achieve this. Not only the data processing and displaying platforms should be robust and user-friendly, but also utilizing modern data analysis methods like machine learning patterns which can predict and interpret algorithms of long-term measurements will aid better and more accurate identifications.

Author's contributions

M.S., A.A., G.H., E.N.Z., M.E.W., O.A., Y.S.H., and N.R. wrote the main manuscript, conceptualized, and finalized the manuscript. All authors reviewed and approved the manuscript.

Declaration of competing interest

All authors declare that there are no competing interests.

Acknowledgment

This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean Government (MSIT) (No. 2022M3J7A1062940, 2021R1A5A6002853, and 2021R1A2C3011585). This work was also supported by the Technology Innovation Program (20015577) funded by the Ministry of Trade, Industry & Energy (MOTIE, Korea).

References

[1] C.F. Markwalter, et al., Inorganic complexes and metal-based nanomaterials for infectious disease diagnostics, Chem. Rev. 119 (2) (2019) 1456–1518.
[2] W. Schweitzer, et al., Implications for forensic death investigations from first Swiss post-mortem CT in a case of non-hospital treatment with COVID-19, Forensic Imaging 21 (2020 Jun) 200378, https://doi.org/10.1016/j.fri.2020.200378. Epub 2020 Apr 18.
[3] A.D. Association, Diagnosis and classification of diabetes mellitus, Diabetes Care 32 (Supplement_1) (2009) S62–S67.
[4] N.H. Cho, et al., IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045, Diabetes Res. Clin. Pract. 138 (2018) 271–281.
[5] L. Guariguata, Contribute data to the 6th edition of the IDF diabetes atlas, Diabetes Res. Clin. Pract. 100 (2) (2013) 280–281.
[6] T. Deckert, J.E. Poulsen, Diabetic nephropathy: fault or destiny? Diabetologia 21 (3) (1981) 178–183.
[7] E.R. Seaquist, et al., Familial clustering of diabetic kidney disease. Evidence for genetic susceptibility to diabetic nephropathy, N. Engl. J. Med. 320 (18) (1989) 1161–1165.
[8] K. Earle, et al., Familial clustering of cardiovascular disease in patients with insulin-dependent diabetes and nephropathy, N. Engl. J. Med. 326 (10) (1992) 673–677.
[9] D. Nathanson, et al., Healthcare cost development in a type 2 diabetes patient population on glucose-lowering drug treatment: a nationwide observational study 2006-2014, Pharmacoecon Open 2 (4) (2018) 393–402.
[10] Y. Zhu, et al., Flexible biosensor based on signal amplification of gold nanoparticles-composite flower clusters for glucose detection in sweat, Colloids Surf. A Physicochem. Eng. Asp. 661 (2023) 130908.
[11] M. Li, et al., Coaxial electrospinning synthesis of size-tunable CuO/NiO hollow heterostructured nanofibers: towards detection of glucose level in human serum, Colloids Surf. B Biointerfaces 222 (2023) 113047.
[12] Y. Yuan, et al., Investigation for terminal reflection optical fiber SPR glucose sensor and glucose sensitive membrane with immobilized GODs, Opt Express 25 (4) (2017) 3884–3898.
[13] M. Jing, M.T. Bowser, Methods for measuring aptamer-protein equilibria: a review, Anal. Chim. Acta 686 (1–2) (2011) 9–18.
[14] M. Pohanka, Overview of piezoelectric biosensors, immunosensors and DNA sensors and their applications, Materials 11 (3) (2018) 448.
[15] S. Laha, et al., A concise and systematic review on non-invasive glucose monitoring for potential diabetes management, Biosensors 12 (11) (2022) 965.
[16] J.D. Yuen, et al., A fully-flexible solution-processed autonomous glucose indicator, Sci. Rep. 9 (1) (2019) 6931.
[17] E. Scarpa, et al., Wearable piezoelectric mass sensor based on pH sensitive hydrogels for sweat pH monitoring, Sci. Rep. 10 (1) (2020) 10854.
[18] P. Kanokpaka, et al., Enabling glucose adaptive self-healing hydrogel based triboelectric biosensor for tracking a human perspiration, Nano Energy 112 (2023) 108513.
[19] G. Yang, et al., A self-powered closed-loop brain-machine-interface system for real-time detecting and rapidly adjusting blood glucose concentration, Nano Energy 93 (2022) 106817.
[20] P. Zhong, et al., Piezoelectric sensing of glucose oxidase activity of Aspergillus Niger spores pretreated by different methods, Food Chem. 370 (2022) 130901.
[21] W. Zhang, et al., Self-powered implantable skin-like glucometer for real-time detection of blood glucose level in vivo, Nano-Micro Lett. 10 (2) (2018) 32.
[22] B.J. Brownlee, et al., Electrochemical glucose sensors enhanced by methyl viologen and vertically aligned carbon nanotube channels, ACS Appl. Mater. Interfaces 10 (34) (2018) 28351–28360.
[23] L.C. Clark Jr., C. Lyons, Electrode systems for continuous monitoring in cardiovascular surgery, Ann. N. Y. Acad. Sci. 102 (1962) 29–45.
[24] A.E.G. Cass, et al., Ferrocene-mediated enzyme electrode for amperometric determination of glucose, Anal. Chem. 56 (4) (1984) 667–671.
[25] P. D'Orazio, Biosensors in clinical chemistry, Clin. Chim. Acta 334 (1–2) (2003) 41–69.
[26] J.D. Newman, A.P. Turner, Home blood glucose biosensors: a commercial perspective, Biosens. Bioelectron. 20 (12) (2005) 2435–2453.
[27] A. Riklin, et al., Improving enzyme-electrode contacts by redox modification of cofactors, Nature 376 (6542) (1995) 672–675.
[28] Y. Degani, A. Heller, Direct electrical communication between chemically modified enzymes and metal electrodes. I. Electron transfer from glucose oxidase to metal electrodes via electron relays, bound covalently to the enzyme, J. Phys. Chem. 91 (6) (1987) 1285–1289.
[29] M.V. Pishko, et al., Direct electrical communication between graphite electrodes and surface adsorbed glucose oxidase/redox polymer complexes, Angew. Chem., Int. Ed. Engl. 29 (1) (1990) 82–84.
[30] Q. Wa, et al., Nanoscale Ni(OH)x films on carbon cloth prepared by atomic layer deposition and electrochemical activation for glucose sensing, ACS Appl. Nano Mater. 2 (7) (2019) 4427–4434.
[31] M. Wang, et al., In situ growth of Ni-B nanoparticles on Ni foam: an efficient 3D integrated anode for enzyme-free glucose detection, J. Alloys Compd. 786 (2019) 530–536.
[32] Z. Zhao, et al., Nonenzymetic glucose sensitive device based on morchella shaped nickel-copper layered double hydroxide, Appl. Surf. Sci. 597 (2022) 153658.
[33] W. Lu, et al., Ni foam: a novel three-dimensional porous sensing platform for sensitive and selective nonenzymatic glucose detection, Analyst 138 (2) (2013) 417–420.
[34] C. Li, et al., A novel amperometric biosensor based on NiO hollow nanospheres for biosensing glucose, Talanta 77 (1) (2008) 455–459.
[35] J. Ding, et al., Electrodeposition of nickel nanostructures using silica nanochannels as confinement for low-fouling enzyme-free glucose detection, J. Mater. Chem. B 8 (16) (2020) 3616–3622.
[36] C. Guo, et al., Non-enzymatic glucose sensor based on three dimensional nickel oxide for enhanced sensitivity, Anal. Methods 5 (2013) 1644–1647.
[37] M. Sg, et al., Fabrication of cerium oxide and β-Ni (OH) 2 nano hexagonal architectures assembled on reduced graphene oxide for non-enzymatic electrochemical detection of glucose, Ionics 28 (4) (2022) 1957–1972.
[38] M. Wang, et al., Ultra-sensitive non-enzymatic glucose sensor based on Ni/Au bilayer nanowire arrays, J. Electron. Mater. 51 (5) (2022) 2490–2499.
[39] S. Ci, et al., NiO-microflower formed by nanowire-weaving nanosheets with interconnected Ni-network decoration as supercapacitor electrode, Sci. Rep. 5 (1) (2015) 11919.
[40] N. Akhtar, et al., One-pot fabrication of dendritic NiO@carbon-nitrogen dot electrodes for screening blood glucose level in diabetes, Adv. Healthcare Mater. 4 (14) (2015) 2110–2119.
[41] Z.H. Ibupoto, et al., Glycine-assisted synthesis of NiO hollow cage-like nanostructures for sensitive non-enzymatic glucose sensing, RSC Adv. 5 (24) (2015) 18773–18781.
[42] N. Pal, S. Banerjee, A. Bhaumik, A facile route for the syntheses of Ni(OH)(2) and NiO nanostructures as potential candidates for non-enzymatic glucose sensor, J. Colloid Interface Sci. 516 (2018) 121–127.
[43] R.A. Soomro, et al., Electrochemical sensing of glucose based on novel hedgehog-like NiO nanostructures, Sensor. Actuator. B Chem. 209 (2015) 966–974.
[44] J. Vilana, et al., Electrochemical deposition of CoNi micro/nanostructures as new materials for electrochemical sensing of glucose, Mater. Lett. 159 (2015) 154–158.
[45] R. Prasad, B.R. Bhat, Multi-wall carbon nanotube–NiO nanoparticle composite as enzyme-free electrochemical glucose sensor, Sensor. Actuator. B Chem. 220 (2015) 81–90.
[46] H. Mizuguchi, et al., A flow-based enzyme-free biosensor fabricated using track-etched membrane electrodes: selective and sensitive detection of uric acid, Sensor. Actuator. B Chem. 383 (2023) 133588.
[47] R. Ahmad, Y.-B. Hahn, Nonenzymatic flexible field-effect transistor based glucose sensor fabricated using NiO quantum dots modified ZnO nanorods, J. Colloid Interface Sci. 512 (2018) 21–28.
[48] D.-U.-J. Jung, R. Ahmad, Y.-B. Hahn, Nonenzymatic flexible field-effect transistor based glucose sensor fabricated using NiO quantum dots modified ZnO nanorods, J. Colloid Interface Sci. 512 (2018) 21–28.
[49] D. Pradhan, F. Niroui, K.T. Leung, High-performance, flexible enzymatic glucose biosensor based on ZnO nanowires supported on a gold-coated polyester substrate, ACS Appl. Mater. Interfaces 2 (8) (2010) 2409–2412.
[50] M. Long, et al., Novel helical TiO2 nanotube arrays modified by Cu2O for enzyme-free glucose oxidation, Biosens. Bioelectron. 59 (2014) 243–250.
[51] G. Li, et al., Dual structural design of platinum-nickel hydrogels for wearable glucose biosensing with ultrahigh stability, Small 19 (16) (2023) 2206868.
[52] B. Li, et al., Emerging multifunctional metal-organic framework materials, Adv. Mater. 28 (40) (2016) 8819–8860.
[53] Z. Zhang, et al., Fe(III)-based metal-organic framework-derived core-shell nanostructure: sensitive electrochemical platform for high trace determination of heavy metal ions, Biosens. Bioelectron. 94 (2017) 358–364.
[54] F. Wang, et al., High-performance non-enzymatic glucose sensor by hierarchical flower-like nickel(II)-based MOF/carbon nanotubes composite, Mater. Sci. Eng. C 96 (2019) 41–50.
[55] M. Lu, et al., Core-shell MOF@MOF composites for sensitive nonenzymatic glucose sensing in human serum, Anal. Chim. Acta 1110 (2020) 35–43.
[56] Q. Balouch, et al., Cobalt oxide nanoflowers for electrochemical determination of glucose, J. Electron. Mater. 44 (10) (2015) 3724–3732.
[57] S.-J. Li, et al., Electrodeposition of cobalt oxide nanoparticles on reduced graphene oxide: a two-dimensional hybrid for enzyme-free glucose sensing, J. Solid State Electrochem. 18 (4) (2014) 1049–1056.

[58] F. Xie, et al., Cobalt nitride nanowire array as an efficient electrochemical sensor for glucose and H2O2 detection, Sensor. Actuator. B Chem. 255 (2018) 1254–1261.
[59] Q. Wang, et al., One-step synthesis of Co(OH)F nanoflower based on micro-plasma: as an effective non-enzymatic glucose sensor, Sensor. Actuator. B Chem. 304 (2020) 127282.
[60] M. Huang, et al., Hierarchical Co(OH)2 nanotube arrays grown on carbon cloth for use in non-enzymatic glucose sensing, Anal. Methods 9 (40) (2017) 5903–5909.
[61] H. Xu, et al., Electrochemical non-enzymatic glucose sensor based on hierarchical 3D Co3O4/Ni heterostructure electrode for pushing sensitivity boundary to a new limit, Sensor. Actuator. B Chem. 267 (2018) 93–103.
[62] S. Mondal, R. Madhuri, P.K. Sharma, Probing the shape-specific electrochemical properties of cobalt oxide nanostructures for their application as selective and sensitive non-enzymatic glucose sensors, J. Mater. Chem. C 5 (26) (2017) 6497–6505.
[63] Y. Zhong, et al., Ultrasensitive non-enzymatic glucose sensors based on different copper oxide nanostructures by in-situ growth, Sensor. Actuator. B Chem. 236 (2016) 326–333.
[64] Z. Yang, et al., Copper oxide nanoleaves decorated multi-walled carbon nanotube as platform for glucose sensing, Anal. Methods 4 (7) (2012) 1924–1926.
[65] R. Ahmad, et al., Highly efficient non-enzymatic glucose sensor based on CuO modified vertically-grown ZnO nanorods on electrode, Sci. Rep. 7 (1) (2017) 5715.
[66] Z. Haghparas, et al., Highly sensitive non-enzymatic electrochemical glucose sensor based on dumbbell-shaped double-shelled hollow nanoporous CuO/ZnO microstructures, Sci. Rep. 11 (1) (2021) 344.
[67] W. Na, et al., Highly sensitive copper nanowire conductive electrode for nonenzymatic glucose detection, J. Ind. Eng. Chem. 69 (2019) 358–363.
[68] Y. Zhang, et al., Ultrasensitive and selective non-enzymatic glucose detection using copper nanowires, Biosens. Bioelectron. 31 (1) (2012) 426–432.
[69] J. Ye, et al., Well-aligned Cu@C nanocubes for highly efficient nonenzymatic glucose detection in human serum, Sensor. Actuator. B Chem. 305 (2020) 127473.
[70] Y. Song, et al., Ratiometric electrochemical glucose biosensor based on GOD/AuNPs/Cu-BTC MOFs/macroporous carbon integrated electrode, Sensor. Actuator. B Chem. 257 (2018) 792–799.
[71] X. Wang, et al., An ultrasensitive non-enzymatic glucose sensors based on controlled petal-like CuO nanostructure, Electrochim. Acta 259 (2018) 225–232.
[72] P. Arul, S. Abraham John, Electrodeposition of CuO from Cu-MOF on glassy carbon electrode: a non-enzymatic sensor for glucose, J. Electroanal. Chem. 799 (2017) 61–69.
[73] X. Zhang, et al., Ultrasensitive binder-free glucose sensors based on the pyrolysis of in situ grown Cu MOF, Sensor. Actuator. B Chem. 254 (2018) 272–281.
[74] M. Shamsipur, et al., Highly sensitive non-enzymatic electrochemical glucose sensor by Nafion/SBA-15-Cu (II) modified glassy carbon electrode, J. Electroanal. Chem. 799 (2017) 406–412.
[75] B. Zheng, et al., A sensitive AgNPs/CuO nanofibers non-enzymatic glucose sensor based on electrospinning technology, Sensor. Actuator. B Chem. 195 (2014) 431–438.
[76] Z. Yu, et al., Hydrothermal synthesis of Fe2O3/graphene nanocomposite for selective determination of ascorbic acid in the presence of uric acid 158 (2015) 264–270.
[77] S. Felix, A.N. Grace, R. Jayavel, Sensitive electrochemical detection of glucose based on Au-CuO nanocomposites, J. Phys. Chem. Solid. 122 (2018) 255–260.
[78] K. Dhara, et al., Pt-CuO nanoparticles decorated reduced graphene oxide for the fabrication of highly sensitive non-enzymatic disposable glucose sensor, Sensor. Actuator. B Chem. 195 (2014) 197–205.
[79] B. Haghighi, et al., Fabrication of a nonenzymatic glucose sensor using Pd-nanoparticles decorated ionic liquid derived fibrillated mesoporous carbon, Mater. Sci. Eng., C 52 (2015) 219–224.
[80] S. Nantaphol, et al., Bimetallic Pt-Au nanocatalysts electrochemically deposited on boron-doped diamond electrodes for nonenzymatic glucose detection, Biosens. Bioelectron. 98 (2017) 76–82.
[81] W. Meng, et al., A novel electrochemical sensor for glucose detection based on Ag@ZIF-67 nanocomposite, Sensor. Actuator. B Chem. 260 (2018) 852–860.
[82] M. Li, et al., Electrodeposition of nickel oxide and platinum nanoparticles on electrochemically reduced graphene oxide film as a nonenzymatic glucose sensor, Sensor. Actuator. B Chem. 192 (2014) 261–268.
[83] H. Naeim, et al., Ionic liquid/reduced graphene oxide/nickel-palladium nanoparticle hybrid synthesized for non-enzymatic electrochemical glucose sensing, Electrochim. Acta 282 (2018) 137–146.
[84] P. Li, B. Zhang, T. Cui, Towards intrinsic graphene biosensor: a label-free, suspended single crystalline graphene sensor for multiplex lung cancer tumor markers detection, Biosens. Bioelectron. 72 (2015) 168–174.
[85] S.S. Mahshid, et al., Electrodeposition and electrocatalytic properties of Pt/Ni–Co nanowires for non-enzymatic glucose detection, J. Alloys Compd. 554 (2013) 169–176.
[86] D. Geng, X. Bo, L. Guo, Ni-doped molybdenum disulfide nanoparticles anchored on reduced graphene oxide as novel electroactive material for a non-enzymatic glucose sensor, Sensor. Actuator. B Chem. 244 (2017) 131–141.
[87] Y.J. Zhai, et al., MoS2 microflowers based electrochemical sensing platform for non-enzymatic glucose detection, J. Alloys Compd. 672 (2016) 600–608.
[88] J.M. Jeong, et al., High performance electrochemical glucose sensor based on three-dimensional MoS(2)/graphene aerogel, J. Colloid Interface Sci. 506 (2017) 379–385.
[89] Y.-B. Choi, et al., The electrochemical glucose sensing based on the chitosan-carbon nanotube hybrid, Biochem. Eng. J. 144 (2019) 227–234.
[90] B. Fall, et al., Highly efficient non-enzymatic electrochemical glucose sensor based on carbon nanotubes functionalized by molybdenum disulfide and decorated with nickel nanoparticles (GCE/CNT/MoS2/NiNPs), Sensors and Actuators Reports 5 (2023) 100136.
[91] S. Phetsang, et al., Copper/reduced graphene oxide film modified electrode for non-enzymatic glucose sensing application, Sci. Rep. 11 (1) (2021) 9302.
[92] U. Schwedes, M. Siebolds, G. Mertes, Meal-related structured self-monitoring of blood glucose: effect on diabetes control in non-insulin-treated type 2 diabetic patients, Diabetes Care 25 (11) (2002) 1928–1932.
[93] C. Li, et al., Design of cyclic peptide based glucose receptors and their application in glucose sensing, Anal. Chem. 89 (19) (2017) 10431–10438.
[94] B. Tolaieb, C.J.L. Constantino, R.F. Aroca, Surface-enhanced resonance Raman scattering as an analytical tool for single molecule detection, Analyst 129 (4) (2004) 337–341.
[95] Y. Li, et al., Immobilized optical fiber microprobe for selective and high sensitive glucose detection, Sensor. Actuator. B Chem. 255 (2018) 3004–3010.
[96] B. Luo, et al., Novel glucose sensor based on enzyme-immobilized 81° tilted fiber grating, Opt Express 22 (25) (2014) 30571–30578.
[97] J. Huang, et al., Temperature controlling fiber optic glucose sensor based on hydrogel-immobilized GOD complex, Sensor. Actuator. B Chem. 237 (2016) 24–29.
[98] A. Deep, et al., Immobilization of enzyme on long period grating fibers for sensitive glucose detection, Biosens. Bioelectron. 33 (1) (2012) 190–195.
[99] K.C. Liao, et al., Percutaneous fiber-optic sensor for chronic glucose monitoring in vivo, Biosens. Bioelectron. 23 (10) (2008) 1458–1465.
[100] W. Niu, et al., A chemiluminescence sensor array for discriminating natural sugars and artificial sweeteners, Anal. Bioanal. Chem. 402 (1) (2012) 389–395.
[101] L. Shang, S. Dong, G.U. Nienhaus, Ultra-small fluorescent metal nanoclusters: synthesis and biological applications, Nano Today 6 (4) (2011) 401–418.
[102] M. Moskovits, Surface-enhanced Raman spectroscopy: a brief retrospective, J. Raman Spectrosc. 36 (6–7) (2005) 485–496.
[103] D. Atias, et al., Chemiluminescent optical fiber immunosensor for the detection of IgM antibody to dengue virus in humans, Sensor. Actuator. B Chem. 140 (1) (2009) 206–215.
[104] J.M. Lin, et al., Luminol chemiluminescence in unbuffered solutions with a cobalt(II)-ethanolamine complex immobilized on resin as catalyst and its application to analysis, Anal. Chem. 73 (21) (2001) 5043–5051.
[105] W. Wu, et al., Specific glucose-to-SPR signal transduction at physiological pH by molecularly imprinted responsive hybrid microgels, Biomaterials 33 (29) (2012) 7115–7125.
[106] P.D. Skottrup, M. Nicolaisen, A.F. Justesen, Towards on-site pathogen detection using antibody-based sensors, Biosens. Bioelectron. 24 (3) (2008) 339–348.
[107] S.-K. Kim, et al., Hyaluronate–gold nanoparticle/glucose oxidase complex for highly sensitive wireless noninvasive glucose sensors, ACS Appl. Mater. Interfaces 11 (40) (2019) 37347–37356.
[108] K.V. Kong, et al., Sensitive SERS glucose sensing in biological media using alkyne functionalized boronic acid on planar substrates, Biosens. Bioelectron. 56 (2014) 186–191.
[109] I. Al-Ogaidi, et al., A gold@silica core-shell nanoparticle-based surface-enhanced Raman scattering biosensor for label-free glucose detection, Anal. Chim. Acta 811 (2014) 76–80.
[110] R. Botta, A. Rajanikanth, C. Bansal, Silver nanocluster films for glucose sensing by Surface Enhanced Raman Scattering (SERS), Sens. Bio-Sens. Res. 9 (2016) 13–16.
[111] K.P. Sooraj, et al., SERS based detection of glucose with lower concentration than blood glucose level using plasmonic nanoparticle arrays, Appl. Surf. Sci. 447 (2018) 576–581.
[112] K.V. Kong, et al., A transition metal carbonyl probe for use in a highly specific and sensitive SERS-based assay for glucose, J. Am. Chem. Soc. 135 (48) (2013) 18028–18031.
[113] D. Yang, et al., Glucose sensing using surface-enhanced Raman-mode constraining, Anal. Chem. 90 (24) (2018) 14269–14278.
[114] A. Bhide, S. Muthukumar, S. Prasad, CLASP (Continuous lifestyle awareness through sweat platform): a novel sensor for simultaneous detection of alcohol and glucose from passive perspired sweat, Biosens. Bioelectron. 117 (2018) 537–545.
[115] J.R. Sempionatto, et al., Wearable chemical sensors for biomarker discovery in the omics era, Nat. Rev. Chem 6 (12) (2022) 899–915.
[116] A. Sharma, et al., Wearable biosensors: an alternative and practical approach in healthcare and disease monitoring, Molecules 26 (3) (2021) 748.
[117] Y.-C. Lin, et al., Favoring the selective H2O2 generation of a self-antibiofouling dissolved oxygen sensor for real-time online monitoring via surface-engineered N-doped reduced graphene oxide, ACS Appl. Mater. Interfaces 15 (36) (2023) 42520–42531.
[118] P. Kanokpaka, et al., Self-powered molecular imprinted polymers-based triboelectric sensor for noninvasive monitoring lactate levels in human sweat, Nano Energy 100 (2022) 107464.
[119] Y.-X. Wang, et al., Boron-doped graphene quantum dots anchored to carbon nanotubes as noble metal-free electrocatalysts of uric acid for a wearable sweat sensor, ACS Appl. Nano Mater. 5 (8) (2022) 11100–11110.
[120] Y.-C. Lin, et al., A non-invasive wearable sweat biosensor with a flexible N-GQDs/PANI nanocomposite layer for glucose monitoring, Sensor. Actuator. B Chem. 383 (2023) 133617.
[121] H. Lee, et al., Enzyme-based glucose sensor: from invasive to wearable device, Adv. Healthcare Mater. 7 (8) (2018) 1701150.
[122] M. Dervisevic, et al., Skin in the diagnostics game: wearable biosensor nano- and microsystems for medical diagnostics, Nano Today 30 (2020) 100828.

[123] A.S. Campbell, J. Kim, J. Wang, Wearable electrochemical alcohol biosensors, Curr. Opin. Electrochem. 10 (2018) 126–135.
[124] P. Lorwongtragool, et al., A Novel Wearable Electronic Nose for Healthcare Based on Flexible Printed Chemical Sensor Array 14 (10) (2014) 19700–19712.
[125] Y.-H. Chang, et al., Self-powered triboelectric sensor with N-doped graphene quantum dots decorated polyaniline layer for non-invasive glucose monitoring in human sweat, Nano Energy 112 (2023) 108505.
[126] H. Lee, et al., Wearable/disposable sweat-based glucose monitoring device with multistage transdermal drug delivery module, Sci. Adv. 3 (3) (2017) e1601314.
[127] H. Yoon, et al., Wearable, robust, non-enzymatic continuous glucose monitoring system and its in vivo investigation, Biosens. Bioelectron. 117 (2018) 267–275.
[128] M.J. Tierney, et al., Clinical evaluation of the GlucoWatch biographer: a continual, non-invasive glucose monitor for patients with diabetes, Biosens. Bioelectron. 16 (9–12) (2001) 621–629.
[129] J. Kim, A.S. Campbell, J. Wang, Wearable non-invasive epidermal glucose sensors: a review, Talanta 177 (2018) 163–170.
[130] J. Kim, et al., Noninvasive alcohol monitoring using a wearable tattoo-based iontophoretic-biosensing system, ACS Sens. 1 (8) (2016) 1011–1019.
[131] V.F. Curto, et al., Real-time sweat pH monitoring based on a wearable chemical barcode micro-fluidic platform incorporating ionic liquids, Sensor. Actuator. B Chem. 171–172 (2012) 1327–1334.
[132] H. Lee, et al., A graphene-based electrochemical device with thermoresponsive microneedles for diabetes monitoring and therapy, Nat. Nanotechnol. 11 (6) (2016) 566–572.
[133] A. Koh, et al., A soft, wearable microfluidic device for the capture, storage, and colorimetric sensing of sweat, Sci. Transl. Med. 8 (366) (2016) 366ra165.
[134] L. Lipani, et al., Non-invasive, transdermal, path-selective and specific glucose monitoring via a graphene-based platform, Nat. Nanotechnol. 13 (6) (2018) 504–511.
[135] L. Lipani, et al., Non-invasive, transdermal, path-selective and specific glucose monitoring via a graphene-based platform, Nat. Nanotechnol. 13 (6) (2018) 504–511.
[136] J. Kim, et al., Battery-free, stretchable optoelectronic systems for wireless optical characterization of the skin, Sci. Adv. 2 (8) (2016) e1600418.
[137] Y. Chen, et al., Skin-like biosensor system via electrochemical channels for noninvasive blood glucose monitoring, Sci. Adv. 3 (12) (2017) e1701629.
[138] A. Matsumoto, et al., Synthetic "smart gel" provides glucose-responsive insulin delivery in diabetic mice, Sci. Adv. 3 (11) (2017) eaaq0723.
[139] M.X. Chu, et al., Soft contact lens biosensor for in situ monitoring of tear glucose as non-invasive blood sugar assessment, Talanta 83 (3) (2011) 960–965.
[140] H. Kudo, et al., A flexible and wearable glucose sensor based on functional polymers with soft-MEMS techniques, Biosens. Bioelectron. 22 (4) (2006) 558–562.
[141] H. Yao, et al., A contact lens with embedded sensor for monitoring tear glucose level, Biosens. Bioelectron. 26 (7) (2011) 3290–3296.
[142] Y.T. Liao, et al., A 3-$\mu\hbox{W}$ CMOS glucose sensor for wireless contact-lens tear glucose monitoring, IEEE J. Solid State Circ. 47 (1) (2012) 335–344.
[143] H.-J. Jeon, et al., Optical assessment of tear glucose by smart biosensor based on nanoparticle embedded contact lens, Nano Lett. 21 (20) (2021) 8933–8940.
[144] B.P. Gurale, et al., Indirect detection of glycosidases using amperometry, Anal. Chem. 88 (8) (2016) 4248–4253.
[145] J. Zhang, et al., Low-cost and highly efficient DNA biosensor for heavy metal ion using specific DNAzyme-modified microplate and portable glucometer-based detection mode, Biosens. Bioelectron. 68 (2015) 232–238.
[146] A. Das, et al., Detection of enzymes, viruses, and bacteria using glucose meters, Anal. Chem. 90 (19) (2018) 11589–11598.
[147] X. Cui, et al., Highly specific and rapid glycan based amperometric detection of influenza viruses, Chem. Sci. 8 (5) (2017) 3628–3634.
[148] J. Zhang, et al., Dose-dependent response of personal glucose meters to nicotinamide coenzymes: applications to point-of-care diagnostics of many non-glucose targets in a single step, Angew. Chem. Int. Ed. 55 (2) (2016) 732–736.
[149] Y. Du, et al., A sweet spot for molecular diagnostics: coupling isothermal amplification and strand exchange circuits to glucometers, Sci. Rep. 5 (1) (2015) 11039.
[150] R. Chavali, et al., Detection of Escherichia coli in potable water using personal glucose meters, Anal. Methods 6 (16) (2014) 6223–6227.
[151] D. Kwon, et al., Facile method for enrofloxacin detection in milk using a personal glucose meter, Sensor. Actuator. B Chem. 254 (2018) 935–939.
[152] S. Huang, et al., Highly sensitive detection of mercury ion based on T-rich DNA machine using portable glucose meter, Sensor. Actuator. B Chem. 242 (2017) 347–354.