Enzymatic Glucose Biosensors: A Review on Recent Progress in Materials and Fabrication Techniques

Bentolhoda Mahdizadeh[a,*], Arezoo Nouri[b], Leila Baharinikoo[c] and Batool Lotfalipour[d]

[a]Department of Biomedical Engineering, Islamic Azad University, South Tehran Branch, Tehran, Iran
[b]Department of Chemistry, University of Sistan and Baluchestan, Zahedan, Iran
[c]Department of Analytical Chemistry, Faculty of Chemistry, University of Mazandaran, Babolsar, Iran
[d]Department of Community Health Nursing, School of Nursing and Midwifery, Kerman University of Medical Sciences, Kerman, Iran

In recent years, biosensors are used in various applications ranging from biomedical and pharmaceutical to food and chemical products. As an example, biosensors can be used for glucose assessment in blood and regulation of insulin usage in diabetic patients. In this regard, it is anticipated that many diseases could be diagnosed in the near future at an early stage regarding further progress in nanotechnology. The advancement in nanotechnology meets the technological requirements for the increased demand for sensors in biomedical applications. Enzymes play a significant role among various biologic elements exerted in the design of biosensors. Glucose oxidase is an enzyme and biocatalysts that accelerate the process of turning glucose to oxygenated water. Recent surveys have reported the novel qualitative and quantitative approaches used to enhance the sensitivity, detection limit and biocompatibility of biosensors. Furthermore, they have confirmed the enhanced performance of glucose-based biosensors in both response and detection limits in their implementation. This review aims to summarize recent progress in sensitivity, selectivity, response time, and stability of the enzymatic biosensor based on the versatile fabrication of glucose by semi-permeable membranes.

Keywords: Biosensor, Glucose biosensor, Enzyme, Glucose oxidase

INTRODUCTION

Biosensors are analytical media that could identify a compound(s) by specific reactions based on the intrinsic properties of biological materials. The resultant product of such a reaction may be in a form of chemical, optical, or electrical signals. One of the main applications of sensors is in medical diagnosis. Recently, glucose biosensors have been considered as the most successful biosensors used for measuring glucose concentration in blood [1]. In general, each biosensor has the following components: analytes, recognition elements, and transducers. Analyte (substrate) is a material produced or consumed in chemical processes and is quantified by the biosensor [2]. Recognition elements

prevent the intervention of pesky materials for certain conditions that lead to deviation in the measurement method. Also, a recognition element may catalyze the substrate in the reaction. Using an enzyme as a recognition element is more common than other materials. Finally, a Transducerturns the visible physical or chemical change to a measurable signal in the way that its magnitude is proportional to an assessable material or a group of materials [3]. From the medical landscape, the progress of sensitive biosensors of glucose for the precise identification of the level of blood glucose is of great importance to manage diabetics [4]. Glucose oxidase (GOx)-based enzymatic is the most extensively used model enzyme. There are two significant restrictions in immobilizing enzymes on the solid electrodes: (1) poor electrical relationship between the electrode and the active site of the

*Corresponding author. E-mail: kamalim448@gmail.com

enzyme and (2) leaching of the enzyme. To dominate these issues, selecting an appropriate immobilization matrix with the antifouling trait, stability and good electrical conductivity is compulsory to prepare highly effective biosensors of glucose [5]. Chemicals with an electrochemical effect are known as redox mediators. In a bioelectrocatalysis reaction, mediators can exchange electrons with fuels or oxidants at the biocatalyst reaction sites, then diffuse to the electrode surface and exchange electrons there. The mediator acts as an electron shuttle between the biocatalyst and the electrode during this step, which is repeated. A lot of research has been done on [6]. Oxygen is required as a co-substrate for determining glucose through first-generation biosensors of glucose. However, it has a main disadvantage known as 'oxygen deficit', as oxygen may not be available in all the systems and its concentration cannot be fixed in biological fluids [7]. By replacing oxygen with redox mediators, the issue of 'oxygen deficit' can be addressed [8-12]. Metal phthalocyanines (MPcs) are among the appropriate electrocatalysts and redox mediators to mediate glucose oxidation. These enzymes have prominent physicochemical and electrochemical attributes of MPcs like fast electron transmission kinetics, biocompatibility, rich redox attributes, high thermal and chemical constancies [13-16]. Some of the introduced MPcs based mediated biosensors of glucose include poly(ethylene glycol)/GOx/cobalt octaethoxy phthalocyanine [CoPc (OEt)$_8$] [13], ether-linked cobalt(II) phthalocyanine (CoPc)-cobalt(II) tetraphenylporphyrin pentamer [8], polymetallophthalocyanines/polypyrrole-GOx [14], GOx-CoPcboron-doped diamond electrode [15] and nanoscaled CoPc-GOx [16]. CoPc and its derivatives are the most suitable phthalocyanines for the biosensor of glucose usages. There are several reviews on glucose sensing, however, some imperative features in this regard are not completely comprehended attracting not much interest. The fast development of peripheral and core technologies and the great clinical and scientific importance of glucose sensors also need continuous updating in the research prominences. The present review chiefly explains the principles of GOx-based enzymatic glucose biosensors, their current status and recent developments, the major strategies to enhance their performance, and the key opportunities and challenges in their further applications and development.
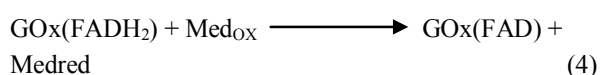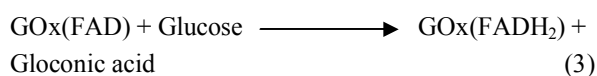
Glucose Biosensor

T2D diabetes outbreak is one of the most important issues concerning global health based on the official statistics about the disease. The rapid development of the disease, which is related to lifestyle and individual genetics, is quickly spreading around the world. Meantime, in order to deal with the prevalence and the development of the disease an easy-to-use and quick technology to adequately discover biomarkers is highly valued [17]. Developing biosensors was traced back to the invention of an oxygen electrode aims to at measuring the concentration of glucose in the blood by L. Clark at Cincinnati USA in 1962. Later on, its electrode surface was covered by an enzyme to associate glucose oxidation in order to measure glucose in the blood and known as the first enzymatic biosensor. Measurement of glucose is of significance due to its role in the human metabolic process; as well it is particularly important for patients suffered from diabetes. Glucose biosensors are working based on a phenomenon in which glucose oxidase enzyme enables to turn glucose oxidation to gluconic acid whilst the, oxygen plays as an oxidation factor [18,19]. The consumption of oxygen causes electrochemical reduction at the platinum electrode or graphite (Auxiliary electrode: It is made of platinum or graphite rod. Any reaction that takes place on the surface of the working electrode, the opposite reaction takes place on the surface of this electrode. As a result, a current is applied between this electrode and the working electrode). Glucose oxidation reaction with oxidase enzyme could be shown as equations below:

$$\text{Glucose} + O_2 \xrightarrow{\text{GOx}} \text{Gloconic acid} + 2H_2O_2 \tag{1}$$

$$O_2 + 4e^- + 4H^+ \longrightarrow 2H_2O \tag{2}$$
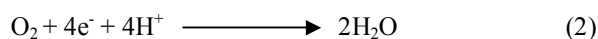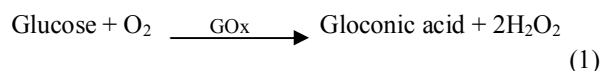
Three Generations of Glucose Biosensors Exist Based on Enzyme

The biocatalytic reaction of glucose biosensing based on GOx includes reducing the flavin groups in the enzyme (GOx (FAD)) that reacts with glucose to yield the reduced

enzyme form (GOx(FADH$_2$)) (Eq. (3)), after reoxidizing GOx (FADH$_2$) via the electron acceptor (Medox) for regenerating the oxidized form of the enzyme (GOx(FAD)), (Eq. (4)). Regenerating the original state of GOx(FAD) is vital in the enzymatic cycle, then, one enzyme molecule can be impacted only once while ceasing the subsequent enzymatic reaction cycle.

$$GOx(FAD) + Glucose \longrightarrow GOx(FADH_2) + Gloconic\ acid \tag{3}$$

$$GOx(FADH_2) + Med_{OX} \longrightarrow GOx(FAD) + Medred \tag{4}$$

Amperometric glucose biosensors are categorized into three generations based on the nature of Medox as follows: The electrode potentiostated at a potential positive of the formal potential of GOx using artificial (synthetic) electron acceptor, and the physiological mediator O$_2$, the GOx(FAD) is regenerated by Medox in the first, second and third-generation amperometric glucose biosensors, respectively [20].

First-generation Glucose Biosensors

The physiological mediator O$_2$ is taken by the first-generation amperometric glucose biosensors as the Medox to create GOx(FAD) and discover glucose in terms of monitoring the O$_2$ consumption or the generation of H$_2$O$_2$ within the enzymatic reaction process. O$_2$ is the GOx's physiological electron acceptor, therefore, very fast electron communication is essential. Although electrochemical reduction of O$_2$ is normally utilized for monitoring the O$_2$ consumption for glucose quantification, both cathodic reduction and anodic oxidation of H$_2$O$_2$ are used for monitoring the H$_2$O$_2$ enzymatic generation, moreover, the H$_2$O$_2$ anodic oxidation positively regenerates or replenishes O$_2$ to enhance the enzymatic cycling. Stability, simplicity, and the ability for using miniaturized tools are the advantages of the first-generation biosensing mode in terms of measuring the O$_2$ consumption or H$_2$O$_2$ creation. The first-generation glucose sensors' response is associated directly with the O$_2$ concentration in solution; therefore, oxygen tension has a key role in determining. The normal O$_2$ concentrations have a magnitude of nearly 1 order lower than the physiological glucose level, this is called ''oxygen deficit''. The ''oxygen deficit'' greatly reduces the upper linearity limit of first-generation amperometric glucose biosensors and the O$_2$ concentration in solution restricts their sensitivity to glucose. It was attempted to overcome these disadvantages of O$_2$-based amperometric glucose biosensors. Using a mass transport-limiting film was proposed to increment the O$_2$/glucose permeability ratio for addressing the ''oxygen deficit'', here, the 2D cylindrical electrode designed by Gough's group is a prosperous instance in this regard [21-23]. Oxygen-rich carbon paste enzyme electrodes were also designed by scientists or an air diffusion biocathode was constructed utilizing O$_2$ directly from the air for enhancing the O$_2$ supply to overcome the O$_2$ restriction [24-26]. It is expected that other materials able to effectively supplement O$_2$ are also used in the first-generation amperometric glucose biosensors for solving the problem of O$_2$-limit. One of the fundamentals of an effective biosensor is an anti-interferent capability. Several coexisting oxidizable types in biological fluids are co-oxidized at relatively higher potentials including uric acids, ascorbic acid and some drugs (like acetaminophen), which are utilized for H$_2$O$_2$ electro-oxidation. Hence, they all have a role in the present response and cooperate with the accuracy and selectivity of measuring glucose. There are significant efforts on improving the anti-interferent capability of first-generation amperometric glucose biosensors. Mainly, two effective protocols exist to minimize the interferences including first, immobilization of the enzyme via a permselective film diminishing or inhibiting the electroactivity of interferents while allowing the adequately high electroactivity of O$_2$ or H$_2$O$_2$ at the enzyme electrode [27]. Second, reducing the H$_2$O$_2$-detecting potential via catalysts immobilized at the enzyme electrode [28]. Prussian blue (PB), known as ''artificial peroxidase'' has been extensively used as a result of its high catalytic activity and selectivity for reducing H$_2$O$_2$, in the greatly selective biosensing of glucose at low potentials. In the study of Zhao *et al*., the enzymatically created H$_2$O$_2$ was catalyzed at low potentials and inhibited the interferents' responses by preparing poly(diallyl dimethylammonium chloride) (PDDA)-protected PB nanoparticles. Li *et al.* used the enzymatic effect of GOx and an inorganic PB catalytic polymer to make a molecularly imprinted electrochemical

sensor with high sensitivity in terms of double amplification [29]. GOx was also incorporated into Langmuir-Blodgett films in terms of PB to an amperometric glucose biosensor acting at very low potentials. In the present work, we found the glucose-sensitive determination in H_2O_2-reduction and H_2O_2-oxidation modes on a PB modified Au electrode with immobilized GOx [30]. Moreover, electropolymerized poly film (toluidine blue O) was effectively used as the redox mediator contributing to the lower potential discovery of glucose at a glassy carbon electrode modified with carbon nanotube. It was demonstrated that different nanomaterials are effective in enhancing the selectivity of resulting GOx-based amperometric biosensors like CNTs, platinum nanoparticles [31,32], metalized carbons, and composite nanomaterials [33,34]. They reduce the determination potential of H_2O_2 through virtue of the superior catalytic effects of nanomaterials. Moreover, some biological enzymes for H_2O_2 (like horseradish peroxidase (HRP)) were co-immobilized for developing bienzymatic amperometric electrodes for cathodic detecting H_2O_2. Coimmobilizing HRP for example, to catalyze the reduction of H_2O_2 generated by GOx at lower potentials effectively enhances the glucose sensors' selectivity [35]. Moreover, the high technical sophistication levels in the amperometric detection tool can enhance efficiently the selectivity for the glucose assay such as introducing an interferent-pretreatment unit for electrochemically removing the interfering species prior to reaching the biosensor surface [36,37].

Second Generation Amperometric Glucose Biosensors

The 10-fold extra glucose over oxygen in blood yields the ''oxygen deficit'' as the most severe problem for the first-generation amperometric biosensors [38]. Using another artificial Medox is a greatly successful method for increasing the electron-transfer rates of biosensors for mediating the GOx cycling rather than oxygen. The artificial Medox is a solution-state mediator diffusing out of and into the enzyme active site, or it is entrapped by an immobilized mediator attaching directly to the enzyme within the enzyme film. Moreover, it can use a redox-conducting polymer shuttling its electrons and creating the enzymatic active site [39]. The biosensors that use artificial electron acceptors for shuttling electrons from the enzyme's

redox center to the electrode's surface are called second-generation biosensors [40]. Ferrocene derivatives, conducting organic salts (mainly TTF-TCNQ, tetrathiafulvalene-tetracyanoquinodimethane), transition-metal complexes, ferricyanide, quinone compounds and phenoxazine and phenothiazine compounds are the effective mediators for GOx [41,42]. Fascinatingly, in some reports, ferricyanide is not suggested as a greatly efficient electron mediator for GOx. However, the molecular mechanism is still not known [43]. There are three steps in the catalytic procedure of second-generation amperometric glucose biosensors including first, transferring electrons (and protons) from glucose to the two FAD reaction centers of GOx decreased to $FADH_2$, second, transporting electrons from the $FADH_2$ centers to the artificial mediators, hence, the mediators transform from Medox to their decreased state Medred, and third, transferring electrons *via* the artificial mediators to the electrodes. The present signals created by oxidizing Medred are utilized to determine glucose in the second-generation biosensing state. Hence, the effective interactions between enzymes and mediators that are essential for realizing the effective shuttling of electrons between electrode and GOx redox-active centers. This is necessary for the second-generation biosensing state. This demand is well-satisfied by diffusion mediators. Nevertheless, the soluble mediating species are utilized in implantable probes [44]. Different approaches were proposed to tailor the mediators in the electrode-supported enzyme film. The mediators are chemically bound with the polymer backbone to make the biosensor is extensively used for stabilizing artificial mediators. In the study of Hale *et al.*, some systems were assessed with chemically binding mediating species to the polysiloxane to permit the close connection between the enzyme's $FAD/FADH_2$ centers and the mediator, however, the second case was prohibited from diffusion away from the electrode surface [45]. Dong's group indicated supramolecular organized multilayers made by ferrocene derivatized poly(allylamine) redox polymer and GOx-modified MWCNTs via electrostatic self-assembly and constructed a reagentless biosensor. Using hydrogels comprising Os complexes, second-generation amperometric biosensors were fabricated with extensive utilization in important practical applications and fundamental science [46]. Utilizing a redox hydrogel

electron based on conducting crosslinked polyaniline (PANI) created in one step at pH 7.2, the GOx was wired electrically and an effective glucose electrooxidation catalyst was formed. Thus, the electro-oxidizing glucose was realized at 0.3 V *vs*. Ag/AgCl [47]. The electrically contacted CNTs/ferrocene/GOx electrodes were integrated to fabricate Willner's group and to detect the glucose bioelectrocatalycally. Glucose sensing was realized by co-immobilizing hydroquinone sulfonate ions in polypyrrole films with GOx in the nonexistence of mediator in solution. There are also wide reports on the direct connection between redox mediators or relays and the enzymes. The electron-transfer was reported by Schuhmann *et al.* between electrodes and GOx through redox mediators bound with flexible chains to the enzyme surface. Attempts were made by scientists to bind covalently the ferrocene derivative to the enzyme molecule; however, it was indicated that this is less successful and more complicated [48]. Nonetheless, Sekretaryova *et al.* successfully immobilized the mediator and enzyme stably, which avoided covalent bouns of the mediator through exposing the enzymes to water-organic mixtures with a high content of organic solvent [38]. We believe that contrary to a second-generation amperometric enzyme electrode including a solution-state artificial mediator (diffusion-based), a compromise should be made by the immobilized mediator case between the three events. These events occur simultaneously but mutually contradictory below to some extent including, immobilizing the mediator stably (restricted movement), the higher electron-exchange efficacy between the electrode surface and immobilized mediator, and the high electron/proton-exchange efficiency between the immobilized mediator and enzyme. Therefore, it is essential to immobilize the artificial mediator both near the electrode surface and near the enzyme's redox center for the quick mass or electron transfer between the mediator, the electrode, and the enzyme. Then, the amperometric signaling efficacy or the enzyme-mediating efficacy will reduce or even completely dwindle.

Third-generation Amperometric Glucose Biosensors

The third-generation amperometric glucose biosensors are attractive as a result of their function in the best biosensing model without mediators. The GOx's direct electrical communication can also have a role in detecting glucose at lower and slightly positive redox potentials of the GOx (about 0.2~0.5 V *vs*. Ag/AgCl). Obtaining the enzymes' direct electron communication is considerably based on the distance between the electrode surface and the redox-active cofactor [49,50]. There are several efforts to solve the long electron-tunneling distance and understand the enzymes' direct electrochemistry. Reconstituting apo-enzymes on cofactor functionalized Au nanoparticles and apoproteins on cofactor-modified electrodes had extensive application as a versatile technique for aligning redox enzymes on electrodes [51-53]. Though this technique is operative to wire redox enzymes electrically with electrodes, it has less use practically due to complicated procedures. A method was reported by Yehezkeli *et al.* for wiring the enzyme electrically and transforming it to oxidize to a hydrogenase through biocatalytically inserting Pt nanoclusters into GOx. They thermodynamically reduced various metal salts to metallic nanoclusters with the decreased cofactor $FADH_2$. It was reported that different nanomaterials yield the direct electrochemistry of GOx [54]. In the study of Shan *et al.*, it was indicated the direct electrochemistry of glucose biosensing and GOx in terms of polyvinylpyrrolidone-sheltered graphene. Alwarappan *et al.* attempted to use graphene-GOx for the detection of glucose and promoting glucose biosensing, they found the direct electrochemistry of GOx using graphene [55,56]. Glucose was found by Wang *et al.* in terms of the direct electron transfer reaction of GOx immobilized on greatly ordered PANI nanotubes [36]. Gao *et al.* developed amine-terminated ionic liquid functionalized CNTs AuNPs to assess the GOx direct electron transfer [58]. The direct electrical communication was established by Holland et al. between electrode and GOx *via* a simply site-based modifying of GOx to represent a free thiol group close to its active site. They simplified the site-based connection of a maleimide-modified gold nanoparticle to the enzymes [58]. Though several studies achieved well-determined voltammetric peaks of GOx direct electrochemistry, detecting glucose in terms of the direct transferring of electrons for GOx was rarely understood. GOx mainly displaying decent direct electrochemical peaks of GOx are still required mediators for catalyzing the glucose oxidation

[59]. Indeed, in some reports on GOx electrochemistry, it was not clearly demonstrated the direct electrochemistry originating from the intact (or still adequately bioactive) enzyme. Therefore, adequate care should be paid for any statements on the third generation amperometric glucose biosensing. In [60] the achieved well-determined voltammetric peaks of GOx direct electrochemistry may be originated from the enzyme molecules with greatly reducing activity by the damage of enzyme conformation or releasing flavin. used the EQCM (electrochemical quartz crystal microbalance) to measure the electroactivity of sodium dodecyl benzene sulfonate (SDBS)-treated GOx adsorbed on an MWCNTs/Au electrode as the enzymatic specific activity's function (determined as the enzymatic activity per unit enzyme mass) of the adsorbed GOx. Hence, experimentally we initially found that the enzymatic specific activity and the electroactivity of the immobilized GOx had an opposite response in the existence of SDBS and MWCNTs. Moreover, the adsorbed GOx portion representing electrochemical activity displayed nearly no enzymatic activity [60]. Yao and Wang made a similar experimental conclusion [61]. It is essential to consider the significance of understanding this direct electrochemistry of fully or partially denatured GOx for glucose detection. Conceptually, determining glucose in terms of enzyme electro-reduction using O_2 at lower potentials (near the GOx's redox potential) needs to be based on the first-generation amperometric glucose, not the third-generation biosensors. However, for a glucose biosensor based on an effective third-generation GOx, an increment in the oxidation current of the direct electrochemistry of GOx and a notable reduction in the reduction current should be observed simultaneously while existing glucose (versus its absence). Therefore, a glucose biosensor based on third-generation GOx can efficiently act at the potentials to some extent positive of the GOx redox potential about 0.2~0.5 V *vs*. Ag/AgCl (for example at 0.2~0.3 V *vs*. Ag/AgCl). In general, it is essential to conformational alter the enzyme for the direct electron communication within the electrode surface and the deeply buried redox-active center of the enzyme since it may lead to a clear loss in enzymatic activity. A proper balance is vital between the electrochemical and enzymatic activities for the third-generation amperometric glucose biosensors. It appears that

the third generation amperometric biosensing is realized optimistically and globally *via* effective connection of the enzyme's redox-active center to the electrode utilizing nano or subnanosized conducting wires of less interference to the confirmation of the enzyme [54].

Oxidase Glucose Enzyme

Flavo-protein catalyses the D-β glucose oxidase to δ-molecule of gluconolacton and hydrogen peroxide *via* transfer electron to the oxygen molecules. This enzyme is obtained from fungi and honey bees. Glucose oxidase obtained from asperigillus fungus as an enzyme constituted from two segments while its molecular weight is 150 kDA. The Activity and thermodynamic stability of such enzyme depends on its structure and 3-D construction affected by environmental factors. Glucose could be converted to exolactone and oxygenated water through catalytic oxidation process. The biocatalyst used in this process is glucose oxidase enzyme with compatibility to glucose [62]. In glucoseoxidase the flavin group (FAD) presents in its active center reacting with glucose produces by reduction of flavin (FADH2) and then it is turned to primary state based on the type of mediator shown in two following reactions. Reproduction of enzymes is a vital process in which if not done leads to its eliminations from reaction cycle. The performance of enzymes is strongly dependent on processing parameters such as temperature, pH and substrate concentration. Using a conveyor for enzyme stabilization may change these conditions that these changes may lead to some problems for its performance. Therefore, the closer these conditions in stabilized and free sates to each other, the stabilization will be better [63].

Recent Advances in Enzymatic Glucose Biosensors

In recent years, a great class of nano-carbonous materials such as single-wall and multi-wall carbon nanotubes, carbon nanofibers, and graphene has been used in biosensors applications. This is due to their high surface area and electrical properties leads to ameliorate the detection limit sensitivity and responding time by using gold nanoparticles [64], carbon nanotubes [65] and Sulfide Cadmium [66]. In addition, increased, bio-compatibility of sensor *in vivo* by using biological polymer materials was reported [67]. Other studies were addressed a reduction in

costs accompanied by improving electrical properties. Due to the utilization of gold and palatine nanoparticles [68]. The study was performed by Sternberg *et al.* in which they improved different ways for immobilizing glucose oxidase enzyme on a membrane of cellulose acetate [69]. Their research concentrated on the generation of stable and thin membranes. The optimum way was a covalent connection of cellulose acetate membrane to bovine serum albumin (BSA) and with the GOx that was then activated with *p*-benzoquinone. Such research provided thin membranes of 5-20 micrometer with the stability of up to3 months and high surface activities of 1-3 U/cm^3. Lately, the membrane of cellulose acetate has re-surfaced as a semi-penetrable membrane for enzymatic biosensors of glucose. Biosensors of glucose developed by Setti *et al.* consisted of a conductive blend of poly(3,4-ethylenedioxythiophene/ polystyrenesulphonic acid (PEDOT/PSS) inkjet printed on an indium tin oxide glass layer [70]. This tool was enclosed in a capsule in a cellulose acetate semi-permeable membrane *via* dip-covering. The resultant biosensor of glucose had a linear response up to 60 mM and 0.00643 mA mM^{-1} cm^{-2} sensitivity.

Recently, Khan *et al.,* 2019, utilized the GOx enzyme with the functionalized graphene oxide on a gold-sputtered screen-printed carbon electrode for detection of glucose. Here, to functionalize graphene oxide, hydroxyl groups and epoxide bonds were broken and the thiol group was obtained carrying graphene oxide (GO-SH), which enhanced electrical conductivity as a result of regenerating the sp2 carbon network. The GO-SH layer provided conductive support between enzyme and Au-sputtered SPE. The successful sensor formation was confirmed by SEM images of the GO-SH-Au-SPE bare and the SPE. The electrode's stability was revealed by SEM images of the GO-SH-Au-SPE prior and followed by the electrochemical measurements [71]. CV was used to examine the sensor performance while existing glucose. Increasing the glucose concentration in the specimen reduced the current signal of O$_2$ reduction. The reduction in anodic CV current was linear within the range of 3-9 mM with a LOD of 0.319 mM. Other carbon-based nanomaterials can be used along with graphene, in enzyme-based glucose sensors such as carbon nanotubes, and graphene quantum dots [72]. For example, the GOx enzyme was immobilized on GCE using

MWCNTs (multi-walled carbon nanotubes) covered with semiconductor CoS nanoparticles. Glucose can be discovered by the resultant nanocomposite at lower potential values representing a LOD of 5 µM [73].

A ratiometric glucose sensor was fabricated using a similar method of integrating gold nanoparticles (AuNPs). Cu-BTC MOFs (Cu-trimesic acid metal-organic frameworks) in addition to AuNPs were also employed on a 3D macroporous carbon integrated electrode (3D-KSCs). GOx was immobilized on AuNPs followed by electrodepositing AuNPs over the MOFs. The signal differences between the analyte and internal reference are measured using ratiometric sensors and intrinsic signal errors are created by built-in signal correction [74,75]. The O$_2$ reduction was catalyzed by AuNPs-supported GOx to water improving the electrocatalytic activity of MOFs. The glucose oxidation was catalyzed by Cu-BTC MOFs to present reference signals. CuBTC reduction current incremented by adding glucose, however, the oxygen reduction current reduced using oxygen *via* GOx-catalyzed glucose oxidation reaction. Hence, the ratio of the present densities of these reduction reactions ($j_{o2}/j_{cu\text{-}BTC}$) was regarded as the sensor's response. Differential pulse voltammetry (DPV) was used to examine the performance of the sensor for the detection of glucose at 0.2 M O$_2$-saturated PBS (pH 7.0). Increasing the glucose concentration to 4 mM, reduced $j_{cu\text{-}BTC}$ linearly, and increased linearly. Moreover, it remained constant for concentrations over 4 mM, and the only j_{o2} linearly decreased by reaching the catalytic limits of Cu-BTC MOF and continuing catalyzation of glucose oxidation by GOx. The sensor could measure various 44.6 µM-19 mM while revealing a LOD of 14.77 µM.

High selectivity is essential for sensing applications. Kim *et al.*, enhanced selectivity by red blood cell membranes (RBCM) within an electrochemical enzymatic sensor as a diffusing barrier for keeping the interfering molecules away from the electrode. In general, cell membranes avoid penetration of small molecules and ions into the cell, however, transportation of glucose is facilitated by glucose transporter-1 (GLUT1) protein on the cell membrane *via* the cell membrane. Moreover, RBCMs carrying excess quantity of GLUT1 can be utilized as a diffusion barrier permitting glucose completely for reaching

the electrode. To fabricate such a sensor, a screen-printed gold electrode (SPGE) was initially coated with an enzyme composite comprising pyrroloquinoline (PQQ), glucose dehydrogenase (GDH), buffer and mediator. Then, the sensor platform was covered with RBCM gathered from human blood. The enhanced thickness of 200 nm was considered for the RBCM layer. The atomic force microscopy (AFM) and SEM images indicated a significant reduction in the sensor's surface roughness revealing the complete coverage of the surface by the RBCM layer. The chronoamperometry was used to test the RBCM coated enzymatic sensor for the detection of glucose. A linear association was observed between the glucose concentration and sensor response within the range of 0-10 mM with a LOD of 1.06 mM. Moreover, the sensor performance was assessed in human serum specimens spiked with glucose. Decent linear responses were provided by the RBCM sensor with a LOD of 1.11 mM in human serum specimens. However, poor performance was exhibited by the sensor with no RBCM layer (LOD: 2.51 mM) proving that the measurement performance is improved by the RBCM layer on the sensor [76].

Enzyme immobilizing in sensor applications can be performed using conductive polymers (CP). Schiff base polymers (SBP) are conductive, biocompatible and stable polymers with good catalytic and mechanical features. Presently, electroactive SBP nanosheets have been employed to develop an enzymatic ratiometric glucose sensor and immobilize enzymes [77]. Schiff base polymer was synthesized using pbenzaldehye carrying aldehyde functional groups on both sides and thionine carrying two main amine groups on both sides of the ring. The enzyme GOx and polymer were covered on GCE. Using DPV, the sensor performance was investigated for the detection of glucose. The ratio of changing the oxygen reduction current density to the polymer ($\Delta j_{o2}/j_{SBP}$) current density was defined as a sensor response. The sensor response resulted in good linearity within the range of 0.82 µM-4 mM with a LOD of 0.27 µM using the polymer signal at -0.05 V as the reference. Correspondingly, to immobilize GOx for glucose sensing application a new conductive polymer was utilized [78]. Hence, the monomer with thiazolothiazole and furan units was synthesized first. Then, electropolymerizing the monomer was performed on the graphite electrode *via* CV

to achieve poly(2,5-di(furan-2-yl)thiazolo[5,4-d]thiazole) (PTTzFr). Glutaraldehyde was used as a crosslinking agent to drop coat GOx on the PTTzFr. Such an electrode was used for the detection of glucose and a linear correlation was found within the sensor response and glucose concentration for a range of 5 µM-0.7 mM with an LOD of 12.8 µM. It should be noted that similar readings were exhibited by the sensor in real sample analysis with a small error. It is indicated that the sensor can be used for analytical objectives. A disposable glucose sensor was made *via* inkjet printing technology using a conductive polymer poly(3,4-ethylene dioxythiophene) doped with polystyrene sulfonate (PEDOT:PSS) as the electronic component [79]. Coupling GOx with ferrocene-chitosan mixture mediated the electron transfer between the electrode and enzyme. Such a sensor was able to discover glucose linearly in saliva within the range of 28 µM-0.85 mM.

Invasive approaches are mainly required by conventional glucometers, which cause pain and discomfort for the patients. Lee *et al.*, established non-invasive and wearable glucose sensors as patient-friendly tools [80]. Cao *et al.*, represented a paper-based microfluidic electrochemical integrated device (3D-PMED) for the detection of glucose in sweat for non-invasive and wearable sensing. Such a sensor was made by patterning the cellulose paper with wax *via* a heat source and mesh, the waxed paper was then cut and folded. For the detection of glucose, a three-electrode sensor with GOx is immobilized on the working electrode. The Prussian blue was covered on the counter and working electrode as a redox mediator for detecting H_2O_2. Over successive glucose additions in a beaker, the sensor performance was examined with amperometry. The good linearity was shown by the amperometric response within the range of 0-1.9 mM and a LOD of 5 µM was revealed. Moreover, the sensor merged with a 3D-PMED structure was investigated by successively adding PBS and glucose. The resultant responses had good linearity, however, the sensitivity reduced owing to an unstirred system rather than a stirred beaker. Moreover, the sensing tool was examined for the detection of glucose in sweat on human skin, however, the subjects were simultaneously exercised. Though variances occurred in metabolism rate and measured current within the subjects, the change was realized by the device in the glucose of the

sweat with exercise [81].

Lipani *et al.*, established an impressive sensing platform with PtNPs decorated graphene and GOx immobilized hydrogel for transdermal and non-invasive glucose detection. The sensor has the advantage that glucose extracted from skin follows hair follicle preferentially such as paths. After extracting glucose from the skin *via* reverse iontophoresis, flowing into GOx-hydrogel occurs. By oxidizing glucose in GOx-hydrogel, H_2O_2 is produced which is then discovered by PtNPs decorated graphene sensor. By the pixelated sensor, each pixel resembles one skin follicle extracting glucose. This permits verification of the extracted glucose dilution, hence, the quantized measurements were achieved with no calibration. The sensor was examined *ex vivo* with porcine skin yielding an LOD value of 0.76 μM. Furthermore, *in vivo* measurement was conducted by the researchers through a sensor patch on a human forearm and following the blood glucose level with a commercial glucose meter. A close matching was obtained by the records of the pixelated sensor with blood glucose levels [82].

GOx was dissolved by Saha *et al.* within an electrolyte solution rather than connecting to an electrode surface to avoid problems caused by the immobilization procedure. Here, y oxidizing glucose *via* GOx in the electrolyte produced H_2O_2, which was found by CdS nanoribbons on the ITO electrode for quantifying glucose. To prepare the electrolyte for detecting glucose, 0.1 M PBS (pH ~ 7) was used with 1 mg ml^{-1} GOx. The amperometric signal of H_2O_2 decreased on CdS ribbons were linearly changed by glucose concentration up to 225 μM with a LOD of 0.1 μM. This alternative method of GOx introduction to the electrolyte leads to higher sensitivity compared to the immobilization of GOx on the electrode surface. Glucose could be also measured by the electrode in diluted blood serum specimens, in which, the sensor readings had a good consistency with the commercial glucometer [83].

Harrison *et al.* altereda Pt electrode with GOx followed by covering of nafion [84]. The nafion membrane thickness was 1.7 μm enabling to persistent evaluation of glucose in the blood at 37 degrees Celsius *in vitro*. A linear response of up to 28 mM with a response time varying from 5 to 17 s was seen. It was higher than those cellulose acetate membranes coated with bioelectrodes.

A novel mixed membrane matter including laponite gel and nafion was utilized to encapsulate GOx for modulating the enzyme loading in the bio-membrane. The glucose sensor sensitivity was found to be directly adequate to the content of enzyme in the gel membrane. A mixture of GOx to laponite in a ratio of 3.3 attained a sensibility of 132 mA mM^{-1} cm^{-2} over a linear dynamic limit from 0.01 mM to 20 mM. The impact of interfering components like acetaminophen, ascorbate, and urate was decreased by a factor of 4 using polyphenol oxidase and nafion membrane [85]. Carbon Nano-tubes have been investigated as electrode substrates due to their benefits over other glassy carbon and metallic electrodes. Some of the benefits consist of high aspect ratios and strong bonding between the tubes and the atoms resulting to increase the surface area and conductivity for immobilization of the enzyme. Current research has been indicated that GOx and palladium Nano-particles can be quickly co-deposited on a nafion-solubilized carbon nano-tube [86]. The produced biosensor of glucose indicateda linear response of up to 12 mM with 0.15 mM identification limit with 3SNR. The nafion covering removed the impacts of common mediating species like ascorbic acid and uric acid was eliminated by nafion coating. The exploitation of carbon nano-tubes as the electrode substrates for immobilization of enzyme was an efficient strategy and led to the exploration of carbon nano-wires as a compact assembled chain of multi-walled carbon nano-tubes which were utilized as the substrates for loading high-density enzyme.

Shan *et al.* used graphene planes for covalent stabilization of glucose oxidase enzyme firstly in 2009. They functionalized polyethylenimine with polyethylene ionized functionalized which has a high dispersion and solubility in water for graphene scattering in the electrode structure. The linear domain of biosensor was between 2-14 mM of glucose which compared to previous methods had a wider domain of carbonic nanotubes. This was due to a higher electrical property of graphene compared to other nanocarbonus materials [87].

Zhou *et al.* with a more interesting initiative for preventing from re-aggregation of graphene planes separated from each other combined them with SO_3 so that they opposed loads on these planes repulse them. Shan used nafionas a common polymer in manufacturing biosensors.

Zhou *et al.* increased biosensor activity from 15 mM to 5.8 mM by addition of gold nanoparticles as well as a higher (without gold nanoparticle) repeatability based on combining gold and graphene. The detection limit of biosensor designed by Zhou was 5 mM while its response time is 5 s. In addition, which required less time for responding compared to CNT-based biosensors. But comparing glucose biosensors stabilized on Silica needed more time and this required time for responding was just due to enzyme stabilization [88].

Due to the nature of redox-switchable, by Ramanavičius *et al.* Polypyrrole was used in the development and design of glucose biosensors. In this study, nano-particles of glucose oxidase were encapsulated within a membrane of polypyrrole. The insertion of polypyrrole, a very conductive polymer, was indicated to enhance the rate of reaction (Kcat) and the Michalis-Menten constant (KM). Another method was used to electropolymerized m-phenylene diamine film with GOx, glutamate oxidase and lactate oxidase on a carbon fiber electrode concealed with an electro-metalized ruthenium layer [89]. This biosensor displayed a relatively small dynamic limit up to 4 milimolar for glucose with 0.5 µM identification range with an SNR of 3. Its functionality was constant over ten hours in a dynamic environment at pH = 7.4 and 36 degrees Celsius. Although this system allowed to monitor the glucose *in vivo*, it was unable of identifying normal levels of glucose also hyperglycemia due to its very thin dynamic limit. In addition, composite polymer layers like nafion and polyurethane gain the attentions to complete screening against mediating component such as ascorbic acid, L-cysteine, uric acid, *etc.* [90]. In addition, a co-polymer hydrogel including of 1,3-diaminobenzene has been utilized in the design of a new biosensor array enables simultaneously detecting glucose, glutamine, lactate and glutamate. The system contained a gold electrode and a glass chip with integrated biosensor array to supply electrical durability. This biosensor system runover a wide dynamic limitof 0.1 mM-35 mM. However, the biosensor sensibility was very low (520 nA mM^{-1} cm^{-2}). This biosensor system indicated a low operational constancy over 4 week's whilst its storage stability almost near two years with less than 0.5 mM in respond to interference.

Another biosensor of glucose was designed by immobilization of glucose oxidase on Pt electrode, yielded a dynamic range at low glucose concentration while its sensitivity reached 30 mA mM^{-1} cm^{-2}. This biosensor was covered with a perm selective membrane poly(4-vinylpyridine-co-styrene) [91]. This membrane was found to be a successful medium for the removal of the impacts of *p*-acetaminophen, ascorbic acid, and urate. In another study, GOx was inactivated in the presence of BSA on a nano-yarn carbon nano-tube followed by covering with epoxy-polyurethane to enhance the susceptibility of the glucose biosensor. A 7.5-fold gain in the glucose susceptibility was achieved compared to the utilization of Pt-Ir coil-based electrode while its operating constancy reached 70 days [92]. Similarly, Baby *et al.* [93] exploited gold nanoparticles in presence of palatine as filler between graphene planes. These particles in addition to graphene planes aggregation led to enhancing the limit of detection of biosensor almost near 1 mM.

Liu *et al.* published a paper in which showed that there is an interaction between glucose oxidase amine group to carbocyclic acid group in graphene. This interaction leads to create a strong amide bond whilst it is compatible with the environment. For proving the environmental compatibility of the biosensor, it was tested on PRE cellular class. The results showed that due to the environmental compatibility of graphene sensors, this category of biosensors could be used for measuring blood glucose *in vivo*. Furthermore, this study showed that the repeatability of this biosensor was reduced only after a month from manufacturing [94].

Alwarappan *et al.* reduced the glucose limit of detection to 3 mM by stabilizing glucose oxidase enzyme on graphene oxide and putting this compound on polypirol conductive polymer which was deposited on carbon electrode by chemical method. The polypirol deposited on carbon electrode had a high porous structure which led to increasing in electrode effective level as well as increasing in electrochemical exchanges between reagent and enzyme. In fact, he had used two methods for linking to surface as well as entrapping in order to enzyme stabilization. He hypothesized that by creating a covalent bond between glucose oxidase and graphene oxide, the active segment of enzyme which plays a paramount role in oxidation of glucose get closer to graphene surface and thus, the secondary electrochemical process would be performed on

reaction product, which is oxygenated water in graphene surface. In this work, the limit of detection of his biosensor was reported 3 mM [95].

Another study performed by Wang *et al.* was based on a strategy to dope nitrogen atoms to enhance the graphene electrical properties as well as increased the biocompatibility of biosensors and ameliorate the tendency for functionalization. Besides, to dope nitrogen to nanotube structures, ammonium plasma was used instead of nitrogen plasma and he controlled the doped nitrogen rate in graphene structure by manipulating the plasma pressure. In this regards, doping process was performed at pressure of 750 mPa whilst the plasma production source was in 10 V. The results showed that due to graphene doping with nitrogen, three various nitrogen types enter graphene structure, leading to influence on formic potential and band gaps in electron structure as well as the electrical features of graphene. Limit of detection of this biosensor was 10 mM which was higher than that of previous methods. However, it should be noted that this biosensor will be more cost efficient than biosensors based on gold nanoparticles. In addition, compare to the biosensore based on porous polymers, the limit of detection was reduced [67].

Zeng *et al.* introduced combined biosensors made by chitosan and graphene. This biosensor which was stabilized by palladium had a limit of detection of 0.2 Mm and a linear range of micro to mM. The inclusion of chitosan to graphene caused to increasing in the hydrophobicity of graphene and enhancing in the compatibility of biosensors which was suitable for using *in vivo*. Repeatability of these biosensors after 60 tests exhibited 91% of primary activity after 1 week and 80% after three weeks which was orginating from a strong covalant bond between enzyme and chitosan. In this study, Jiang *et al.* examined intrusions due to natural oxidation factors like ascorbic acid and urea may be present along with glucose and it was shown that the impact of these intrusions was observed at the voltage below -0.5 V [65].

Yin *et al.* utilized the electrolysis process to eliminate the effects of strong oxidizing reagents and secondary reducer in the synthesis of graphene oxide. It is noteworthy that the Hammer method is a prevalent technique to synthesis the graphene in a way that a mixture of reducer and strong acid is used whilst the existing defects within graphene are functionalized by oxide factors. Subsequently, to achieve graphene electrical features, graphene oxide is partially reduced by a reducing factor like hydrazine. Accordingly, some circular carbonic structures were also produced during this process. These particles prevented graphene aggregation by creating spatial prevention between graphene planes. The linear range sensitivity was reported between 0.4-20 mM while its limit of detection was 0.1 mM [96].

Zhang *et al.* designed a sensor by the combination of single-wall and multi-wall functionalized carbon nanotubes accompanied with gold nanoparticles by lamination method. This sensor enabled to measure the glucose of human salvia non-invasive and with high resolution. The advantages of this sensor were repeatability, ease of measuring, speed of measuring, and continuous supervision was among for assessing the salvia glucose [97].

Nor *et al.* provided a biosensor that consisted of Indimtyn oxide with iron oxide nanoparticles along with nafion. In this report, high electrochemical function was reported. In this sensor, nanoparticles of Iron oxide acted like a catalyst and helped to improve the speed of electron relocation between glucose oxidase and Indimtyn oxide electrode. Meanwhile, thin nafion film prevented the interference and resulted in chemical stability. This biosensor had a sensitivity of 70.1 $\mu A \ mM^{-1}$ and linear range of 1.0-8.0 mM [98].

One of the prominent approaches to improve the electron transmission rate was indicated by Liu *et al.,* wherein GOx was trapped in a composite consisted of a mixture of chitosan and carbon nano-tube in order to enhancement in the direct electron transmission rate (7.73/s). This enhancement was more than one-fold in GOx-absorbed on carbon nano-tubes (3.10/s) [99]. In addition, the susceptibility was 0.577 $mA \ mM^{-1} \ cm^{-2}$. The application of chitosan membrane resulted in entrapment of the enzymes leading to the enhancement in the constancy of the biosensor. Because metal surfaces have high empathy for immobilization of enzyme, Zeng *et al.* immobilized GOx on nano-particles of palladium altered with chitosan membrane [64]. Improvement in hydrophilicity and biocompatibility was seen with a low constant of reaction rate ensuring the enhancement of the enzyme dependency to glucose. The sensor presented a linear dynamic limit from 1 μM to 1 mM

with an identification range of 0.2 μM at SNR of 3 and a sensibility of 0.031 mA mM^{-1} cm^{-2}. Ang *et al.* progressed a biosensor of glucose and specified it in a fruit recently [100]. The glucose biosensor was created from a Pt electrode altered with glucose oxidase immobilized in a membrane of chitosan. An enhancement in the reaction rate compared to the system developed by Zeng *et al.* was reported. The range of identification for this biosensor was 0.05 mM at an SNR of 3. Accompanied with good constancy at high enzyme maintenance activity.

In this decay, scientists have been used nanomaterials such as nanoparticles, nan-fibers, nanotubes, and nano-composites in designing biosensor to ameliorate thier properties. Kaushik *et al.* introduced a biosensor containing iron oxide nanoparticles contained chitosan in tin Indium oxide solution which was stable for 8 weeks and its limit of detection was 100-400 mg dL^{-1} [101].

Nouira *et al.* conducted a study to show the possibility of implementation of biosensors contained two types of nanoparticles including gold and magnetic nanoparticles. They modified nanoparticles of Alyl amine hydrochloride (PAH) and achieved the best sensitivity by using magnetic nanoparticles (limit of detection of 3 μM and 70 mM) compared to gold nanoparticles (9 μM and 45 mM) and glucose oxidase (50 μM and 30 mM). The implemented method was amperometry while a three-days stability was reported [102].

Wu *et al.* designed a hybrid micro gel made from silver nanoparticles at a complex environment of physiologic pH enabled the optical monitoring of glucose levels with high selectivity. In fact, the resonance response belonged to hybrid micro gel enabled to identify glucose without interference effects in more than one range of clinical glucose concentration from 0.1-20 μM. This biosensor was tested on human blood serum [103].

Ahmad *et al.* produced ployvinylpyrolidon nanofibers on acetate with electrospinning technique 195-350 nm. Then, each nano-fiber covered on a gold electrode with physical absorbance of glucose oxidase; this action was performed for developing a very sensitive glucose electrochemical biosensor. Their work showed that this nanomaterial could provide optimal stability and long-term storage (more than 4 months) like an anti-interference capability [104].

To easily monitor glucose, a sensor based on a reusable smartphone was established requiring the software and settlement of disposable enzymatic pellets onto a bare sensor strip over the phone case [105]. Then, the sample is introduced by the user to the sensor surface and the data are measured and transmitted by the electronic module. Enhanced pellets contained Rh-C as catalysis for oxidizing H$_2$O$_2$, GOx with trehalose lyophilized in the buffer, graphite, and Ni. Amperometric measurements were conducted to achieve a calibration curve with various glucose concentrations. Vargas *et al.*, established a dual marker biosensor in another work, for simultaneous detecting insulin and glucose. The sensor utilized two gold working electrodes for insulin and glucose detection. By immobilizing GOx within permeable chitosan onto TTF redox mediator, the current during reoxidation was created. Such a sensor was able to measure insulin and glucose in spiked saliva specimens and whole blood without dilution [106].

A conductive ink made of automotive varnish and graphite was used to develop a disposable electrochemical glucose sensor [107]. A working electrode was obtained by printing the conductive ink on an adhesive paper sheet. Dihexadecyl phosphate and GOx were cast on the electrode and used for glucose detection, indicating a linear range of 1-10 μM with a LOD of 0.21 μM. Table 1 represents other essential enzymatic glucose sensors reported from 2016 briefly. Also, several advantages and disadvantages residing within the above-reviewed glucose sensing methods based on different sensor components are listed in Table 2.

CONCLUSIONS

This review addresses recent significant advances in the field of electro-spun nanofiber-based glucose sensors using different mechanisms. Introducing the glucose assays provides a great opportunity for the efficient immobilization of enzymes on their surface with elevated interaction with analytes, enhanced oxidation process and prolonged constancy. Many studies have been conducted on using nanomaterials such as gold, palatine, palladium, silver and graphene to reduce the limit of the detection of blood glucose. These studies have been carried out to reduce the limit of detection and biocompatibility of nanoparticles in the body and enzyme repeatability. Regarding the

Table 1. Overview of the Enzymatic Electrochemical Glucose Sensors

Sensor material	Detection method	Applied voltage (V)	Detection medium	Linear range	LOD (µM)	Sensitivity (µA mM^{-1} cm^{-2})	Selectivity	Long-term stability	Real sample analysis	Ref.
GOx/AuNPs/Cu-BTC MOFs/3D-KSCs	DPV	-	O$_2$-sat 0.1 M PBS	44.6 µM-4 mM 4-19 mM	14.77	-	AA, UA, U, Cys, Fru, Suc, Man	16 Days, 91.2% retained	Blood serum	[74]
RBCM	Amperometry	-0.3	0.1 M PBS	0-10 mM	1.06 mM	-	AA, UA, Gal	3 Weeks	Human serum	[76]
GOx/SPE/3D-PMED	Amperometry	-0.1	0.01 M PBS	0-1.9 mM	5	35.7	AA, UA, Lactate, NaCl	-	Human sweat	[81]
CdS/ITO with GOx mixed electrolyte	Amperometry CV	0.55	0.1 M PBSb	2-225 µM	0.1	1.345 **µA µM^{-1} cm^{-2}**	AA, DA, UA	20 Days 80% retained	Human blood serum	[83]
PtNWA/AuNP/GOx	Amperometry CV	0.3	0.1 M PBS (pH 7.2)	15 µM-2.5 mM	15	184	AA, CA, UA	21 Days	Rabbit blood serum	[108]
GOx/3D MoS$_2$/graphene aerogel	Amperometry	-0.45	-	2-20 mM	0.92 mM	3.36 µA mM^{-1}	AA, DA, UA	-	-	[109]
Pin- based sensor	Amperometry	-0.2	0.1 M PBSb	0.05-1 mM	30	-	AA, Fru	-	Honey, juice	[110]
PVI-Os/PEGDGE/PQQ GDH on CME	Amperometry CV	0.35	0.1 M PBb	0 -15 mM	16	5.16 pA mM^{-1}	-	Poor	-	[111]
Collagen based ECH-GOx	Amperometry	0.6	PBS (pH 7.4)	0-4 mM	-	-	-	27 Days	Porcine meat	[112]
GOx/Pt-MWCNTs/CSF	Amperometry CV	0.65	0.01 M PBS pH 7.4	0-5 mM	50	288.86	AA, UA AP	15 Days, 94% retained	-	[113]
GOx/CNT-Mucin/Pt	Amperometry	-	0.1 M PBSb	2 µM-3.2 mM	3 µM	15 mA M^{-1} cm^{-2}	AA	300 Days	Human blood plasma	[113]
Fc-C$_3$-LPEI/p-GOX	Amperometry	0.35	0.05 mM PBb	-	-	-	-	-	-	[115]
GOx/Au-ZnO/GCE	CV	-	O$_2$-sat 0.1 M PBSb	1-20 mM	20	1.409 µA mM^{-1}	AA, UA, DA,	15 Days, 5.6% decrease	Human serum	[116]
GOx/Cu-hemin MOFs	LSV	-	O$_2$-sat 0.1 M PBSb	9.1 µM-36 mM	2.73 µM	22.77	AA, UA, Fru, Gal, Man	30 Days, 87.5% retained	Human serum	[117]

Table 1. Continued

GOx/AuNPs/graphene	Amperometry	-0.2 V	0.1 M PBSb	0-40 mg dL^{-1}	0.3 mg dL^{-1}	-	AA, DA, UA NaCl	-	-	[118]
PAA-rGO/VS-ANI/LuPc2/GOx-MFH	Amperometry CV	0.3	0.1 M PBSb	2-12 mM	25	15.31	AA, UA	3 Months > 98% retained	Juice, human serum	[119]
4-ATP/PVA/PEI/GOxAuNPs	EIS	-	0.1 M PBS (pH 5)	0.01-0.2 mM	0.9	25 kΩ log-1 [Glucose]	AA, UA,	4 Days	-	[120]
GOx/Nafion/ScPdNF/G FET-type sensor	ISD, VG = -100 mV	-	1 M NaOH 0.1 M PBS	1 nM-1 µM	1 nM	-	AA, UA	-	-	[121]
Prussian blue NPs@filter paper/GOx	Amperometry	-0.1	0.05 M PB	0-25 mM	-	-	AA, AP, UA	-	Human blood	[122]
GOx/Au/Ni/Au NW	Potentiometry	-	Buffer	0.5- 10 mM	-	123.3 mV decade^{-1}	Ca^{2+}, Cl$^-$, K$^+$, Na$^+$	-	-	[123]
(CS-GLM)7-GCE	CV	-	0.1 M PBS	0.01-10 mM	1.31 µM	-	-	7 Days, 72% retained	Juice	[124]
SiC@C/Pt NWE/GOx	Amperometry CV	0.6	PBS	0-1 mM	41 µM	20.72 pA mM^{-1}	-	8 Days, 84% retained	HUVECs, LO2 cells	[125]
GOx/Au/MoS2/Au	Amperometry	-0.1	PBS	10-500 nM	10 nM	-	AA, UA	-	Human serum	[126]
GOx/Pt/rGO/P3ABA/SPE	Amperometry	0.5	0.1 M PBS pH 7.4	0.25-6 mM	44.3	22.01	AA, UA, Cho, Suc	7 Days, 86% retained	Human serum	[127]
PTTzFr/GOx on graphite	Amperometry	-0.7	0.05 M PB	0.005-0.7 mM	12.8	65.44	CA, U	-	Beverage	[128]
GOx/SBP$_{Thi}$/GCE	DPV	-	O$_2$-sat 0.2 M PBS	0.82 µM-4 mM	0.27	-	AA, UA, NaCl, KCl, H$_2$O$_2$, Cys	2 Weeks 5.6% decrease	Blood serum	[129]

Table 2. The Merits and Demerits of Sensor Components Employed in Glucose Sensing Methods

Components	Disadvantages	Advantages	Ref.
Enzyme	Deactivation in the presence of ionic detergents Instable above 40 °C Bioactivity is affected by pH and humidity	Good selectivity and sensitivity	[130,131]
Metal oxides	High oxidation potentials Poor conductivity Alkaline conditions are needed usually	Cost-effectivity High stability Easy chemical modification and preparation	[132,133]
Graphene	Heterogeneity of samples	Enhanced electrical conductivity due to high carrier mobility Good mechanical strength Biocompatibility	[134,135]
Noble metals	Poor sensitivity due to slow kinetics Expensive for commercial use Activity of the electrode is hindered in presence of oxidation intermediates and chloride ions	Higher stability compared to enzyme High electrocatalytic activity for glucose oxidation	[136]
MIPs	Template removal conditions must be optimized for efficient binding	Robustness Cost-effective and facile synthesis Physical and chemical stability Ability to easily attain high binding affinity with a target molecule	[137,138]
Carbon nanotubes	Involvement of possible contamination or degradation of nanotubes Tedious post-synthesis separation processes	Thermal and chemical stability, high mechanical strength, high surface area High electrocatalytic properties	[139,140]

significance of biosensors and their very useful efficiency, we hope that researchers can design stable, accurate, and sensitive sensors using these methods.

SUMMARY

Some of the most utilized biosensors in the market are electrochemical biosensors mainly due to glucose monitoring.

Electrochemical biosensors are inherently inexpensive, easily miniaturized and need simple electronics for read-out and conditioning, making them perfect for point-of-care usages.

Amperometric biosensors evaluate flows due to electroactive species, often utilizing mediators to improve electron transition.

Electrochemical impedance spectroscopy-based biosensors are among the most encouraging electrochemical sensors for systems with well-defined charges like DNA.

Nowadays, thanks to the extraordinary attributes of nanomaterials like graphene and carbon nanotubes, electrochemical nano-bio sensors with very low limits of detection are being developed.

AUTHORS' CONTRIBUTIONS

Authors read and approved the final manuscript.

ACKNOWLEDGEMENTS

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of Interest
The authors declare that they have no competing interests.

Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent
Informed consent was obtained from all individual participants included in the study.

REFERENCE

[1]   E. Burcu Aydın, M. Aydın, M. Kemal Sezgintürk. Int. J. Environ. Anal. Chem. 100 (2020) 602.

[2]   P. Fioretto, M.W. Steffes, D.E. Sutherland, F.C. Goetz, M. Mauer, N. Engl. J. Med. 339 (1998) 69.

[3]   B.R. Eggins, Chem. Sens. Biosens., Vol. 28, John Wiley & Sons, 2008.

[4]   M. Takase, E. Takahashi, M. Murata, H. Ohnuki, K. Hibi, H. Ren, H. Endo, Int. J. Environ. Anal. Chem. 93 (2013) 125.

[5]   M. Rahmani, H. Ghafoori Fard, M.T. Ahmadi, K. Rahmani. Int. J. Environ. Anal. Chem. 97 (2017) 1024.

[6]   P. Wang, H. Jia, in Bioprocessing for Value-Added Products from Renewable Resources, 2007

[7]   A.A. Karyakin, O.V. Gitelmacher, E.E. Karyakina, Anal. Chem. 67 (1995) 2419.

[8]   T. Kaku, H.I. Karan, Y. Okamoto, Anal. Chem. 66 (1994) 1231.

[9]   G.F. Khan, W. Wernet. Anal. Chem. 69 (1997) 2682.

[10] R. Pauliukaite, A. Malinauskas, G. Zhylyak, U.E. Spichiger-Keller, Electroanalysis 19 (2007) 2491.

[11] N. Mano, F. Mao, A. Heller, J. Electroanal. Chem. 574 (2005) 347.

[12] M.E. Ghica, C.M. Brett, Anal. Chim. Acta 532 (2005) 145.

[13] F. Mizutani, S. Yabuki, S. Iijima, Anal. Chim. Acta 300 (1995) 59.

[14] Z. Sun, H. Tachikawa, Anal. Chem. 64 (1992) 1112.

[15] T. Kondo, M. Horitani, M. Yuasa, Int. J. Electrochem. 2012 (2012) 943957.

[16] K. Wang, J.J. Xu, H.Y. Chen, Biosens. Bioelectron. 20 (2005) 1388.

[17] A. Salek-Maghsoudi, F. Vakhshiteh, R. Torabi, S. Hassani, M.R. Ganjali, P. Norouzi, M. Hosseini, M. Abdollahi, Biosens. Bioelectron. 99 (2018) 122.

[18] J. Wang, Anal. Electrochem. Third ed., John Wiley & Sons, Inc., Hoboken, NJ, 2006, pp. 165-200.

[19] L.C. Clark Jr, C. Lyons, Ann. N. Y. Acad. Sci. 102 (1962) 29.

[20] K.E. Toghill, R.G. Compton. Int. J. Electrochem. Sci. 5 (2010) 1246.

[21] G. Reach, G.S. Wilson, Anal. Chem. 64 (1992) 381A.

[22] D.A. Gough, J.Y. Lucisano, P.H. Tse, Anal. Chem. 57 (1985) 2351.

[23] J.C. Armour, J.Y. Lucisano, B.D. McKean, D.A. Gough, Diabetes 39 (1990) 1519.

[24] J. Wang, F. Lu, J. Am. Chem. Soc. 120 (1998) 1048.

[25] J. Wang, J.W. Mo, S. Li, J. Porter, Anal. Chim. Acta 441 (2001) 183.

[26] R. Kontani, S. Tsujimura, K. Kano, Bioelectrochemistry 76 (2009) 10.

[27] F. Moussy, S. Jakeway, D.J. Harrison, R.V. Rajotte,

Anal. Chem. 66 (1994) 3882.

[28] S.A. Emr, A.M. Yacynych, Electroanalysis 7 (1995) 913.

[29] J. Li, Y. Li, Y. Zhang, G. Wei, Anal. Chem. 84 (2012) 1888.

[30] C. Chen, Y. Fu, C. Xiang, Q. Xie, Q. Zhang, Y. Su, L. Wang, S. Yao, Biosens. Bioelectron. 24 (2009) 2726.

[31] L. Bahshi, M. Frasconi, R. Tel-Vered, O. Yehezkeli, I. Willner, Anal. Chem. 80 (2008) 8253.

[32] Y. Fu, P. Li, Q. Xie, X. Xu, L. Lei, C. Chen, C. Zou, W. Deng, S. Yao, Adv. Funct. Mater. 19 (2009) 1784.

[33] S. Hrapovic, Y. Liu, K.B. Male, J.H. Luong, Anal. Chem. 76 (2004) 1083.

[34] J. Wu, L. Yin, ACS Appl. Mater. Interfaces 3 (2011) 4354.

[35] E.W. Stein, D.V. Volodkin, M.J. McShane, G.B. Sukhorukov, Biomacromolecules 7 (2006) 710.

[36] Z. Wang, S. Liu, P. Wu, C. Cai, Anal. Chem. 81 (2009) 1638.

[37] K. Wang, D. Zhang, T. Zhou, X.H. Xia, Chem. - Eur. J. 11 (2005) 1341.

[38] A.N. Sekretaryova, D.V. Vokhmyanina, T.O. Chulanova, E.E. Karyakina, A.A. Karyakin, Anal. Chem. 84 (2012) 1220.

[39] R. Rajagopalan, A. Aoki, A. Heller, J. Phys. Chem. C 100 (1996) 3719.

[40] L. Zheng, J. Li, J. Xu, L. Xiong, D. Zheng, Q. Liu, W. Liu, Y. Li, S. Yang, J. Xia, Analyst 135 (2010) 1339.

[41] C. Qin, C. Chen, Q. Xie, L. Wang, X. He, Y. Huang, Y. Zhou, F. Xie, D. Yang, S. Yao, Anal. Chim. Acta 720 (2012) 49.

[42] C. Chen, L. Wang, Y. Tan, C. Qin, F. Xie, Y. Fu, Q. Xie, J. Chen, S. Yao, Biosens. Bioelectron. 26 (2011) 2311.

[43] E.J. Calvo, R. Etchenique, C. Danilowicz, L. Diaz, Anal. Chem. 68 (1996) 4186.

[44] Y. Kajiya, H. Sugai, C. Iwakura, H. Yoneyama, Anal. Chem. 63 (1991) 49.

[45] P.D. Hale, T. Inagaki, H.I. Karan, Y. Okamoto, T.A. Skotheim, J. Am. Chem. Soc. 111 (1989) 3482.

[46] T.J. Ohara, R. Rajagopalan, A. Heller, Anal.

Chem. 65 (1993) 3512.

[47] N. Mano, J.E. Yoo, J. Tarver, Y.L. Loo, A. Heller, J. Am. Chem. Soc. 129 (2007) 7006.

[48] W. Schuhmann, T.J. Ohara, H.L. Schmidt, A. Heller, J. Am. Chem. Soc. 113 (1991) 1394.

[49] S. Alwarappan, S.R. Singh, S. Pillai, A. Kumar, S. Mohapatra, Anal. Lett. 45 (2012) 746.

[50] P. Si, S. Ding, J. Yuan, X.W. Lou, D.H. Kim, ACS Nano 5 (2011) 7617.

[51] L. Fruk, C.H. Kuo, E. Torres, C.M. Niemeyer, Angew. Chem., Int. Ed. 48 (2009) 1550.

[52] M. Zayats, B. Willner, I. Willner, Electroanalysis 20 (2008) 583.

[53] F. Patolsky, Y. Weizmann, I. Willner, Angew. Chem. 116 (2004) 2165.

[54] O. Yehezkeli, S. Raichlin, R. Tel-Vered, E. Kesselman, D. Danino, I. Willner, J. Phys. Chem. Lett. 1 (2010) 2816.

[55] C. Shan, H. Yang, J. Song, D. Han, A. Ivaska, L. Niu, Anal. Chem. 81 (2009) 2378.

[56] S. Alwarappan, S. Boyapalle, A. Kumar, C.Z. Li, S. Mohapatra, J. Phys. Chem. C 116 (2012) 6556.

[57] R. Gao, J. Zheng, Electrochem. Commun. 11 (2009) 608.

[58] J.T. Holland, C. Lau, S. Brozik, P. Atanassov, S. Banta, J. Am. Chem. Soc. 133 (2011) 19262.

[59] X. Liu, L. Shi, W. Niu, H. Li, G. Xu, Biosens. Bioelectron. 23 (2008) 1887.

[60] Y. Su, Q. Xie, C. Chen, Q. Zhang, M. Ma, S. Yao, Biotechnol. Prog. 24 (2008) 262.

[61] Y. Wang, Y. Yao. Microchim. Acta 176 (2012) 271.

[62] J.P. Lowry, K. McAteer, S.S. El Atrash, A. Duff, R.D. O'Neill, Anal. Chem. 66 (1994) 1754.

[63] D. Brady, J. Jordaan, Biotechnol. Lett. 31 (2009) 1639.

[64] N.M. Nor, Z. Lockman, K.A. Razak, Procedia Chem. 19 (2016) 50.

[65] Q. Zeng, J.S. Cheng, X.F. Liu, H.T. Bai, J.H. Jiang, Biosens. Bioelectron. 26 (2011) 3456.

[66] H. Du Toit, M. Di Lorenzo, Electrochim. Acta 138 (2014) 86.

[67] Y. Wang, Y. Shao, D.W. Matson, J. Li, Y. Lin, ACS Nano 4 (2010) 1790.

[68] S. Alwarappan, C. Liu, A. Kumar, C.Z. Li, J. Phys.

Chem. C 114 (2010) 12920.

[69] R. Sternberg, D.S. Bindra, G.S. Wilson, D.R. Thevenot, Anal. Chem. 60 (1988) 2781.

[70] L. Setti, A. Fraleoni-Morgera, B. Ballarin, A. Filippini, D. Frascaro, C. Piana, Biosens. Bioelectron. 20 (2005) 2019.

[71] M.A. Akhtar, R. Batool, A. Hayat, D. Han, S. Riaz, S.U. Khan, L. Niu, ACS Appl. Nano Mater. 2 (2019) 1589.

[72] B.D. Mansuriya, Z. Altintas, Mater. 13 (2020) 96.

[73] J. Li, Y. Liu, X. Tang, L. Xu, L. Min, Y. Xue, X. Hu, Z. Yang, Microchim. Acta 187 (2020) 1.

[74] Y. Song, M. Xu, C. Gong, Y. Shen, L. Wang, Y. Xie, L. Wang, Sens. Actuators, B 257 (2018) 792.

[75] H. Cheng, X. Wang, H. Wei, Anal. Chem. 87 (2015) 8889.

[76] I. Kim, D. Kwon, D. Lee, T.H. Lee, J.H. Lee, G. Lee, D.S. Yoon, Biosens. Bioelectron. 102 (2018) 617.

[77] L. Wang, M. Xu, Y. Xie, C. Qian, W. Ma, L. Wang, Y. Song, Sens. Actuators, B 285 (2019) 264.

[78] S. Soylemez, H.Z. Kaya, Y.A. Udum, L. Toppare, Org. Electron. 65 (2019) 327.

[79] E. Bihar, S. Wustoni, A.M. Pappa, K.N. Salama, D. Baran, S. Inal, npj Flexible Electron. 2 (2018) 1.

[80] H. Lee, C. Song, S. Baik, D. Kim, T. Hyeon, D.H. Kim, Adv. Drug Delivery Rev. 127 (2018) 35.

[81] Q. Cao, B. Liang, T. Tu, J. Wei, L. Fang, X. Ye, RSC Adv. 9 (2019) 5674.

[82] L. Lipani, B.G. Dupont, F. Doungmene, F. Marken, R.M. Tyrrell, R.H. Guy, A. Ilie, Nat. Nanotechnol. 13 (2018) 504.

[83] B. Saha, S.K. Jana, S. Majumder, S. Banerjee, Sens. Actuators, B 283 (2019) 116.

[84] D.J. Harrison, R.F. Turner, H.P. Baltes, Anal. Chem. 60 (1988) 2002.

[85] S. Poyard, N. Jaffrezic-Renault, C. Martelet, S. Cosnier, P. Labbe, Anal. Chim. Acta 364 (1998) 165.

[86] S.H. Lim, J. Wei, J. Lin, Q. Li, J. KuaYou, Biosens. Bioelectron. 20 (2005) 2341.

[87] C. Shan, H. Yang, J. Song, D. Han, A. Ivaska, L. Niu, Anal. Chem. 81 (2009) 2378.

[88] K. Zhou, Y. Zhu, X. Yang, C. Li, Electroanalysis 22 (2010) 259.

[89] A. Ramanavičius, A. Kaušaitė, A. Ramanavičienė,

[90] O.M. Schuvailo, O.O. Soldatkin, A. Lefebvre, R. Cespuglio, A.P. Soldatkin, Anal. Chim. Acta 573 (2006) 110.

[91] S. Poyard, C. Martelet, N. Jaffrezic-Renault, S. Cosnier, P. Labbe, Sens. Actuators, B 58 (1999) 380.

[92] N.G. Poulos, J.R. Hall, M.C. Leopold, Langmuir 31 (2015) 1547.

[93] T.T. Baby, S.J. Aravind, T. Arockiadoss, R.B. Rakhi, S. Ramaprabhu, Sens. Actuators, B 145 (2010) 71.

[94] Y. Liu, D. Yu, C. Zeng, Z. Miao, L. Dai, Langmuir 26 (2010) 6158.

[95] S. Alwarappan, C. Liu, A. Kumar, C.Z. Li, J. Phys. Chem. C 114 (2010) 12920.

[96] H. Yin, Y. Zhou, X. Meng, K. Shang, S. Ai, Biosens. Bioelectron. 30 (2011) 112.

[97] W. Zhang, Y. Du, M.L. Wang, Sens. Biosens. Res. 4 (2015) 96.

[98] N.M. Nor, Z. Lockman, K.A. Razak, Procedia Chem. 19 (2016) 50.

[99] J. Liu, A. Chou, W. Rahmat, M.N. Paddon-Row, J.J. Gooding, Electroanalysis 17 (2005) 38.

[100] L.F. Ang, L.Y. Por, M.F. Yam, PLoS One 10 (2015) e0111859.

[101] A. Kaushik, R. Khan, P.R. Solanki, P. Pandey, J. Alam, S. Ahmad, B.D. Malhotra, Biosens. Bioelectron. 24 (2008) 676.

[102] W. Nouira, A. Maaref, H. Elaissari, F. Vocanson, M. Siadat, N. Jaffrezic-Renault, Mater. Sci. Eng. C 33 (2013) 298.

[103] W. Wu, J. Shen, Y. Li, H. Zhu, P. Banerjee, S. Zhou, Biomater. 33 (2012) 7115.

[104] M. Ahmad, C. Pan, Z. Luo, J. Zhu, J. Phys. Chem. C 114 (2010) 9308.

[105] A.J. Bandodkar, S. Imani, R. Nunez-Flores, R. Kumar, C. Wang, A.V. Mohan, J. Wang, P.P. Mercier, Biosens. Bioelectron. 101 (2018) 181.

[106] E. Vargas, H. Teymourian, F. Tehrani, E. Eksin, E. Sánchez-Tirado, P. Warren, A. Erdem, E. Dassau, J. Wang, Angew. Chem., Int. Ed. 58 (2019) 6376.

[107] L.O. Orzari, R.C. de Freitas, I.A. de Araujo Andreotti, A. Gatti, B.C. Janegitz, Biosens. Bioelectron. 138 (2019) 111310.

[108] Z. Li, F. Gao, Z. Gu, Sens. Actuators, B 243 (2017)

1092.

[109] J.M. Jeong, M. Yang, D.S. Kim, T.J. Lee, B.G. Choi, J. Colloid Interface Sci. 506 (2017) 379.

[110] E.C. Rama, A. Costa-García, M.T. Fernández-Abedul, Biosens. Bioelectron. 88 (2017) 34.

[111] M. Marquitan, T. Bobrowski, A. Ernst, P. Wilde, J. Clausmeyer, A. Ruff, W. Schuhmann, J. Electrochem. Soc. 165 (2018) G3008.

[112] R. Ravichandran, J.G. Martinez, E.W. Jager, J. Phopase, A.P. Turner, ACS Appl. Mater. Interfaces 10 (2018) 16244.

[113] C. Chen, R. Ran, Z. Yang, R. Lv, W. Shen, F. Kang, Z.H. Huang, Sens. Actuators, B 256 (2018) 63.

[114] F.N. Comba, M.R. Romero, F.S. Garay, A.M. Baruzzi, Anal. Biochem. 550 (2018) 34.

[115] N.P. Godman, J.L. DeLuca, S.R. McCollum, D.W. Schmidtke, D.T. Glatzhofer, Langmuir 32 (2016) 3541.

[116] L. Fang, B. Liu, L. Liu, Y. Li, K. Huang, Q. Zhang, Sens. Actuators, B 222 (2016) 1096.

[117] J. He, H. Yang, Y. Zhang, J. Yu, L. Miao, Y. Song, L. Wang, Sci. Rep. 6 (2016) 36637.

[118] Z. Pu, R. Wang, J. Wu, H. Yu, K. Xu, D. Li, Sens. Actuators, B 230 (2016) 801.

[119] H. Al-Sagur, S. Komathi, M.A. Khan, A.G. Gurek, A. Hassan, Biosens. Bioelectron. 92 (2017) 638.

[120] E. Sapountzi, M. Braiek, F. Vocanson, J.F. Chateaux, N. Jaffrezic-Renault, F. Lagarde, Sens. Actuators, B 238 (2017) 392.

[121] D.H. Shin, W. Kim, J. Jun, J.S. Lee, J.H. Kim, J. Jang, Sens. Actuators, B 264 (2018) 216.

[122] S. Cinti, R. Cusenza, D. Moscone, F. Arduini, Talanta 187 (2018) 59.

[123] M.H. Asif, A. Razaq, N. Akbar, B. Danielsson, I. Sultana, Mater. Res. Express. 6 (2019) 095028.

[124] H. Guan, D. Gong, Y. Song, B. Han, N. Zhang, Colloids Surf., A 574 (2019) 260.

[125] Q.L. Liao, H. Jiang, X.W. Zhang, Q.F. Qiu, Y. Tang, X.K. Yang, Y.L. Liu, W.H. Huang, Nanoscale 11 (2019) 10702.

[126] J. Yoon, S.N. Lee, M.K. Shin, H.W. Kim, H.K. Choi, T. Lee, J.W. Choi, Biosens. Bioelectron. 140 (2019) 111343.

[127] S. Phetsang, J. Jakmunee, P. Mungkornasawakul, R. Laocharoensuk, K. Ounnunkad, Bioelectrochemistry 127 (2019) 125.

[128] S. Soylemez, H.Z. Kaya, Y.A. Udum, L. Toppare, Org. Electron. 65 (2019) 327.

[129] L. Wang, M. Xu, Y. Xie, C. Qian, W. Ma, L. Wang, Y. Song, Sens. Actuators B Chem. 285 (2019) 264.

[130] A. Weremfo, S. Tung, C. Fong, A. Khan, D.B. Hibbert, C. Zhao, Electrochim. Acta 231 (2017) 20.

[131] S. Park, H. Boo, T.D. Chung. Anal. Chim. Acta 556 (2006) 46.

[132] G. He, L. Tian, Y. Cai, S. Wu, Y. Su, H. Yan, W. Pu, J. Zhang, L. Li, Nanoscale Res. Lett. 13 (2018) 3.

[133] H. Zhu, L. Li, W. Zhou, Z. Shao, X. Chen, J. Mater. Chem. B 4 (2016) 7333.

[134] H. Lee, T.K. Choi, Y.B. Lee, H.R. Cho, R. Ghaffari, L. Wang, H.J. Choi, T.D. Chung, N. Lu, T. Hyeon, S.H. Choi, D.H. Kim, Nat. Nanotechnol. 11 (2016) 566.

[135] F. Wang, L. Liu, W.J. Li, Graphene-Based Glucose Sensors: A Brief Review. IEEE Trans. Nanobioscience 14 (2015) 818.

[136] Q. Zhang, Q. Luo, Z. Qin, L. Liu, Z. Wu, B. Shen, W. Hu, ACS Omega 3 (2018) 3420.

[137] A.F.T. Waffo, C. Yesildag, G. Caserta, S. Katz, I. Zebger, M.C. Lensen, U. Wollenberger, F.W. Scheller, Z. Altintas, Sens. Actuators B Chem. 275 (2018) 163.

[138] D.M. Kim, J.M. Moon, W.C. Lee, J.H. Yoon, C.S. Choi, Y.B. Shim, Biosens. Bioelectron. 91 (2017) 276.

[139] R. Prasad, B.R. Bhat, Sens. Actuators B Chem. 220 (2015) 81.

[140] W. Yang, K.R. Ratinac, S.P. Ringer, P. Thordarson, J.J. Gooding, F. Braet, Angew. Chemie- Int. Ed. 49 (2010) 2114.