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Recent advances in metal oxide, bimetallic nanocomposites, metal-organic frameworks (MOFs), and non-invasive technologies for biofluid-based glucose sensors: A comprehensive review

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ABSTRACT

The field of glucose biosensors for diabetes control has experienced enormous scientific and technological developments since it was first introduced in the 1960s, with electrochemical biosensors emerging as the most promising platform for real-time, dynamic glucose monitoring due to the high precision, versatility and compatibility with wearable devices. Over the past decade, wearable healthcare technologies have significantly advanced, enabling non-invasive or minimally invasive monitoring of biomarkers in peripheral biofluids such as sweat, saliva, tears and interstitial fluid (ISF) through electrochemical sensing. While enzymatic biosensors, particularly those employing glucose oxidase (GOx), remain prevalent for their sensitivity, challenges such as enzyme instability and limited shelf life persist. In response, non-enzymatic have gained prominence, leveraging nanostructure materials like metal oxides (e.g., NiO, CuO, ZnO), metal-organic frameworks (MOFs) and bimetallic composites (e.g., CuCo-MOFs) to achieve superior sensitivity, stability and catalytic performance. These materials exploit high surface-to-volume ratios, tuneable porosity and synergistic effects to overcome limitations such as pH sensitivity and poor conductivity. Innovations in material design, including laser-induced (LIG) and hybrid composites (eg., MXene/rGO), further enhance electron transfer and these materials enable low detection limits, wide linear ranges and rapid response time. This review comprehensively examines recent enzyme-free glucose sensors, focusing on the advancement of nanomaterials and their integration into wearable platforms such as microneedle-based ISF monitor contact lens sensors for tear analysis and hydrogel patches for sweat glucose detection. We critically evaluate the current state of biofluid sensing, addressing challenges in accuracy mad scalability while highlighting the convergence of advanced nanomaterials.

1. Introduction

Over the past ten years, wearable healthcare has advanced significantly in health monitoring [1]. Personalised diagnostics and physiological health monitoring have benefited from the rapid advancement of technology. The advances include the development of wearable sensing technology, a promising and rapidly developing area of research that is confidently moving forward from tracking physical activity to monitoring health issues [1,2]. Recent research has focused on designing non-invasive and /or minimally invasive wearable devices to track constantly changing health-related biomarkers in peripheral biofluids such as tears, sweat, saliva and interstitial fluid (ISF) [1,3]. Electrochemical biosensors remain the most widely used biosensing platform since their inception, offering distinct advantages including rapid detection, cost effectiveness, portability and instrument simplicity, making them particularly suitable for point-of-care diagnostics and immunoassays. To date, they represent the most clinically significant category encompassing both enzymatic and non-enzymatic biosensors that primarily use amperometric techniques. While enzymatic sensors utilize biological recognition elements, their non-enzymatic counterparts operate through direct electrochemical oxidation of glucose [4]. These biosensors operate based on the amperometric principle,

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continuously measuring the current generated by the oxidation or reduction of an electroactive species in a biological reaction [5]. Glucose biosensors have evolved through four generations of enzymatic systems, primarily utilising glucose oxidase (GOx) and glucose dehydrogenase (GDH) with their respective cofactors. Among these, GOx is particularly valued for its glucose selectivity and stability under varying pH and temperature conditions. However, maintaining enzymatic activity remains challenging due to their inherent instability and limited lifespan. Beyond biosensing applications, blood glucose monitoring also relies on other enzymes such as glucose dehydrogenase (G-6-PD), hexokinase (HK) and GDH, which play critical roles in metabolic pathways [6].

In enzymatic sweat glucose sensors, glucose oxidase converts glucose into gluconic acid ($C_6H_{12}O_7$) and hydrogen peroxide (H_2O_2). In contrast, non-enzymatic sensors rely on nanomaterial modifiers (e.g., metals, alloys and metal oxides) to directly oxidise glucose without enzyme mediation. Liu et al. [7] showed a mechanism that outlines the redox process where cobalt-iron with MOF catalyses the oxidation of glucose to gluconolactone.

$$[Co(II)Fe(II)(MI)_{4)}]_n + nOH^- \rightarrow [Co(III)Fe(III)MI_4(OH)_2]_n + ne^- \quad (1)$$

$$[Co(III)Fe(III)(MI)_4(OH)_2]_n + nOH^- \rightarrow [Co(IV)Fe(III)(MI)_4(OH)_3]_n + ne^- \quad (2)$$

$$[Co(II)Fe(II)(MI)_{3)}]_n + glucose \rightarrow [Co(III)Fe(II)MI_4(OH)_2]_n + H_2O + gluconolactone \quad (3)$$

$$[Co(III)Fe(II)(MI)_4(OH)_2]_n + glucose \rightarrow [Co(III)Fe(II)MI_4]_n + H_2O + gluconolactone \quad (4)$$

Recently, simple and flexible matrices have garnered significant attention due to their suitability for immobilising biomolecules (e.g., proteins, enzymes, DNA) and developing sensitive enzymatic biosensors. Self-assembled monolayer-based interfaces are essential for constructing enzymatic biosensors due to their highly ordered molecular structure. These systems offer convenience, flexibility and excellent sensitivity and selectivity. Furthermore, these monolayers offer molecular biological activities which promote the direct electron-transfer process and the electrocatalytic ability of biomolecules [8]. They use different immobilisation techniques, such as adsorption, crosslinking electro-polymerisation, and polymerisation. These biosensors have a short shelf life which is influenced by enzyme degradation and chemical interferences [9,10]. A biocompatible membrane, such as lipids, polymers and hydrogels is used together with enzymes and mediators to limit contamination and unwanted responses. Considering the limitations of enzyme-based biosensors, non-enzymatic biosensors do not require the use of biological molecules like enzymes [11,12]. Moreover, non-enzymatic biosensors' surface area can be enhanced with catalysts or immobilisation platforms, and functionalised nanomaterials can improve the sensitivity and specificity of detection [13]. Non-enzymatic sensors remain superior in terms of stability and cost-effectiveness, and the incorporation of nanostructured metals and metal oxides onto the electrode surfaces greatly improves sensitivity, playing a crucial role in the progress of non-enzymatic biosensors [14]. The current review primarily focuses on the detection of glucose using non-enzymatic biosensors and different biofluids, with a specific emphasis on the latest advancement of non-enzymatic biosensors based on surface modification and encompassing metal oxides and metal-organic frameworks (MOFs). Additionally, the review covers the wide variety of materials used, the underlying detection principles, and an in-depth evaluation of the sensors' effectiveness in detecting glucose levels in biofluids such as sweat, saliva, tears and interstitial fluids (ISF). The review highlights considerable progress made in this area, the promising future, and the capabilities of non-invasive biosensors in biofluids.

2. Metal nanomaterial composites on non-enzymatic glucose sensing

Metal oxides have been extensively studied for the detection of non-enzymatic glucose in an alkaline environment [15]. The metal oxides, including nickel oxide (NiO), Zinc oxide (ZnO), iron oxide (Fe_3O_4), copper oxide (CuO), Cerium oxide (CeO_2), and manganese dioxide (MnO_2) [16], are combined with other elements or compounds to form composites. Metal oxide nanomaterials have garnered significant interest as immobilizing matrices for biosensors due to their advantageous characteristics, such as biocompatibility [17], ease of preparation [18], controllable shape and size, chemical stability [19], optical and catalytic properties, electro-transfer kinetics, and strong adsorption capability [20]. They also possess unique physicochemical properties, including fluorescence, UV absorption, photocatalytic activity, and dielectric and magnetic properties [21]. Metal oxide-based biosensors fall short of commercialization standards because they fail to meet clinical detection requirements. This shortfall is due to the enzyme's sensitivity to pH variations, storage conditions temperature fluctuations [22]. Additionally, they must support enzyme immobilization for glucose oxidation in a neutral pH environment [23]. The current trends to date include the integration of metal oxides with other functional materials such as conducting polymers and carbon materials (e.g., graphene and graphene oxide) to create a synergistic effect with non-enzymatic glucose [24,25]. This approach improves sensitivity and addresses the limitations of enzyme-based biosensors, including pH and temperature fluctuations, as well as the loss of enzyme functionality under harsh conditions [25]. Studies have been done to highlight nickel and its compounds in electrocatalysis and energy storage, specifically the electrochemical activity of nickel-based compounds, particularly the Ni(II) and Ni(III) couple. The interest lies mainly in the oxidation of carbohydrates, which include glucose, on nickel oxide in the application of nonenzymatic glucose sensing [26]. For example, Vu et al.[27] reported the NiO nanohives distributed on Ni foam, which showed sensitivity towards glucose compared to nickel (II) oxide materials reported prior. The synthesised NiO/Ni electrodes demonstrate excellent glucose sensing performance with a sensitivity of 10.08 $mM^{-1}.cm^{-2}$ and a limit of detection of 7.25 μA, showing strong potential for clinical glucose monitoring applications. Eprilia et al.[28] proposed a nickel foam modified with a hollow-like structure of $NiCo_2O_4$ to minimise Ni instability and high overpotential in glucose sensing. The prepared Ni foam/$NiCo_2O_4$ at a ratio of 1:2 nickel to cobalt ratio showed a sensitivity of 0.060 mA μM^{-1} and a detection limit of 0.060 μM. The enhanced pore volume and the surface of Ni foam/$NiCo_2O_4$ relative to the unmodified Ni Foam facilitate electrolyte diffusion to the electrodes' active, thereby improving its electrochemical performance. Zhou et al.[29] presented a glucose electrochemical sensor on a reduced graphene oxide (rGO) sheet to assist the Fe and Co bimetallic oxides. The introduction of iron (Fe) can prevent the agglomeration of nanomaterials and increase their homogeneity [30,31]. Fe also alters the microstructure of cobalt (Co) oxides, which enhances electrocatalytic efficiency by creating oxygen vacancies, and defects, and improving the adsorption of reaction intermediates. Additionally, the synergistic effect of metal ions may further improve electrocatalytic performance [31,32]. The Fex-$CoyO_4$-rGO modified electrode showed enhanced electrocatalysis and exhibited excellent detection performance for glucose in tears with a detection limit as low as 0.07 μM and a sensitivity of 1510 μM^{-1} $cm^{-2}mA^{-1}$ [32]. Wei et al.[33] designed a 3D hybrid structure combining Au and Cu_2O on a copper foil for glucose detection. The resultant hierarchical Au/Cu_2O nanowires demonstrated significant electrocatalytic activity, a large surface area, and a fast electron transfer rate, outperforming previously reported sensors utilising Au and Cu_2O-based composite modified electrodes, exhibiting enhanced sensitivity at lower detection potentials. The Au/Cu_2O NWAs supported on a conductive substrate showed low glucose LOD (1.5 μM) at a lower voltage of 0.4 V, and a higher sensitivity of 2.098 mA mM^{-1}. cm^{-2} and a

limit of detection of 1.50 μM. The stability of the sensor was evaluated by measuring its current response to glucose at three-day intervals over a month. After 30 days, the sensor maintained 94.7 % of its original sensitivity to glucose. Three possible reasons for this exceptional detection sensitivity as compared to other non-enzymatic glucose sensors made with Cu and Cu hybrids: (1) The incorporation of Au nanoparticles onto Cu_2O improves the material's conductivity and introduces extra active sites for glucose oxidation. (2) The nanowire array configuration of the electroactive materials provides a high density of active sites, enhancing the electrocatalytic oxidation of glucose. (3) The lack of binders enables efficient and rapid electron transfer among glucose, the electrocatalyst, and the current collector [33]. Shao et al.[34] developed a novel sonochemical synthesis method to regulate transient cavitation intensity during the fabrication of transition metal oxides (TMOs) on self-supported electrodes. Polydopamine (PDA) was used as an additive to stabilise CuO growth, ensuring a more uniform size distribution of CuO nanoparticles on the Carbon Cloth (CC) substrate. This method led to a precisely controlled nanostructure and improved interfacial properties, leading to the successful application of the CuO/PDA/CC electrode for glucose detection. The resulting flexible electrode demonstrated a significantly larger electrochemically active surface area (4.61 mF. cm^{-2}) than CuO/PDA/CC and CuO/CC electrodes, along with a high sensitivity of 1.843 μA cm^{-2}. mM^{-1}, demonstrating remarkable stability [34]. The application of metallic Cu and its oxides to fabricate glucose sensors has been widely used due to their low cost and high catalytic behaviour. Since the discovery of graphene in the sensor field, research has been done to combine graphene, metallic Cu, and Cu oxides. However, the interaction between graphene and Cu is significant, resulting in a slower rate of electron transfer, which deteriorates the sensor's performance as reported by Hidalgo-Manrique et al.[35]. To overcome this shortfall, a graphene modification together with free-standing Cu/Cu_2O, and CuO for glucose detection was proposed. Ren et al.[36] demonstrated the incorporation of graphene, along with the synergistic effects of Cu_0, Cu_1, and Cu_2, significantly enhances the rate of electron transfer, thereby improving the overall sensing properties. A nonenzymatic glucose biosensor developed utilizing a hybrid of copper oxides combined with Cu and graphene, mitigates the adverse effects of metals on graphene through the insertion of an intermediate Cu oxide layer. This self-supporting Cu–CuO–CuO glucose sensor exhibits remarkable resistance to interference, strong cycling and temporal stability, as well as a high sensitivity of 3102 A/mM.cm within a linear concentration range of 0.0022–2.88 mM. The enhanced catalytic performance is attributed to the synergistic effects of the Cu–CuO–CuO multi-oxidation system and the accelerated electron transfer rate facilitated by graphene. This enhancement is achieved by minimizing the interaction between copper and graphene through the presence of a Cu oxide intermediate layer. Moreover, the catalytic potential of graphene, associated with its inherent defects, is further amplified [36–38]. Different metal oxides have shown great catalytic activity when applied to glucose sensing. However, metal oxide tends to have low conductivity, preventing electron transfer between the catalyst and the electrode. To overcome this challenge, metal oxides are combined with conductive materials, forming binary, ternary, or multi-compound-based composites for non-enzymatic glucose sensing. Gopal et al.[39] reported using a ternary composite made from Cu_2O based on MXene supported on reduced graphene oxide (rGO). MXene, a two-dimensional material, is integrated with metal oxide nanoparticles onto rGO sheets to form a composite electrode. The composite exhibits excellent electrocatalytic activity towards glucose oxidation, enabling efficient glucose detection, rGO inhibits the stacking of MXene sheets, which boosts the electron transfer rate and creates more active sites. This results in a higher peak and spike current in the MG–Cu_2O composite. The prepared MXene sheet-Cu_2O composite shows good selectivity, stability, reproducibility, and sensitivity of 125.6 μAmM^{-1}.cm^{-2} for glucose analysis. The MG–Cu_2O modified electrode's reproducibility was validated by conducting chronoamperometry (CA) tests on six different electrodes, all of which exhibited consistent current changes, demonstrating the material's performance [36,39]. More importantly, the use of metal oxides, which face challenges with low sensitivity due to restacking or internal sheet aggregation, combined with the addition of polymeric nanofibers in the composites, helps to address this limitation. Using metal/metal oxide nanoparticles to modify carbon nanofibers in activated carbon fibre (ACF) is a coherent and expandable technique to promote effective glucose sensing. Saravanan et al. introduced a flower-like CuO/NiO nanostructure integrated with activated carbon nanofiber (ACNF) membranes to enhance electron transfer and provide a high surface area, thereby improving glucose electrooxidation kinetics. The resulting CuO/NiO/ACNF composite exhibited flexibility, binder-free fabrication, recyclability and cost and time-efficient production, simplifying glucose detection. The fabricated sensor demonstrated high sensitivity (247 μA mM^{-1}.cm^{-2}) and a low detection limit (146 nM) [40]. To build a synergistic electrocatalytic composite with a three-dimensional network that possesses high electrical conductivity and effective sensing area, Au and CO_3O_4 composite was proposed by Coyle et al.[41]. Although Co_3O_4 exhibits poor electronic conductivity, its application as a sensor material was aided by incorporating Co_3O_4 into the Au scaffold structure, resulting in an improvement of the electrochemical sensing capabilities. The material showed excellent sensitivity towards glucose of 2.014 mA.mM^{-1}.cm^{-2} at the low concentration range of 20 μM^{-1}.mM [41]. The CuO-graphene and Cu_2O-graphene composites typically involve complex procedures, such as hydrothermal or annealing techniques, often supplemented with surfactants or stabilising agents. These methods regulate the dispersion and dimensions of the produced oxides. However, they present challenges in scalability, making it difficult to manufacture the products in significant quantities [35]. Table 1 summarises the advantages and disadvantages of different metals and metal oxides found to be favourable in glucose sensing.

Zinc Oxide exhibits a strong optical response and can be used in the fabrication of colometric glucose sensing. Among its various properties,

Table 1
Analytical comparison of electrochemical sensors modified with metal oxides and noble metal nanoparticles as reported in various studies.

Materials	Target analytes	Limit of detection (μM)	Sensitivity (μA mM^{-1} cm^{-2})	References
Cu/Cu_2O aerogels	Glucose	0.6	1.95×10^3	[42]
TiO_2/CuO nanofibers	Glucose	10	–	[43]
Co_3O_4-Au nanowire	Glucose	0.005	12.5	[44]
CuO nanosheets	Glucose	-	5.20×10^2	[45]
TiO_2/I_2/CMC (TIC)	Glucose	400	-	[46]
NiO/C	Glucose	2	30.2	[47]
CuO/GO	Glucose			[48]
CuO-rGO	Glucose	4.7×10^4	1746	[49]
Cu_2O-BSA NPs	Glucose	Up to 100	0.000400	[50]
Au /Co_3O_4 //FTO	Glucose	50	8.20×10^4	[51]
CuO MFs/ Nafion/GC	Glucose	6.5	-	[52]
CoO micro flowers on a nickel foam (NF)	Glucose	0.5	2.82×10^7	[53]
$NiMnO_3$	Glucose	0.01	7560	[54,55]
NN-CuO/N-rGO	Glucose	0.01	0.0340	[55]
$NiCo_2O_4$-rGO	Glucose	100–550	4372	[56]
Pt-NiO/rGO	Glucose	2.7	832	[57]
	Glucose	29	297	[57]
Co_3O_4/MWCNT	Glucose	0.4	63.3	[58]
Co_3O_4/CuO NRA	Glucose	0.4	5405	[59]
Caterpillar-like gold nanotubes Cu_2O	Glucose	1.8	1215	[60]

Table 2
Saliva, tears, sweat and interstitial fluids (ISF)-based glucose monitoring devices comparison.

Biofluid	Advantages	Disadvantages	Electrode material/ Technique	Sensitivity	Linear Range	LOD	Reference
Saliva	• Non-invasive	• Low correlation blood	• Au/CuO/SPCE	236.70 μA mM^{-1} cm^{-2}	2 μM to 397 μM		[81]
	• Easily collected and does not require stimulation	• Many interfering biomarkers • Hysteretic behaviour • Low sensitivity • Prone to breeding bacteria	• NiCo-LDH/MWCNTs	2.25 μA mM^{-1} cm^{-2}	0.1–3000 μM	0.03 μM	[82]
Sweat	• Non-invasive	• Hysteretic behaviour	• Carbon black nanoparticles (CBNPs)	14.64 μA mM^{-1} cm^{-2}	5 μM to 1250 μM	4.83 μM	[38]
	• Easily collected via different stimulation techniques • A good candidate for wearable technology • Continuous monitoring	• Every analysis requires sweat; not suitable for diabetic patient	• Zwitterionic PSBMA-modified thread	255 mM^{-1}		14.7 μM	[82]
Tears	• Non-invasive • Less impurity and interference • A good candidate for wireless transmission technology	• Low comfort • Energy supply problem • Poor precision	• polyvinyl chloride • FC blue light Mini-LEDs		0.2–2 mM 0.1–10 mM	50 μM 2.15 mM	[83] [84]
ISF	• Non-invasive • Higher glucose concentration • Good correlation to blood • Large linear range • High sensitivity	• Skin irritation • Hysteretic behaviour	• CGM device • pH-responsive hydrogel system		0.25–35 mM		[85]

ZnO is non-toxic, has high chemical stability and can be modified into one-dimensional (1D), two-dimensional (2D), and three-dimensional (3D) forms to improve its catalytic performance [61]. Hsu et al.[61] studied the optical properties of ZnO by synthesizing high-density ZnO nanowires and decorating them with platinum nanoparticles. The sensitivity of the glucose sensor was investigated by comparing the use of UV and green LED illumination. The sensitivity was significantly higher under UV illumination at 928 $cm^{-2}.mM^{-1}$ than under green light at 123 $cm^{-2}.mM^{-1}$, primarily due to UV-induced effects such as surface charge localization and overcoming the Schottky barrier.

To exploit ZnO photo-oxidation properties, which is a feature required in fluorescence sensing applications. Dao et al.[62] combined the unique properties of ZnO nanorods with CuO wire mesh to make a non-enzymatic absorbance glucose sensor. Additionally, ZnO was used to photo-oxidise glucose to H_2O_2 using the ferrous oxidation-xylenol orange (FOX) assay technique. The sensor had a sensitivity of 0.394 mM^{-1} and a detection limit of 0.25 mM. The enhanced sensitivity arises from the high surface-to-volume ratio of the ZnO/CuO nanocomposite, which facilitates the adsorption of glucose and gluconic acid. However, these molecules eventually cover the active sites, leading to saturation. This inhibits further molecular interactions, reduces H_2O_2 generation and consequently limits the absorbance response.

2.1. Metal-organic frameworks (MOFs) for non-enzymatic glucose biosensing

Energy storage and electrochemical sensor technology are two areas with numerous potential applications for the design and structural customisation of metal-organic frameworks (MOFs) materials [63]. They also manage to serve as sturdy substrates for detecting material location, indicating a promising application for electrochemical detection. MOFs are large porous crystalline structures formed by coordination bonds of metal ions/clusters and organic ligands with potential unsaturated active sites and large surface areas [64,65]. The MOFs support the immobilisation of small-sized noble metal NPs and inhibit their aggregation, thus resulting in increased catalytic activity and structural stability. According to several studies, MOFs or ZIFs have several drawbacks that limit their use in electrolysis, such as poor chemical activity and undesired conductivity [66–68]. To address this limitation, research then shifted to incorporating additional metallic centres in the framework. Using the benefits of MOFs and the combined effects of Cu and Co metal ions, Song et al.[63] produced bimetallic CuCo-MOFs on the surface of Nickel foam (NF) using hydrothermal synthesis, which allowed for highly sensitive biosensors. The CuCo-MOFs/NF demonstrated a high sensitivity of 8304.4 μA $mM^{-1}.cm^{-2}$ for glucose detection. The sheet-like architecture in NF and the synergistic effect of cobalt (Co) and copper (Cu) metals in the catalysts are responsible for the improvement in electrocatalytic performance. NF improves electronic conductivity and active site accessibility, facilitating rapid charge transport during redox reactions [63]. Li et al.[66] studied the use of 2D MOF nanosheets to enhance the electrocatalytic performance of non-enzymatic biosensors. This was achieved by etching solid gold to create nanoporous gold, which served as a substrate, and the growing of a NiCo-MOFNs array vertically on the substrate surface through in situ methods [66]. The resulting biosensor demonstrated exceptional performance, attributed to the 2D structure and the synergistic interaction between N, Co, and Ni. Key performance metrics include a wide linear range of 1 mm to 8 mM, a high sensitivity of 0.6844 μA $mM^{-1}.cm^{-2}$, a fast response time of under 1 s, and a low detection limit of 0.29 mM. The development of obi- or multi-metallic MOF compounds offers superior catalytic efficiency and electrochemical activity compared to single-metal MOFs and MOF-free bimetallic compounds, due to their synergistic enhancement [69]. Moreover, bimetallic transition materials offer advantages such as multifunctionality, enhanced catalytic efficiency, improved activity and greater stability when compared to single-component monometallic materials [70]. The production of bimetal MOFs with desired morphology and enhanced electrochemical performance remains challenging, despite their enormous potential. To address this, Ma et al.[71] synthesised a nanosized Ni/NiO@C via a one-step calcination method of a yolk-shell hollow morphology [71]. The Ni and NiO particles were evenly distributed within the carbon matrix, which improved their electronic conductivity and provided numerous electrocatalytic active sites. The distinctive yolk-shell hollow sphere structure of the Ni/NiO@C microspheres used to modify the electrode created an efficient pathway for electrochemical sensing. This electrode demonstrated a broad linear range of 0.01–10 mm, a sensitivity to 1291 μA $mM^{-1}.cm^{-2}$, and a detection limit of 0.116 μM for glucose. Additionally, it

exhibited strong selectivity, excellent reproducibility and long-term stability for the two analytes [71]. The study found that increasing the mass concentration of Ni/NiO@C microspheres on electrodes improves the current response for glucose detection, peaking at 2 mg/mL. Beyond this concentration, the current response decreases, suggesting that too much active materials hinder electronic communication with the electrode, while too little is not sufficient for effective glucose oxidation [71]. Due to their high electronegativity and polarisability, halogens impart unique characteristics to halogenated molecules, such as low surface tension and low surface energy. Li et al.[66] reported a one-pot synthesis method for NiCo bimetallic MOF nanoplates using pyridine as a modulator. This approach introduced a polar halogen molecule onto the surface of the MOFs, resulting in halogenated NiCo-MOF nanoplates to enhance sensing activities. The surface halogenation improved the MOF interaction with glucose, and the synthesized NiCoBP-Br showed a high sensitivity of up to 1755.51 μA mM^{-1} cm^{-2} in the range of 0.5–6065.5 μM. The MOF-based electrochemical biosensors have been focused on improved tolerance of strong acidic and basic environments. Kim et al.[72] prepared a chemically stable ZIF-67 by partially replacing cobalt with zinc. The synthesised Zeolitic-imidazolate framework (ZIF) with different ratios of Zn^{2+}/Co^{2+}ZIF-Zn x Co_{1-x} ($0 \leq x \leq 1$) was kept in an aqueous media of 0.1 M NaOH to investigate the chemical stability under a base environment. The ZIF-Zn0.5$Co_{0.5}$ electrode showed superior chemical stability and had good electrocatalytic activity towards glucose oxidation. The ZIF-$Zn_{0.5}Co_{0.5}$ electrode showed sensitivity that is comparable to cobalt-MOFs, with a sensitivity of 1105.6 μA mM^{-1}. cm^{-2}, linear range up to 1.25 mM, and a detection limit of 9 μM. The suggested mechanism for glucose oxidation by Co^{2+}-based ZIF includes two stages, Co^{2+} within the ZIF is oxidised to Co^{3+} when the OH^- is present in the solution; Co^{3+} is subsequently reduced back to Co^{2+} by glucose, which is oxidised to gluconolactone. This reaction enhances the anodic current, as the consumption of Co^{3+} in the second stage promotes the first stage [72]. This method has proven effective in restoring electrocatalysts on the electrode surface to enhance sensor longevity. Metals and metal oxides are synthesised at the nanoscale to increase active sites and surface area; however, nanoparticles often agglomerate due to their high surface energy. Therefore, merging porous carbon materials with the metal/metal oxide nanoparticles with help solve the challenge. Xiao et al.[73] developed a metal/metal oxide@carbon composite (M/MO@C) that was synthesised through the direct carbonisation of a bimetallic Cu/Ni-based MOF, resulting in a three-dimensional porous material. The nanoparticles were evenly distributed within the porous matrix, exhibiting excellent reproducibility, remarkable stability, and high selectivity [73].

2.2. Classification of wearable biosensors

The human body secretes biofluids such as sweat, saliva, tears and intestinal fluids, which contain important biomarkers such as glucose, uric acid and lactate and can be used for disease diagnosis and monitoring [74]. These biofluids are easy to sample and can provide rapid results in a non-invasive approach, such as smart watches, patches, contact lenses, and mouthguards. Furthermore, biofluids have several advantages such as needle-free sampling, reduced physical discomfort and anxiety (especially for frequent testing), no need for trained personnel, healthcare costs-eliminated risk of bloodborne infections for enhanced safety, and greater stability due to the absence of rapid coagulation. Several studies described a relationship between the concentration of blood glucose and the concentration of glucose present in the biofluids, which is lower [75]. Saliva is easily collected, and the concentrations of electrolytes such as magnesium, calcium, sodium, potassium, bicarbonate and phosphate are lower in saliva. Furthermore, saliva is highly contaminated, making it challenging to separate the fluid's natural electrolyte content [76]. Sweat glucose is particularly preferred, as studies have shown that its concentration, ranging from 1–4 mg/dL (0.06–0.22 mM), closely correlates with blood glucose levels. Saliva serves as an easily accessible biomarker with a simple, non-invasive collection process; however, it has a lower concentration of glucose and other analytes. Additionally, the presence of numerous impurities makes it challenging to accurately isolate the intrinsic electrolyte levels in the fluid [77,78]. Tear and interstitial fluid (ISF) have well-maintained volumes and generate consistent glucose concentrations as compared to other biological fluids like saliva and sweat [79, 80]. As a result, indirect blood glucose monitoring techniques have been developed, focusing on measuring glucose levels in tears and analysing their correlation with blood glucose level concentrations [80].

2.3. Saliva non-invasive methods

Saliva is the most accessible biofluid that consists of biomarkers that are used for monitoring glucose. The development of biosensor technologies based on sweat will help facilitate access and potentially, improve healthcare outcomes for low-resource patients [85]. It has a different oral function such as lubrication, protection against pathogens and digestion of food. Saliva is such a complex biological fluid that has a range of molecules, enzymes, hormones, proteins, and genetic material, that can help monitor and identify pathological and physiological changes that happen in the body. The working principle behind the use of saliva as a biomarker is that the blood glucose can diffuse into the glands that produce saliva, where it is excreted. Although there is a time lag between the concentration of saliva and that of blood glucose due to the diffusion of glucose from the bloodstream into the salivary glands, it can be correlated [86]. Other factors that can affect the concentration of salivary glucose range from diet, oral health, salivary flow rate, and sometimes medications. The accuracy of salivary glucose measurements can be affected by these factors, which can also increase variability [87]. Arakawa et al.[88] first reported on the fabrication of non-invasive monitoring of saliva glucose using a detachable oral cavity sensor. The glucose sensor was fabricated on a polyethene terephthalate glycol (PETG) surface and consists of a platinum electrode coated with a glucose oxidase (GOD) and a silver/silver chloride electrode. This novel mouthguard glucose sensor can detect glucose in artificial saliva at 5–1000 mol/L. This glucose sensor can directly measure oral cavity saliva glucose levels without pre-treatment. The substrate material is made from PETG and silver as the substrate material, along with the platinum electrodes coated with cellulose acetate. The proposed glucose sensor could quantify the glucose concentration in the range of 1.75–1000 μmol/L. Although saliva is a promising option for non-invasive sensors, it presents challenges such as the breakdown of food residues and the presence of protein and other active chemicals that can interfere with the detection of target analytes during sensing [88, 89]. To solve this problem different strategies are employed including timing after the most recent meal, including saliva stimulation and mouth washing, in addition to different sample processing including centrifugation and filtration [90]. De Castro et al.[91] developed a colorimetric detection microfluidic paper-based wearable sensor for glucose and nitrite monitoring. The enclosed μPAD (microfluidic paper-based devices) was incorporated into a mouthguard, and the proposed had a detection limit of 27 μmol/L and 7 μmol/L for glucose and nitrite, respectively [91]. Samples were obtained from patients with a prior diagnosis of diabetes mellitus and periodontitis. Liu et al.[92] developed a non-invasive alternative toothbrush glucose sensor for diabetic patients that uses saliva and toothpaste residues as a detecting platform. The two electrodes were constructed from the graphite ink on the working electrode and the Ag/AgCl ink was used on the reference/counter electrode. At the same time, GOD immobilised the working electrode. The sensor showed promising results in glucose detection in 5 min using an amperometric biosensor platform [92]. Additionally, Aparicio-Martínez et al.[93] developed a non-enzymatic salivary glucose sensor using AgNPs/graphene composites to enable direct glucose oxidation without needing an immobilised biomolecule. The sensor featured a reference RE) made of Ag/AgCl ink, a counter

electrode (CE) composed of bare laser-induced graphene (LIG), and a working electrode (WE) constructed from LIG/AgNPs/graphene. The sensor's performance was evaluated from a linear range of 1–10 mM and a narrow range of 1–2 mM. It had an improved LOD of 45 M and an increased sensitivity of 52.2 mA/mM [93]. Panwar et al.[94] designed a 3D-printed optical biosensor strip for non-invasive glucose detection in saliva. The device integrates microfluidic and biochemical methods, with an optical sensor engineered to minimize interferences from ambient light. Clinical testing demonstrated a strong correlation with blood glucose levels, achieving a sensitivity of 26.89 count/(mg/dL) and a detection limit of 28 mg/dL [94]. Qian et al.[95] developed a flexible non-enzymatic glucose sensor designed to replicate an alkaline environment for glucose reaction. The sensor features an alkaline hydrogel patch embedded in situ with Cu-Ni nanocomposite on a carbon-based working electrode. This design exhibited a broad linear detection range (10 μM and 3 mM), high sensitivity, and a low detection of 1 μM. The sensor successfully measured glucose levels in biofluids like sweat and saliva, demonstrating its applicability for both healthy individuals and diabetic patients.

2.4. Sweat -non-invasive methods

Sweat is a vital biofluid that the body produces because it controls body temperature. Sweat contains a variety of biomolecules from forming bigger proteins to hormones, metabolites and electrolytes and it is a great biofluid for non-invasive health monitoring [78]. For continuous disease monitoring, sweat plays a significant role in making non-invasive devices that provide effective data collection and analysis. The sweat glands in the body are eccrine, apocrine and apocrine, which are found in different areas of the body as shown in Fig. 1.

Sweat production in the body is mostly caused by the eccrine sweat glands, which are found in the hypodermis layer of the skin, and Fig. 2 shows the transport mechanism of sweat [98]. More importantly, sweat can be used to determine several biological parameters, such as blood sugar levels and stress. In 2021, the first touch-based prototype for measuring sweat was developed, utilizing a 75 μm-thick, porous polyvinyl alcohol (PVA) hydrogel to sample and transport glucose from the fingertip to the sensor, distinguishing it from earlier touch-based prototypes [99]. A skin-interfaced soft microfluidic device was shown by Koh et al. [100]. This device collects and retains sweat on the skin's surface through natural perspiration, directing it through a microfluidic network and a series of reservoirs for collection and analysis [100]. Lin et al. [101] designed a soft hydrogel patch to detect glucose electrochemically from hand sweat without additional stimulation. Incorporating a Prussian, blue-doped poly (3,4-ethylenedioxythiophene) nanocomposite electrode, the hydrogel enables non-invasive and efficient glucose monitoring while specifically targeting areas that naturally produce sweat [101]. Xiao et al.[102] fabricated a sandwich-structured biosensor using a dielectric layer composed of carboxylated multi-walled carbon nanotubes (MWCNT-COOH) and Prussian blue nanoparticles (PBNPs). It demonstrated rapid, accurate and stable glucose detection within a linear range of 0.01–1.00 mM, achieving a sensitivity of 11.87 μA mM^{-1} $.cm^{-2}$. Glucose oxidase (GOx) was chosen for its ability to efficiently catalyse glucose into gluconic acid and hydrogen peroxide, maintaining high resilience and effectiveness. However, when directly applied to an unmodified electrode surface, GOx often undergoes structural and functional changes, potentially affecting its biological activity [102]. Li et al.[103] explore the use of graphene sponges (GS), also referred to as graphene aerogel or graphene foam, which have an intertwined micro/mesoporous composition of GS to generate additional sites for GOx adsorption and offer convenient pathways for swift ion diffusion. Graphene sponge is characterised by its expansive specific area, significant porosity and impressive electrical conductivity. Effective sweat collection for sensing purposes remains a persistent challenge [103]. To address this, Xu et al.[104] developed a flexible skin patch that incorporates micropillars and micropumps to stimulate and store sweat. The microfluidic chip was fabricated using a Cu-MOF/layered electrode, which demonstrated a detection limit of 2.84 μM within a concentration of 0–1 mM [104].

2.5. Tear non-invasive method

Exploring target biomarkers requires a connection between blood glucose levels and non-invasive body fluids. For instance, the typical glucose concentration is around 0.0 mM in healthy adults, which is adequate for assessing diabetes risk. Tears contain biomarkers including glucose, proteins, vitamin C (ascorbic acid) and pH levels that can be used for various health conditions [106]. The first-generation contact lens glucose sensors relied on optical sensing approaches, such as fluorescence and photonic crystal-based glucose-responsive hydrogels[107]. Parvizs group published a ground-breaking research study in 2011, the first electrochemical contact lens for tear glucose detection [108]. Xie et al.[109] fabricated a non-invasive multifunctional contact lens that monitors glucose levels in tears, intraocular pressure and eyeball movement. They used the one-step hydrothermal reaction to deposit γ-Fe_2O_3@NiO nanosheets on nickel foam. This study successfully introduced flexible biosensors with excellent electrochemical performance, achieving a low detection limit of 0.43 μM and a broad linear range spanning 0.005–0.5 mM and 1.0–6.0 mM. Diabetic patients are at a high risk of diabetic retinopathy and the multifunctional abilities of this contact lens can prevent blindness by its ability to monitor the intraocular pressure immediately. The design of contact lens sensors has improved with recent developments, making the eyes a great window for diagnosing disease, particularly when it comes to the integration of

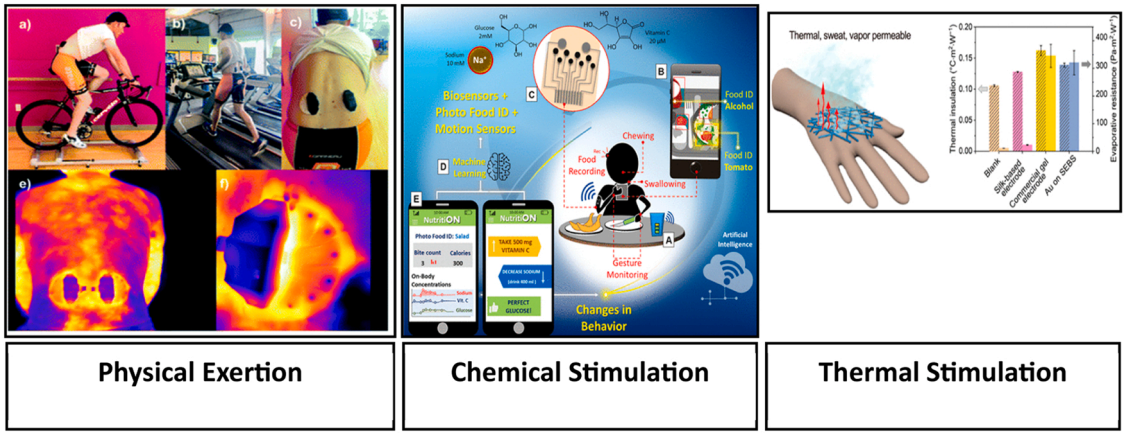


Fig. 1. Active and passive sweat harvesting techniques. Reproduced with permission from [96,97], Published by the American Chemical Society (ACS), 2021.

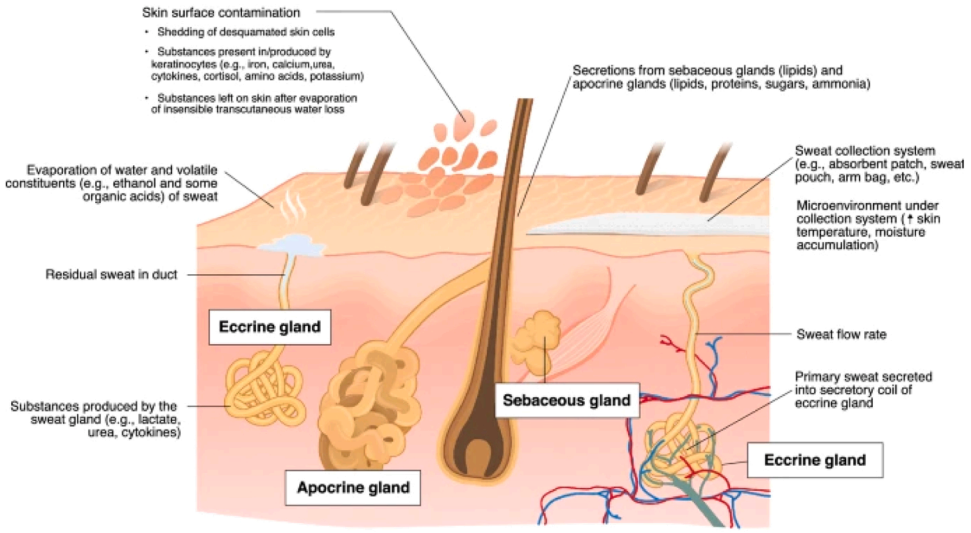


Fig. 2. The transport mechanism of sweat from the sweat glands to the skin surface sweat glands. Copyright©2020 [105], open access article licensed under a Creative Commons Attribution 4.0 International License.

intraocular wearable eye patches that detect multiple biomarkers in human tears [109]. Xu et al.[110] presented a wearable eye patch that has a response period of 30 s and the eye patch biosensor was designed using polyethylene plastic, silicon oil and textiles. Specific colorimetric reactions were incorporated into the sensing regions to enable the selective detection of the desired targets hydrogen ion(pH), ascorbic acid, protein, and glucose [110]. Park et al.[111] designed low-cost colorimetric contact lenses containing cerium oxide nanoparticles to monitor tear glucose levels in diabetic rabbits. The developed wearable was able to accurately detect the blood glucose levels of healthy human volunteers and diabetics while doing non-invasive monitoring of their tears [111]. Wang et al.[112] proposed non-invasive tests that allow diabetic retinopathy to be detected as an advanced diabetic progression. An opto-electrokinetic bead-based immunosensing method was created by the scientists to identify lipocalin 1 (LCN1), which is found in diabetic retinopathy (DR) patients' tears [112]. Gomez et al.[113] designed a fibre optic biosensor that is biofunctionalized to detect LCN1 protein in tears. The label-free biosensor used modern IoT-oriented sensing platforms and has demonstrated the capabilities of detecting the LCN1 protein biomarker [113]. In addition, Park et al.[114] developed a colorimetric disc-type (SD) strip biosensor using a sensing paper coated with glucose oxidase (GOx) and cerium oxide nanoparticles (CNPs). The validation tests demonstrated a strong correlation between glucose levels in tears and blood within the 0–2.5 mM range, with the SD strip biosensor displaying distinct colour change [114]. Seipetdenova et al. [115] introduced a novel approach for detecting two diabetic retinopathy (DR) biomarkers – lipocalin 1 (LCN1) and vascular endothelial growth factor (VEGF)- in artificial tear fluid. The method employs optical biosensors based on semi-distributed interferometry (SDI), which are functionalized with anti-LCN1 and anti-VEGF antibodies for targeted detection. As proof of concept, the research focused on determining the biosensor's key operational parameters and performance characteristics. The results demonstrated high sensitivity and specificity, achieving a detection limit of 5.98 ng/mL for LCN1 and 26.6 fg/mL for VEGF [115].

2.6. *Interstitial stomach fluid (ISF)*

While blood glucose has long been the cornerstone of diabetes management, other analytes may offer a more comprehensive view of metabolic health. The symptoms and complications of diabetes in the case of hyperglycaemia can be mediated via interstitial and cellular effects. Therefore, looking at glucose biosensors that use interstitial fluid (ISF) as an analyte is worth investigating [116]. Normally, the ISF glucose level is the same as the blood glucose under steady-state settings. However, when blood glucose fluctuates rapidly, the difference between blood and ISF glucose may change more gradually, with a delay ranging from five to fifteen minutes[117]. Semi-implantable wearable continuous glucose monitoring (CGM) technology offers excellent monitoring precision without requiring surgical procedures, but it also puts patients at risk for discomfort and infection [1,118]. However, microneedle-based CGM systems provide a promising platform that tracks interstitial fluid instead of blood while being less invasive and offering long-term, pain-free and precise glucose detection [119]. Currently, the available microneedles present two issues: low reliability and low signal-to-noise, because the limited surface area of the valid region for immobilising sensing materials leads to a weak response signal that is readily overwhelmed by the noise signal [120]. Micron-sized needles typically measure between 300 and 1500 μm in length and can be inserted into the dermal layer of the skin to obtain inflammatory stromal cells in a minimally invasive manner [92,121]. Yin et al.[122] introduced a minimally invasive wearable microneedle featuring an integrated circuit for signal processing and transmission. The system incorporates a glucose skin patch to detect glucose levels in transdermal interstitial fluid. Its hollow structural design protects the glucose oxidase (GOD) enzyme from mechanical abrasion and impact, extending the sensor's lifespan to 14 days. Additionally, the hollow architecture enables higher enzyme loading, enhancing detection sensitivity. The study showed an avenue of a cost-effective technique that can detect and monitor in real-time and record fluctuations. Analytes with low molecular weight, such as glucose, urea, pH levels, lactate and urea, etc., have shown similar composition between blood, plasma and ISF [93]. Abbassiasl et al.[123] reported that a laser-drilled hollow microneedle patch was developed for continuous ISF sampling. This system can measure the sensitivity, selectivity, and stability of the sensors while simultaneously monitoring pH and glucose levels in the collected ISF. Its functionality was confirmed through in-vitro and ex-vivo testing of the integrated screen-printed electrodes [123]. Zheng et al.[124] have developed a microneedle (MN) glucose and alcohol hydrogel-based swellable MN patch that was made of methacrylate hyaluronic acid (MeHA). The electrochemical test strip could detect alcohol from 0 mM to 20 mM and glucose from 0 mM to 12 mM in less than a minute after extracting a microlitre of skin ISF [124].

2.7. Flexible materials for non-invasive glucose sensing: textile and polymer-based approaches

Traditional biomedical monitoring devices often rely on invasive methods that frequently restrict the mobility and comfort of the end-user. However, the integration of textile materials in wearable sensors enables a shift towards embedding sensing technology into ordinary garments such as shirts, socks and undergarments [125]. A key benefit of textile-based wearable electronics is their flexibility, lightweight nature and ability to conform to the body. This facilitates a seamless sensors integration into clothing, allowing for continuous, non-intrusive tracking of vital signs like heart rate, breathing patterns and physical activity. Another advantage presented by textile sensors is their expansive coverage, providing a larger surface area for sensing functionality. This proves particularly beneficial for pressure mapping in smart textiles and posture analysis in medical and athletic applications. Additionally, manufacturing these sensors is conveniently incorporated during textile fabrication, enabling a cost-effective and easily scalable manufacturing process [126,127]. Despite their advantages, textile-based sensors present several limitations worth considering. A primary concern is performance caused by mechanical strain, frequent laundering and environmental exposure. Additionally, these sensors pose challenges in complex signal processing as they produce substantial datasets that demand sophisticated analytical algorithms for meaning interpretation. Moreover, their sensitivity and specificity often fall short when compared to conventional rigid sensors [128,129]. Zhao et al. [130] developed a thread-embroided fabric sensing band integrated with a surface-enhanced Raman scattering (SERS) detection system, and it was fabricated with core-shell gold nanorods (AuNRs) coated with Raman reporters (DTNB) for glucose and lactate detection in sweat. The sensing band efficiently measured metabolite levels during different activities by using the capillary actions of threads to passively direct sweat flow and eliminating the need for external pressure. The limits of detection achieved for glucose were 0.125 μM. Current sweat sampling technologies primarily rely on functional hydrophilic materials such as hydrogels, paper and hydrogels. While these materials can absorb sweat passively, they cannot precisely control the sweat and its collection. Recent advances, however, have introduced Janus-type sweat-absorbing materials engineering with anisotropic structures, surface roughness and energy gradients. This material enables on-demand sweat manipulation, allowing for more efficient and targeted fluid handling compared to conventional passive absorption methods [130]. Liu et al.[131] introduce a breathable, patterned Janus textile sweat sensor designed for efficient sweat collection and real-time monitoring of analyte concentrations during continuous exercise. They used a dual-process approach to design the membrane using laser patterning of hydrophobic non-woven fabric (HMN) to create precisely controlled hydrophilic channels, and fiber by electrospinning deposition of a functional nanofiber layer. This hierarchical design enables simultaneous longitudinal fluid transport and lateral sweat droplet aggregation, which allows for the detection of biomarkers such as glucose, pH, lactate, etc [131]. Ren et al.[132] fabricated a Junus fabric by integrating hydrophobic polyurethane (PU) nanofibers with hydrophilic medical gauze via electrospinning to serve as a sweat collection interface. The working electrode was electrodeposited with Prussian blue, followed by functionalization with chitosan, SWCNTs/glucose oxidase, and the developed electrochemical sensor demonstrated a sensitivity of 3.35 μA/mM and a detection limit of 15.32μM [132]. Polymeric materials have enabled the development of highly stretchable, wearable sensors that can be integrated and non-invasively interface with the human body. Their flexibility, biocompatibility, simple processing and low cost, polymers serve as an ideal base material for disposable and skin-adhesive sensors. Flexible and stretchable sensors rely on polymer materials, which can be either conductive or insulating. Conductive polymers such as nanostructured polypyrrole (PPy), PANI and PEDOT combine metal-like conductivity with the mechanical flexibility of plastics [133]. This conductivity arises from their unique molecular structure, unlike non-conductive polymers. PPy has emerged as a versatile material for biosensing devices due to its electrical conductivity, environmental stability and flexibility. Its conductive nature supports efficient electron transfer, essential for high-performance sensing. The material's high surface area and porosity improve biomolecule immobilisation, such as enzymes, enhancing biosensor effectiveness. Additionally, PPy's durability and structural adaptability, especially in highly ordered nanostructures with high aspect ratios, make it valuable for advanced sensor development. For example, Thakur et al.[134] designed a TiO_2-PPy nanocomposite-based non-enzymatic electrochemical sensor for glucose detection. The TiO_2-PPy modified glassy carbon electrode (GCE) exhibits enhanced electrocatalytic activity for glucose oxidation due to a synergistic effect, achieving a sensitivity of 678.57 $\mu A \cdot mM^{-1} \cdot cm^{-2}$. This improvement makes the electrode highly efficient for glucose detection. Additionally, the glucose oxidation signals remain unaffected by interfering substances such as urea, cholesterol and ribose [134]. In another study, Okamoto et al.[135] prepared gold nanoparticles decorated with PPy via electro-polymerisation to improve the catalytic activity in glucose oxidation. Numerous studies have reported on the fabrication of PANI and other metal oxides/nanomaterials for glucose detection [135]. Kailasa et al.[136] synthesised CuO nanoparticles decorated on polyaniline nanobelts using the polymerisation technique. The fabricated sensors demonstrated excellent anti-interference properties, repeatability and long-term stability, highlighting their potential for practical non-enzymatic glucose detection [136]. In their study, Zhai et al.[137] fabricated a glucose biosensor using a PANI hydrogel reinforced with platinum nanoparticles (Pt-NPs), cross-linked with phytic acid. The sensor exhibited a broad linear range (0.01–8 mM) and a fast amperometric response of 3 s [137]. Fang et al.[138] developed a flexible conductive paper-based electrode incorporating PEDOT, PSS and platinum nanohybrids for electrochemical glucose detection. The sensor exhibited a high sensitivity of 21.17 μA mM^{-1} for glucose in both artificial urine and sweat [138].

3. Conclusion: Challenges and prospects of wearable glucose sensors

Non-invasive biosensors for glucose monitoring have made significant progress in research and commercialisation, but the limitations remain. This review is classified based on four different biofluids used for glucose biosensing. Potential biofluids for monitoring blood glucose levels and determining if the concentration correlates with blood glucose levels include ISF, sweat, saliva and tears. ISF has been discovered to have a high concentration because of its proximity to blood capillaries, which closely resemble the biomarkers in blood, which are currently removed from the skin using reverse iontophoresis (RI) or instruments like microneedles [139]. Sweat is the most accessible biofluid since it can be stimulated in a variety of ways. Sweat glucose levels are within the micromolar range and can be determined by using microfluidic channels that collect and hold the sampled sweat or by directly touching a sensor to perspiration on the skin. Although saliva and tears also contain glucose, their biochemical partitioning mechanism is currently poorly understood. Practical uses of contact lens technology have been sluggish to materialise, even though they are one step closer to helping diabetic people better manage their condition. To prevent their influence on contact lens pain, these lenses should be comfortable to use. The correlation between the two salivary indicators, glucose and amylase and the findings is contradictory. Definitive conclusions about the connection between changes in salivary amylase levels in diabetic patients, blood glucose control and the presence of diabetic complications remain unclear. Additional research is necessary to address issues and identify potential salivary biomarkers for diagnostic purposes.

These challenges in saliva, tears and sweat sampling for biosensing include the following:

• Saliva sampling: Variations in flow rate and the complexity of saliva composition pose difficulties in achieving accurate biomarker detection

• Tear sampling: The limited volume of teats and their complex composition require highly selective and sensitive detection methods. Advances in nanomaterials and microfluidics offer promising strategies to improve sensitivity and specificity.

• Sweat sampling: While passive collection is practised for continuous monitoring and is minimally invasive, earlier techniques such as thermal stimulation and intense exercise can lead to dehydration and biomarker fluctuations, reducing long-term reliability. It is necessary to establish a link between the concentration of the target analytes in biofluids and the time delay caused by diffusion.

This review also looked at sensor modification, specifically of metal nanomaterials composites and MOFs which showed that recent breakthroughs in nonenzymatic glucose sensing leverage hierarchically porous electrode materials with engineered surface properties. Laser-induced graphene (LIG) exemplifies this approach, combining 3D interconnected porosity (pore size distribution 50–500 nm), ultrahigh surface area and metallic grade conductivity to achieve unprecedented sensitivity. These innovative materials and integration pave the way for precision health monitoring and show great strides into nonenzymatic glucose sensing. In conclusion, glucose sensors have become indispensable tools for glucose monitoring, enabling accurate and convenient blood glucose monitoring that significantly improves health outcomes. Despite their clinical value, challenges persist in sensor accuracy, durability and affordability, underscoring the need for continued innovation. Future advancements should prioritise (1) Al and machine learning integration for real-time data analytics, (2) novel nanomaterials such as MOFs, laser-induced graphene to enhance sensitivity and stability, and (3) scalable manufacturing techniques to reduce costs. By addressing these critical gaps, next-generation sensors can transform diabetes care, offering millions worldwide improved quality of life through personalised and accessible glucose monitoring solutions.

CRediT authorship contribution statement

NYEMBWE Alain: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Formal analysis, Conceptualization. **Letta Mahlohonolo Ntuli:** Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Methodology, Investigation, Formal analysis, Conceptualization. **Jean Mulopo:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Conceptualization. **Tshimangadzo Munonde:** Writing – review & editing, Visualization, Validation, Methodology, Investigation, Conceptualization. **Gentil Mwengula:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] M. Mansour, M. Saeed Darweesh, A. Soltan, Wearable devices for glucose monitoring: a review of state-of-the-art technologies and emerging trends, Alex. Eng. J. 89 (2024) 224–243, https://doi.org/10.1016/j.aej.2024.01.021.

[2] S.U. Singh, S. Chatterjee, S.A. Lone, H.-H. Ho, K. Kaswan, K. Peringeth, A. Khan, Y.-W. Chiang, S. Lee, Z.-H. Lin, Advanced wearable biosensors for the detection of body fluids and exhaled breath by graphene, Microchim. Acta 189 (2022) 236, https://doi.org/10.1007/s00604-022-05317-2.

[3] S.N. Banitaba, S. Khademolqorani, V.V. Jadhav, E. Chamanehpour, Y.K. Mishra, E. Mostafavi, A. Kaushik, Recent progress of bio-based smart wearable sensors for healthcare applications, Mater. Today Electron 5 (2023) 100055, https://doi.org/10.1016/j.mtelec.2023.100055.

[4] F. Gao, C. Liu, L. Zhang, T. Liu, Z. Wang, Z. Song, H. Cai, Z. Fang, J. Chen, J. Wang, M. Han, J. Wang, K. Lin, R. Wang, M. Li, Q. Mei, X. Ma, S. Liang, G. Gou, N. Xue, Wearable and flexible electrochemical sensors for sweat analysis: a review, Microsyst. Nanoeng. 9 (1) (2023), https://doi.org/10.1038/s41378-022-00443-6.

[5] S. Menon, M.R. Mathew, S. Sam, K. Keerthi, K.G. Kumar, Recent advances and challenges in electrochemical biosensors for emerging and re-emerging infectious diseases, J. Electroanal. Chem. 878 (2020) 114596, https://doi.org/10.1016/j.jelechem.2020.114596.

[6] D.-W. Hwang, S. Lee, M. Seo, T.D. Chung, Recent advances in electrochemical non-enzymatic glucose sensors – a review, Anal. Chim. Acta 1033 (2018) 1–34, https://doi.org/10.1016/j.aca.2018.05.051.

[7] J. Liu, L. Shi, Y. Shi, Q. Zeng, Y. Yang, Glucose sensing performance of bimetallic MOFs CoFe-ZIF/CC for enzyme-free saliva sensor applications, J. Alloy. Compd. 999 (2024) 174733, https://doi.org/10.1016/j.jallcom.2024.174733.

[8] L. Fritea, M. Tertis, R. Sandulescu, C. Cristea, Enzyme–Graphene Platforms for Electrochemical Biosensor Design With Biomedical Applications, in: 2018: pp. 293–333. https://doi.org/10.1016/bs.mie.2018.05.010.

[9] G. Rocchitta, A. Spanu, S. Babudieri, G. Latte, G. Madeddu, G. Galleri, S. Nuvoli, P. Bagella, M. Demartis, V. Fiore, R. Manetti, P. Serra, Enzyme biosensors for biomedical applications: strategies for safeguarding analytical performances in biological fluids, Sensors 16 (2016) 780, https://doi.org/10.3390/s16060780.

[10] W. Putzbach, N. Ronkainen, Immobilization techniques in the fabrication of Nanomaterial-Based electrochemical biosensors: a review, Sensors 13 (2013) 4811–4840, https://doi.org/10.3390/s130404811.

[11] C. Alvarez-Lorenzo, S. Anguiano-Igea, A. Varela-García, M. Vivero-Lopez, A. Concheiro, Bioinspired hydrogels for drug-eluting contact lenses, Acta Biomater. 84 (2019) 49–62, https://doi.org/10.1016/j.actbio.2018.11.020.

[12] J. Lim, G.Y. Lee, H.J. Lee, S.K. Cha, D.S. Choi, S.H. Koo, W.J. Lee, S.O. Kim, Open porous graphene nanoribbon hydrogel via additive-free interfacial self-assembly: fast mass transport electrodes for high-performance biosensing and energy storage, Energy Storage Mater. 16 (2019) 251–258, https://doi.org/10.1016/j.ensm.2018.06.004.

[13] R. Mahmood Khan, M. Pervaiz, Z. Saeed, A. Majid, M. Liaqat, Graphene-Based enzymatic and Non-Enzymatic electrochemical glucose sensors: review of current research and advances in nanotechnology, ChemistrySelect 8 (2023), https://doi.org/10.1002/slct.202303952.

[14] C. Revathi, R.T. Rajendra kumar, Enzymatic and Nonenzymatic Electrochemical Biosensors, in: Fundam. Sens. Appl. 2D Mater., Elsevier, 2019: pp. 259–300. https://doi.org/10.1016/B978-0-08-102577-2.00007-5.

[15] L. Wang, X. Lu, C. Wen, Y. Xie, L. Miao, S. Chen, H. Li, P. Li, Y. Song, One-step synthesis of Pt–NiO nanoplate array/reduced graphene oxide nanocomposites for nonenzymatic glucose sensing, J. Mater. Chem. A 3 (2015) 608–616, https://doi.org/10.1039/C4TA04724A.

[16] M.M. Rahman, A.J.S. Ahammad, J.-H. Jin, S.J. Ahn, J.-J. Lee, A comprehensive review of glucose biosensors based on nanostructured metal-oxides, Sensors 10 (2010) 4855–4886, https://doi.org/10.3390/s100504855.

[17] A.K. Gupta, M. Gupta, Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications, Biomaterials 26 (2005) 3995–4021, https://doi.org/10.1016/j.biomaterials.2004.10.012.

[18] A.A. Ansari, P.R. Solanki, B.D. Malhotra, Sol-gel derived nanostructured cerium oxide film for glucose sensor, Appl. Phys. Lett. 92 (2008), https://doi.org/10.1063/1.2953686.

[19] R. Doong, H. Shih, Array-based titanium dioxide biosensors for ratiometric determination of glucose, glutamate and urea, Biosens. Bioelectron. 25 (2010) 1439–1446, https://doi.org/10.1016/j.bios.2009.10.044.

[20] Y.-B. Hahn, R. Ahmad, N. Tripathy, Chemical and biological sensors based on metal oxide nanostructures, Chem. Commun. 48 (2012) 10369, https://doi.org/10.1039/c2cc34706g.

[21] P. Kumar, R. Rajan, K. Upadhyaya, G. Behl, X.-X. Xiang, P. Huo, B. Liu, Metal oxide nanomaterials based electrochemical and optical biosensors for biomedical applications: recent advances and future prospectives, Environ. Res. 247 (2024) 118002, https://doi.org/10.1016/j.envres.2023.118002.

[22] R. Wilson, A.P.F. Turner, Glucose oxidase: an ideal enzyme, Biosens. Bioelectron. 7 (1992) 165–185, https://doi.org/10.1016/0956-5663(92)87013-F.

[23] X. Li, H. Dong, Q. Fan, K. Chen, D. Sun, T. Hu, Z. Ni, One-pot, rapid microwave-assisted synthesis of bimetallic metal–organic framework for efficient enzyme-free glucose detection, Microchem. J. 179 (2022) 107468, https://doi.org/10.1016/j.microc.2022.107468.

[24] C. Wang, Y. Sun, X. Yu, D. Ma, J. Zheng, P. Dou, Z. Cao, X. Xu, Ag–Pt hollow nanoparticles anchored reduced graphene oxide composites for non-enzymatic glucose biosensor, J. Mater. Sci. Mater. Electron 27 (2016) 9370–9378, https://doi.org/10.1007/s10854-016-4979-2.

[25] M. Li, X. Bo, Z. Mu, Y. Zhang, L. Guo, Electrodeposition of nickel oxide and platinum nanoparticles on electrochemically reduced graphene oxide film as a nonenzymatic glucose sensor, Sens. Actuators B Chem. 192 (2014) 261–268, https://doi.org/10.1016/j.snb.2013.10.140.

[26] R. Sriramprabha, M. Sekar, J. Wilson, N. Ponpandian, C. Viswanathan, Mesoporous nickel oxide nanostructures: influences of crystalline defects and morphological features on mediator-free electrochemical monosaccharide sensor application, Nanotechnology 31 (2020) 215501, https://doi.org/10.1088/1361-6528/ab6fe2.

[27] T.O. Vu, T.X. Chu, D.H. Nguyen, A highly sensitive non-enzymatic glucose electrochemical sensor based on NiO nanohives, Adv. Nat. Sci. Nanosci. Nanotechnol. 12 (2021) 045012, https://doi.org/10.1088/2043-6262/ac4995.
[28] N. Eprilia, A.R. Sanjaya, R.K. Pramadewandaru, T.A.H. Pertiwi, Y.M.T.A. Putri, I. Rahmawati, B.E. Dewi, Y.K. Krisnandi, H. Chung, T.A. Ivandini, Preparation of nickel foam modified by multiwalled hollow spheres of NiCo 2 o 4 as a promising non-enzymatic glucose sensor, RSC Adv. 14 (2024) 10768–10775, https://doi.org/10.1039/D3RA08663A.
[29] F. Zhou, H. Zhao, K. Chen, S. Cao, Z. Shi, M. Lan, Flexible electrochemical sensor with Fe/Co bimetallic oxides for sensitive analysis of glucose in human tears, Anal. Chim. Acta 1243 (2023) 340781, https://doi.org/10.1016/j.aca.2023.340781.
[30] F. Liu, W. Jin, Y. Li, L. Zheng, Y. Hu, X. Xu, Y. Xue, C. Tang, H. Liu, J. Zhang, Defect-rich (Co, Fe)3O4 hierarchical nanosheet arrays for efficient oxygen evolution reaction, Appl. Surf. Sci. 529 (2020) 147125, https://doi.org/10.1016/j.apsusc.2020.147125.
[31] Y. Wang, J. Wu, G. Wang, D. Yang, T. Ishihara, L. Guo, Oxygen vacancy engineering in Fe-doped akhtenskite-type MnO2 for low-temperature toluene oxidation, Appl. Catal. B Environ. 285 (2021) 119873, https://doi.org/10.1016/j.apcatb.2020.119873.
[32] S. Hung, Y. Hsu, C. Chang, C. Hsu, N. Suen, T. Chan, H.M. Chen, Unraveling geometrical site confinement in highly efficient Iron-Doped electrocatalysts toward oxygen evolution reaction, Adv. Energy Mater. 8 (2018), https://doi.org/10.1002/aenm.201701686.
[33] C. Wei, Z. Wang, Y. Xiao, F. Du, Z. Yu, H. Wang, Q. Liu, In-situ construction of Au/Cu2O nanowire arrays for sensitive glucose sensing, Talanta 254 (2023) 124194, https://doi.org/10.1016/j.talanta.2022.124194.
[34] B. Shao, F. Chen, J. Wang, W. Zhai, Cavitation regulated sonochemical synthesis of flexible self-supported CuO@PDA/CC electrode for highly sensitive glucose sensor, Electrochim. Acta 441 (2023) 141801, https://doi.org/10.1016/j.electacta.2022.141801.
[35] P. Hidalgo-Manrique, X. Lei, R. Xu, M. Zhou, I.A. Kinloch, R.J. Young, Copper/graphene composites: a review, J. Mater. Sci. 54 (2019) 12236–12289, https://doi.org/10.1007/s10853-019-03703-5.
[36] Z. Ren, R. Dong, Y. Liu, Free-standing hybrid material of Cu/Cu 2 O/CuO modified by graphene with commercial cu foil using for non-enzymatic glucose detection, Nanotechnology 33 (2022) 505702, https://doi.org/10.1088/1361-6528/ac90cd.
[37] C. Li, H. Yamahara, Y. Lee, H. Tabata, J.-J. Delaunay, CuO nanowire/microflower/nanowire modified cu electrode with enhanced electrochemical performance for non-enzymatic glucose sensing, Nanotechnology 26 (2015) 305503, https://doi.org/10.1088/0957-4484/26/30/305503.
[38] L. Tang, K. Huan, D. Deng, L. Han, Z. Zeng, L. Luo, Glucose sensor based on pd nanosheets deposited on Cu/Cu2O nanocomposites by galvanic replacement, Colloids Surf. B Biointerfaces 188 (2020) 110797, https://doi.org/10.1016/j.colsurfb.2020.110797.
[39] T.S. Gopal, K.E. Alzahrani, A.K. Assaifan, H. Albrithen, A. Alodhayb, M. Muthuramamoorthy, S. Pandiaraj, A.N. Grace, Reduced graphene oxide supported MXene based metal oxide ternary composite electrodes for non-enzymatic glucose sensor applications, Sci. Rep. 12 (2022) 20583, https://doi.org/10.1038/s41598-022-24700-w.
[40] J. Saravanan, M. Pannipara, A.G. Al-Sehemi, S. Talebi, V. Periasamy, S.S. Shah, M.A. Aziz, G. Gnana kumar, Flower-like CuO/NiO nanostructures decorated activated carbon nanofiber membranes for flexible, sensitive, and selective enzyme-free glucose detection, J. Mater. Sci. Mater. Electron 32 (2021) 24775–24789, https://doi.org/10.1007/s10854-021-06927-x.
[41] V.E. Coyle, A.E. Kandjani, M.R. Field, P. Hartley, M. Chen, Y.M. Sabri, S. K. Bhargava, Co3O4 needles on au honeycomb as a non-invasive electrochemical biosensor for glucose in saliva, Biosens. Bioelectron. 141 (2019) 111479, https://doi.org/10.1016/j.bios.2019.111479.
[42] P. Ling, Q. Zhang, T. Cao, F. Gao, Versatile three-dimensional porous Cu@Cu 2 o aerogel networks as electrocatalysts and mimicking peroxidases, Angew. Chem. 130 (2018) 6935–6940, https://doi.org/10.1002/ange.201801369.
[43] L. Tian, W. Hu, X. Zhong, B. Liu, Glucose sensing characterisations of TiO 2 /CuO nanofibres synthesised by electrospinning, Mater. Res. Innov. 19 (2015) 160–165, https://doi.org/10.1179/1433075X14Y.0000000236.
[44] J. Zhao, C. Fu, C. Huang, S. Zhang, F. Wang, Y. Zhang, L. Zhang, S. Ge, J. Yu, Co3O4-Au polyhedron mimic peroxidase- and cascade enzyme-assisted cycling process-based photoelectrochemical biosensor for monitoring of miRNA-141, Chem. Eng. J. 406 (2021) 126892, https://doi.org/10.1016/j.cej.2020.126892.
[45] Z. Ibupoto, K. Khun, V. Beni, X. Liu, M. Willander, Synthesis of novel CuO nanosheets and their Non-Enzymatic glucose sensing applications, Sensors 13 (2013) 7926–7938, https://doi.org/10.3390/s130607926.
[46] B. Sneha Bharat, A.D. Bagde, A.R. Babu, Development of TiO2-Based nanocomposite film for colorimetric detection of glucose, Mater. Sci. Eng. B 298 (2023) 116886, https://doi.org/10.1016/j.mseb.2023.116886.
[47] Z. Cui, H. Yin, Q. Nie, Controllable preparation of hierarchically core–shell structure NiO/C microspheres for non-enzymatic glucose sensor, J. Alloy. Compd. 632 (2015) 402–407, https://doi.org/10.1016/j.jallcom.2015.01.213.
[48] T. Preethi, M.P. Pachamuthu, K. Senthil, S. Bellucci, Antimicrobial, photocatalytic, and Non-Enzymatic glucose sensors applications of nanoplate-structured CuO:rGO Nanocomposites**, ChemistrySelect 8 (2023), https://doi.org/10.1002/slct.202301655.
[49] L. Ruifeng, C. Yue, Y. Weitong, D. Min, L. Xiaoying, J. Qi, Preparation of CuO/rGO nanocomposite with rice granular structure and its application to detect glucose, ECS J. Solid State Sci. Technol. 12 (2023) 057004, https://doi.org/10.1149/2162-8777/acd213.
[50] Z. Dai, A. Yang, X. Bao, R. Yang, Facile Non-Enzymatic electrochemical sensing for glucose based on Cu2O–BSA nanoparticles modified GCE, Sensors 19 (2019) 2824, https://doi.org/10.3390/s19122824.
[51] L.-Y. Xiong, Y.-J. Kim, W.-C. Seo, H.-K. Lee, W.-C. Yang, W.-F. Xie, High-performance non-enzymatic glucose sensor based on Co3O4/rGO nanohybrid, Rare Met 42 (2023) 3046–3053, https://doi.org/10.1007/s12598-023-02318-9.
[52] V. Vinoth, T.D. Shergilin, A.M. Asiri, J.J. Wu, S. Anandan, Facile synthesis of copper oxide microflowers for nonenzymatic glucose sensor applications, Mater. Sci. Semicond. Process 82 (2018) 31–38, https://doi.org/10.1016/j.mssp.2018.03.032.
[53] S. Zhang, W. Zhao, C. Liu, J. Zeng, Z. He, C. Wang, W. Yuan, Q. Wang, Flower-like CoO nanowire-decorated ni foam: a non-invasive electrochemical biosensor for glucose detection in human saliva, Appl. Mater. Today 36 (2024) 102083, https://doi.org/10.1016/j.apmt.2024.102083.
[54] P. Balasubramanian, M. Annalakshmi, S.-M. Chen, T.-W. Chen, Ultrasensitive non-enzymatic electrochemical sensing of glucose in noninvasive samples using interconnected nanosheets-like NiMnO3 as a promising electrocatalyst, Sens. Actuators B Chem. 299 (2019) 126974, https://doi.org/10.1016/j.snb.2019.126974.
[55] S. Yang, G. Li, D. Wang, Z. Qiao, L. Qu, Synthesis of nanoneedle-like copper oxide on N-doped reduced graphene oxide: a three-dimensional hybrid for nonenzymatic glucose sensor, Sens. Actuators B Chem. 238 (2017) 588–595, https://doi.org/10.1016/j.snb.2016.07.105.
[56] M. Dong, H.L. Hu, Y.L. Duan, Preparation of Non-Enzymatic glucose sensing nanocomposite based on NiCo2O4 nanosheets@ reduced graphene oxide and design of glucose detection system, Solid State Phenom. 330 (2022) 145–152, https://doi.org/10.4028/p-w34a36.
[57] N. Hui, J. Wang, Electrodeposited honeycomb-like cobalt nanostructures on graphene oxide doped polypyrrole nanocomposite for high performance enzymeless glucose sensing, J. Electroanal. Chem. 798 (2017) 9–16, https://doi.org/10.1016/j.jelechem.2017.05.021.
[58] T. Zhou, W. Gao, Y. Gao, Q. Wang, A. Umar, Co 3 o 4 nanoparticles/MWCNTs composites: a potential scaffold for hydrazine and glucose electrochemical detection, RSC Adv. 7 (2017) 50087–50096, https://doi.org/10.1039/C7RA10892C.
[59] S. Cheng, S. DelaCruz, C. Chen, Z. Tang, T. Shi, C. Carraro, R. Maboudian, Hierarchical Co3O4/CuO nanorod array supported on carbon cloth for highly sensitive non-enzymatic glucose biosensing, Sens. Actuators B Chem. 298 (2019) 126860, https://doi.org/10.1016/j.snb.2019.126860.
[60] A. Chen, Y. Ding, Z. Yang, S. Yang, Constructing heterostructure on highly roughened caterpillar-like gold nanotubes with cuprous oxide grains for ultrasensitive and stable nonenzymatic glucose sensor, Biosens. Bioelectron. 74 (2015) 967–973, https://doi.org/10.1016/j.bios.2015.07.074.
[61] C.-L. Hsu, J.-H. Lin, D.-X. Hsu, S.-H. Wang, S.-Y. Lin, T.-J. Hsueh, Enhanced non-enzymatic glucose biosensor of ZnO nanowires via decorated Pt nanoparticles and illuminated with UV/Green light emitting diodes, Sens. Actuators B Chem. 238 (2017) 150–159, https://doi.org/10.1016/j.snb.2016.07.060.
[62] Q.K. Dao, T.Q. Mai, T. Van Pham, A.B. Ngac, C.H. Hoang, E. Janssens, H.H. Mai, ZnO nanorods grown on cu wire mesh provide a high sensitivity non-enzymatic absorbance glucose sensor, Microchim. Acta 191 (2024) 753, https://doi.org/10.1007/s00604-024-06845-9.
[63] S. Song, X. Ma, W. Li, B. Zhang, B. Shao, X. Chang, X. Liu, Novel stylophora coral-like furan-based Ni/Co bimetallic metal organic framework for high-performance capacitive storage and non-enzymatic glucose electrochemical sensing, J. Alloy. Compd. 931 (2023) 167413, https://doi.org/10.1016/j.jallcom.2022.167413.
[64] J. Duan, S. Chen, C. Zhao, Ultrathin metal-organic framework array for efficient electrocatalytic water splitting, Nat. Commun. 8 (2017) 15341, https://doi.org/10.1038/ncomms15341.
[65] W. Li, S. Lv, Y. Wang, L. Zhang, X. Cui, Nanoporous gold induced vertically standing 2D NiCo bimetal-organic framework nanosheets for non-enzymatic glucose biosensing, Sens. Actuators B Chem. 281 (2019) 652–658, https://doi.org/10.1016/j.snb.2018.10.150.
[66] P. Li, Y. Bai, G. Zhang, X. Guo, X. Meng, H. Pang, Surface-halogen-introduced 2D NiCo bimetallic MOFs via a modulation method for elevated electrochemical glucose sensing, Inorg. Chem. Front 9 (2022) 5853–5861, https://doi.org/10.1039/D2QI01738E.
[67] Z. Ye, Y. Jiang, L. Li, F. Wu, R. Chen, MOF-related electrocatalysts for sulfur reduction/evolution reactions: composition modulation, structure design, and mechanism research, EScience 3 (2023) 100107, https://doi.org/10.1016/j.esci.2023.100107.
[68] X. Zhuang, C. Han, J. Zhang, Z. Sang, W. Meng, Cu/Cu2O heterojunctions in carbon framework for highly sensitive detection of glucose, J. Electroanal. Chem. 882 (2021) 115040, https://doi.org/10.1016/j.jelechem.2021.115040.
[69] Y. Zhou, R. Abazari, J. Chen, M. Tahir, A. Kumar, R.R. Ikreedeegh, E. Rani, H. Singh, A.M. Kirillov, Bimetallic metal–organic frameworks and MOF-derived composites: recent progress on electro- and photoelectrocatalytic applications, Coord. Chem. Rev. 451 (2022) 214264, https://doi.org/10.1016/j.ccr.2021.214264.
[70] S. eun Kim, A. Muthurasu, Metal-organic framework–assisted bimetallic Ni@Cu microsphere for enzyme-free electrochemical sensing of glucose, J. Electroanal. Chem. 873 (2020) 114356, https://doi.org/10.1016/j.jelechem.2020.114356.
[71] X. Ma, K. Tang, M. Yang, W. Shi, W. Zhao, Metal–organic framework-derived yolk–shell hollow Ni/NiO@C microspheres for bifunctional non-enzymatic

glucose and hydrogen peroxide biosensors, J. Mater. Sci. 56 (2021) 442–456, https://doi.org/10.1007/s10853-020-05236-8.
[72] K. Kim, J. Kim, Y.-S. Bae, Zn–Co bimetallic zeolitic imidazolate frameworks as nonenzymatic electrochemical glucose sensors with enhanced sensitivity and chemical stability, ACS Sustain. Chem. Eng. 10 (2022) 11702–11709, https://doi.org/10.1021/acssuschemeng.2c04306.
[73] X. Xiao, S. Peng, C. Wang, D. Cheng, N. Li, Y. Dong, Q. Li, D. Wei, P. Liu, Z. Xie, D. Qu, X. Li, Metal/metal oxide@carbon composites derived from bimetallic Cu/Ni-based MOF and their electrocatalytic performance for glucose sensing, J. Electroanal. Chem. 841 (2019) 94–100, https://doi.org/10.1016/j.jelechem.2019.04.038.
[74] S. Kumari, M. Samara, R. Ampadi Ramachandran, S. Gosh, H. George, R. Wang, R. P. Pesavento, M.T. Mathew, A review on Saliva-Based health diagnostics: biomarker selection and future directions, Biomed. Mater. Devices 2 (2024) 121–138, https://doi.org/10.1007/s44174-023-00090-z.
[75] A. Ornelas-González, M. Ortiz-Martínez, M. González-González, M. Rito-Palomares, Enzymatic methods for salivary biomarkers detection: overview and current challenges, Molecules 26 (2021) 7026, https://doi.org/10.3390/molecules26227026.
[76] S. Patle, D. Rotake, Recent advances, technological challenges and requirements to predict the future treads in wearable sweat sensors: a critical review, Microchem. J. 200 (2024) 110457, https://doi.org/10.1016/j.microc.2024.110457.
[77] I.T. Gug, M. Tertis, O. Hosu, C. Cristea, Salivary biomarkers detection: analytical and immunological methods overview, TrAC Trends Anal. Chem. 113 (2019) 301–316, https://doi.org/10.1016/j.trac.2019.02.020.
[78] J. Xu, Y. Fang, J. Chen, Wearable biosensors for Non-Invasive sweat diagnostics, Biosensors 11 (2021) 245, https://doi.org/10.3390/bios11080245.
[79] Y.-H. Lee, D.T.W. Wong, Saliva: an emerging biofluid for early detection of diseases, Am. J. Dent. 22 (2009) 241–248.
[80] G. Li, D. Wen, Wearable biochemical sensors for human health monitoring: sensing materials and manufacturing technologies, J. Mater. Chem. B 8 (2020) 3423–3436, https://doi.org/10.1039/C9TB02474C.
[81] W. Park, H. Seo, J. Kim, Y.-M. Hong, H. Song, B.J. Joo, S. Kim, E. Kim, C.-G. Yae, J. Kim, J. Jin, J. Kim, Y. Lee, J. Kim, H.K. Kim, J.-U. Park, In-depth correlation analysis between tear glucose and blood glucose using a wireless smart contact lens, Nat. Commun. 15 (2024) 2828, https://doi.org/10.1038/s41467-024-47123-9.
[82] M.Y. Ali, H.B. Abdulrahman, W.-T. Ting, M.M.R. Howlader, Green synthesized gold nanoparticles and CuO-based nonenzymatic sensor for saliva glucose monitoring, RSC Adv. 14 (2024) 577–588, https://doi.org/10.1039/D3RA05644A.
[83] Z.T. Ye, S.F. Tseng, S.X. Tsou, C.W. Tsai, High-sensitivity flip chip blue Mini-LEDs miniaturized optical instrument for non-invasive glucose detection, Discov. Nano 19 (2024) 6, https://doi.org/10.1186/s11671-023-03948-9.
[84] L. Fiore, A. Sinha, N. Seddaoui, J. di Biasio, F. Ricci, G.M. Stojanovic, F. Arduini, Paper card-like electrochemical platform as a smart point-of-care device for reagent-free glucose measurement in tears, Chem. Commun. 59 (2023) 4300–4303, https://doi.org/10.1039/D2CC06561D.
[85] R. Tiongco, A. Bituin, E. Arceo, N. Rivera, E. Singian, Salivary glucose as a non-invasive biomarker of type 2 diabetes mellitus, J. Clin. Exp. Dent. (2018), https://doi.org/10.4317/jced.55009.
[86] R.S.P. Malon, S. Sadir, M. Balakrishnan, E.P. Córcoles, Saliva-Based biosensors: noninvasive monitoring tool for clinical diagnostics, Biomed. Res. Int. 2014 (2014) 1–20, https://doi.org/10.1155/2014/962903.
[87] Y. Cui, H. Zhang, J. Zhu, Z. Liao, S. Wang, W. Liu, Correlations of salivary and blood glucose levels among six saliva collection methods, Int. J. Environ. Res. Public Health 19 (2022) 4122, https://doi.org/10.3390/ijerph19074122.
[88] T. Arakawa, Y. Kuroki, H. Nitta, P. Chouhan, K. Toma, S. Sawada, S. Takeuchi, T. Sekita, K. Akiyoshi, S. Minakuchi, K. Mitsubayashi, Mouthguard biosensor with telemetry system for monitoring of saliva glucose: a novel cavitas sensor, Biosens. Bioelectron. 84 (2016) 106–111, https://doi.org/10.1016/j.bios.2015.12.014.
[89] T. Arakawa, K. Tomoto, H. Nitta, K. Toma, S. Takeuchi, T. Sekita, S. Minakuchi, K. Mitsubayashi, A wearable cellulose acetate-coated mouthguard biosensor for in vivo salivary glucose measurement, Anal. Chem. 92 (2020) 12201–12207, https://doi.org/10.1021/acs.analchem.0c01201.
[90] J. Giaretta, R. Zulli, T. Prabhakar, R.J. Rath, S. Naficy, S. Spilimbergo, P.S. Weiss, S. Farajikhah, F. Dehghani, Glucose sensing in saliva, Adv. Sens. Res. 3 (2024), https://doi.org/10.1002/adsr.202400065.
[91] L.F. de Castro, S.V. de Freitas, L.C. Duarte, J.A.C. de Souza, T.R.L.C. Paixão, W.K. T. Coltro, Salivary diagnostics on paper microfluidic devices and their use as wearable sensors for glucose monitoring, Anal. Bioanal. Chem. 411 (2019) 4919–4928, https://doi.org/10.1007/s00216-019-01788-0.
[92] Y. Liu, W. Yue, Y. Cui, Development of an amperometric biosensor on a toothbrush for glucose, Sens. Actuators Rep. 5 (2023) 100133, https://doi.org/10.1016/j.snr.2022.100133.
[93] E.P. Aparicio-Martínez, A. Vega-Rios, V. Osuna, R.B. Dominguez, Salivary glucose detection with laser induced Graphene/AgNPs Non-Enzymatic sensor, Biosensors 13 (2023) 207, https://doi.org/10.3390/bios13020207.
[94] S. Panwar, P. Sarkar, D.S. Kasim, R. Anand, A. Priya, S. Prakash, S.K. Jha, Portable optical biosensor for point-of-care monitoring of salivary glucose using a paper-based microfluidic strip, Biosens. Bioelectron. X 17 (2024) 100452, https://doi.org/10.1016/j.biosx.2024.100452.
[95] X. Qian, A. Ko, H. Li, C. Liao, Flexible non-enzymatic glucose strip for direct non-invasive diabetic management, Microchem. J. 197 (2024) 109818, https://doi.org/10.1016/j.microc.2023.109818.
[96] J.R. Sempionatto, V.R.-V. Montiel, E. Vargas, H. Teymourian, J. Wang, Wearable and mobile sensors for personalized nutrition, ACS Sens. 6 (2021) 1745–1760, https://doi.org/10.1021/acssensors.1c00553.
[97] Q. Li, G. Chen, Y. Cui, S. Ji, Z. Liu, C. Wan, Y. Liu, Y. Lu, C. Wang, N. Zhang, Y. Cheng, K.-Q. Zhang, X. Chen, Highly Thermal-Wet comfortable and conformal Silk-Based electrodes for on-skin sensors with sweat tolerance, ACS Nano 15 (2021) 9955–9966, https://doi.org/10.1021/acsnano.1c01431.
[98] T. Saha, R. Del Caño, E. De la Paz, S.S. Sandhu, J. Wang, Access and management of sweat for Non-Invasive biomarker monitoring: a comprehensive review, Small 19 (2023), https://doi.org/10.1002/smll.202206064.
[99] L. Wang, T. Xu, X. He, X. Zhang, Flexible, self-healable, adhesive and wearable hydrogel patch for colorimetric sweat detection, J. Mater. Chem. C. 9 (2021) 14938–14945, https://doi.org/10.1039/D1TC03905A.
[100] A. Koh, D. Kang, Y. Xue, S. Lee, R.M. Pielak, J. Kim, T. Hwang, S. Min, A. Banks, P. Bastien, M.C. Manco, L. Wang, K.R. Ammann, K.-I. Jang, P. Won, S. Han, R. Ghaffari, U. Paik, M.J. Slepian, G. Balooch, Y. Huang, J.A. Rogers, A soft, wearable microfluidic device for the capture, storage, and colorimetric sensing of sweat, Sci. Transl. Med. 8 (2016), https://doi.org/10.1126/scitranslmed.aaf2593.
[101] P.-H. Lin, S.-C. Sheu, C.-W. Chen, S.-C. Huang, B.-R. Li, Wearable hydrogel patch with noninvasive, electrochemical glucose sensor for natural sweat detection, Talanta 241 (2022) 123187, https://doi.org/10.1016/j.talanta.2021.123187.
[102] Y. Xiao, L. Hou, M. Wang, R. Liu, L. Han, M. Nikolai, S. Zhang, C. Cheng, K. Hu, Noninvasive glucose monitoring using portable GOx-Based biosensing system, Anal. Chim. Acta 1287 (2024) 342068, https://doi.org/10.1016/j.aca.2023.342068.
[103] B. Li, X. Wu, C. Shi, Y. Dai, J. Zhang, W. Liu, C. Wu, Y. Zhang, X. Huang, W. Zeng, Flexible enzymatic biosensor based on graphene sponge for glucose detection in human sweat, Surf. Interfaces 36 (2023) 102525, https://doi.org/10.1016/j.surfin.2022.102525.
[104] W. Xu, Y. Cao, H. Shi, X. Jia, Y. Zheng, Z. Tan, R. Zhao, H. Wu, Skin-interfaced sweat monitoring patch constructed by flexible microfluidic capillary pump and Cu-MOF sensitized electrochemical sensor, Talanta 291 (2025) 127895, https://doi.org/10.1016/j.talanta.2025.127895.
[105] L.B. Baker, A.S. Wolfe, Physiological mechanisms determining eccrine sweat composition, Eur. J. Appl. Physiol. 120 (2020) 719–752, https://doi.org/10.1007/s00421-020-04323-7.
[106] Y. Zhu, J. Qian, K. Xu, W. Ouyang, J. Yang, N. Yang, Hollow nanocages heterostructured NiCo-LDH/MWCNTs electrocatalyst for highly sensitive and non-invasive detection of saliva glucose, Chem. Eng. J. 485 (2024) 149795, https://doi.org/10.1016/j.cej.2024.149795.
[107] R.C. Tseng, C.-C. Chen, S.-M. Hsu, H.-S. Chuang, Contact-Lens biosensors, Sensors 18 (2018) 2651, https://doi.org/10.3390/s18082651.
[108] H. Yao, A.J. Shum, M. Cowan, I. Lähdesmäki, B.A. Parviz, A contact lens with embedded sensor for monitoring tear glucose level, Biosens. Bioelectron. 26 (2011) 3290–3296, https://doi.org/10.1016/j.bios.2010.12.042.
[109] M. Xie, G. Yao, T. Zhang, Q. Wang, X. Mo, Q. Dong, W. Lou, F. Lu, T. Pan, M. Gao, D. Jiang, K. Zhao, Y. Lin, Multifunctional flexible contact lens for eye health monitoring using inorganic magnetic oxide nanosheets, J. Nanobiotechnol. 20 (2022) 202, https://doi.org/10.1186/s12951-022-01415-8.
[110] J. Xu, X. Tao, X. Liu, L. Yang, Wearable eye patch biosensor for noninvasive and simultaneous detection of multiple biomarkers in human tears, Anal. Chem. 94 (2022) 8659–8667, https://doi.org/10.1021/acs.analchem.2c00614.
[111] S. Park, J. Hwang, H.-J. Jeon, W.R. Bae, I.-K. Jeong, T.G. Kim, J. Kang, Y.-G. Han, E. Chung, D.Y. Lee, Cerium oxide nanoparticle-containing colorimetric contact lenses for noninvasively monitoring human tear glucose, ACS Appl. Nano Mater. 4 (2021) 5198–5210, https://doi.org/10.1021/acsanm.1c00603.
[112] J.-C. Wang, H.-Y. Ku, T.-S. Chen, H.-S. Chuang, Detection of low-abundance biomarker lipocalin 1 for diabetic retinopathy using optoelectrokinetic bead-based immunosensing, Biosens. Bioelectron. 89 (2017) 701–709, https://doi.org/10.1016/j.bios.2016.11.014.
[113] A.W. Gomez, Z. Myrkhiyeva, M. Tilegen, T.T. Pham, A. Bekmurzayeva, D. Tosi, Optical fiber ball resonator biosensor as a platform for detection of diabetic retinopathy biomarkers in tears, IEEE Sens. J. 24 (2024) 11127–11135, https://doi.org/10.1109/JSEN.2024.3363219.
[114] S. Park, D.Y. Nam, H.-J. Jeon, J.H. Han, D. Jang, J. Hwang, Y.-S. Park, Y.-G. Han, Y.Bin Choy, D.Y. Lee, Chromophoric cerium oxide nanoparticle-loaded sucking disk-type strip sensor for optical measurement of glucose in tear fluid, Biomater. Res. 27 (2023), https://doi.org/10.1186/s40824-023-00469-5.
[115] S. Seipetdenova, T.O. Oladejo, A. Bekmurzayeva, C.K.L. Tan, M. Yang, W. Blanc, D. Tosi, Label-free multiplexed detection of diabetic retinopathy biomarkers using fiber optic biosensors: towards lab-in-the-tear, Opt. Lasers Eng. 189 (2025) 108943, https://doi.org/10.1016/j.optlaseng.2025.108943.
[116] M.S. Boyne, D.M. Silver, J. Kaplan, C.D. Saudek, Timing of changes in interstitial and venous blood glucose measured with a continuous subcutaneous glucose sensor, Diabetes 52 (2003) 2790–2794, https://doi.org/10.2337/diabetes.52.11.2790.
[117] E. Cengiz, W.V. Tamborlane, A tale of two compartments: interstitial versus blood glucose monitoring, Diabetes Technol. Ther. 11 (2009) S-11–S-16, https://doi.org/10.1089/dia.2009.0002.
[118] F. Boscari, M. Vettoretti, F. Cavallin, A.M.L. Amato, A. Uliana, V. Vallone, A. Avogaro, A. Facchinetti, D. Bruttomesso, Implantable and transcutaneous continuous glucose monitoring system: a randomized cross over trial comparing accuracy, efficacy and acceptance, J. Endocrinol. Invest 45 (2022) 115–124, https://doi.org/10.1007/s40618-021-01624-2.

[119] C. Chen, X.-L. Zhao, Z.-H. Li, Z.-G. Zhu, S.-H. Qian, A. Flewitt, Current and emerging technology for continuous glucose monitoring, Sensors 17 (2017) 182, https://doi.org/10.3390/s17010182.
[120] J.J. García-Guzmán, C. Pérez-Ràfols, M. Cuartero, G.A. Crespo, Microneedle based electrochemical (Bio)Sensing: towards decentralized and continuous health status monitoring, TrAC Trends Anal. Chem. 135 (2021) 116148, https://doi.org/10.1016/j.trac.2020.116148.
[121] G.-S. Liu, Y. Kong, Y. Wang, Y. Luo, X. Fan, X. Xie, B.-R. Yang, M.X. Wu, Microneedles for transdermal diagnostics: recent advances and new horizons, Biomaterials 232 (2020) 119740, https://doi.org/10.1016/j.biomaterials.2019.119740.
[122] S. Yin, Z. Yu, N. Song, Z. Guo, W. Li, J. Ma, X. Wang, J. Liu, M. Liang, A long lifetime and highly sensitive wearable microneedle sensor for the continuous real-time monitoring of glucose in interstitial fluid, Biosens. Bioelectron. 244 (2024) 115822, https://doi.org/10.1016/j.bios.2023.115822.
[123] T. Abbasiasl, F. Mirlou, H. Mirzajani, M.J. Bathaei, E. Istif, N. Shomalizadeh, R. E. Cebecioğlu, E.E. Özkahraman, U.C. Yener, L. Beker, A wearable Touch-Activated device integrated with hollow microneedles for continuous sampling and sensing of dermal interstitial fluid, Adv. Mater. 36 (2024), https://doi.org/10.1002/adma.202304704.
[124] M. Zheng, Y. Zhang, T. Hu, C. Xu, A skin patch integrating swellable microneedles and electrochemical test strips for glucose and alcohol measurement in skin interstitial fluid, Bioeng. Transl. Med. 8 (2023), https://doi.org/10.1002/btm2.10413.
[125] M. Azeem, M. Shahid, I. Masin, M. Petru, Design and development of textile-based wearable sensors for real-time biomedical monitoring; a review, J. Text. Inst. 116 (2025) 80–95, https://doi.org/10.1080/00405000.2024.2318500.
[126] J.S. Heo, M.F. Hossain, I. Kim, Challenges in design and fabrication of Flexible/Stretchable Carbon- and Textile-Based wearable sensors for health monitoring: a critical review, Sensors 20 (2020) 3927, https://doi.org/10.3390/s20143927.
[127] J.S. Meena, S.Bin Choi, S.-B. Jung, J.-W. Kim, Electronic textiles: new age of wearable technology for healthcare and fitness solutions, Mater. Today Bio 19 (2023) 100565, https://doi.org/10.1016/j.mtbio.2023.100565.
[128] B. Niu, T. Hua, H. Hu, B. Xu, X. Tian, K. Chan, S. Chen, A highly durable textile-based sensor as a human-worn material interface for long-term multiple mechanical deformation sensing, J. Mater. Chem. C. 7 (2019) 14651–14663, https://doi.org/10.1039/C9TC04006D.
[129] M.M. Hasan, M.M. Hossain, Nanomaterials-patterned flexible electrodes for wearable health monitoring: a review, J. Mater. Sci. 56 (2021) 14900–14942, https://doi.org/10.1007/s10853-021-06248-8.
[130] Z. Zhao, Q. Li, Y. Dong, J. Gong, Z. Li, J. Zhang, Core-shell structured gold nanorods on thread-embroidered fabric-based microfluidic device for ex situ detection of glucose and lactate in sweat, Sens. Actuators B Chem. 353 (2022) 131154, https://doi.org/10.1016/j.snb.2021.131154.
[131] S. Liu, Y. Dong, Z. Zhang, W. Xue, F. Li, Z. Hou, X. Li, K. Zhang, Y. Ke, T. Fang, G. Feng, A patterned janus textile patch for monitoring multiple biomarkers, Sens. Actuators B Chem. 440 (2025) 137954, https://doi.org/10.1016/j.snb.2025.137954.
[132] J. Ren, Q. Li, K. Feng, J. Gong, Z. Li, X. Liu, L. Yang, J. Zhang, A wearable sensor based on janus fabric upon an electrochemical analysis platform for sweat glucose detection, Talanta 284 (2025) 127236, https://doi.org/10.1016/j.talanta.2024.127236.
[133] Z. Golsanamlou, M. Mahmoudpour, J. Soleymani, A. Jouyban, Applications of advanced materials for Non-Enzymatic glucose monitoring: from invasive to the wearable device, Crit. Rev. Anal. Chem. 53 (2023) 1116–1131, https://doi.org/10.1080/10408347.2021.2008227.
[134] A. Thakur, S. Pal, U. Sharma, A. Sharma, M. Choudhary, M.C. Joshi, H. D. Setiabudi, P.P. Singh, A. Singh, S.K. Shukla, Advanced TiO2-polypyrrole nanostructures enhance glucose detection accuracy with cutting-edge non-enzymatic electrochemical capabilities, Chem. Phys. Impact 10 (2025) 100818, https://doi.org/10.1016/j.chphi.2025.100818.
[135] K. Okamoto, H. Kawakami, Y.-A. Chien, T. Kurioka, W.-T. Chiu, P. Chakraborty, T. Nakamoto, Y.-J. Hsu, M. Sone, T.-F.M. Chang, Gold/MnO2 particles decorated on electrodeposited polyaniline toward non-enzymatic electrochemical sensor for glucose, Micro Nano Eng. 18 (2023) 100175, https://doi.org/10.1016/j.mne.2023.100175.
[136] S. Kailasa, B.G. Rani, M.S. Bhargava Reddy, C. Harish, K.V. Rao, T.V. Rao, Enzyme-free glucose sensor based on twisted polyaniline nanobelts decorated with copper oxide nanoparticles, Inorg. Chem. Commun. 179 (2025) 114732, https://doi.org/10.1016/j.inoche.2025.114732.
[137] D. Zhai, B. Liu, Y. Shi, L. Pan, Y. Wang, W. Li, R. Zhang, G. Yu, Highly sensitive glucose sensor based on Pt nanoparticle/polyaniline hydrogel heterostructures, ACS Nano 7 (2013) 3540–3546, https://doi.org/10.1021/nn400482d.
[138] S. Fang, X. Zhou, L. Lin, L. Fang, H. Liu, B. Liang, A flexible and conductive paper electrode based on PEDOT:PSS and platinum nanohybrids for glucose detection, Microchem. J. 212 (2025) 113555, https://doi.org/10.1016/j.microc.2025.113555.
[139] A.Y. Sari, A.S. Eko, K. Candra, D.P. Hasibuan, M. Ginting, P. Sebayang, P. Simamora, Synthesis, properties and application of glucose coated fe 3 o 4 nanoparticles prepared by Co-precipitation method, IOP Conf. Ser. Mater. Sci. Eng. 214 (2017) 012021, https://doi.org/10.1088/1757-899X/214/1/012021.