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REVIEW

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Nanomaterials-based portable electrochemical sensing and biosensing systems for clinical and biomedical applications

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Abstract

Miniaturized electrochemical sensing systems are employed in day-to-day uses in the several area from public health to scientific applications. A variety of electrochemical sensor and biosensor systems may not be effectively employed in real-world diagnostic laboratories and biomedical industries due to their limitation of portability, cost, analytical period, and need of skilled trainer for operating devices. The design of smart and portable sensors with high sensitivity, good selectivity, rapid measurement, and reusable platforms is the driving strength for sensing glucose, lactate, hydrogen peroxide, nitric oxide, mRNA, etc. The enhancement of sensing abilities of such sensor devices through the incorporation of both novel sensitive nanomaterials and design of sensor strategies are evidenced. Miniaturization, cost and energy efficient, online and quantitative detection and multiple sensing ability are the beneficial of the nanostructured-material-based electrochemical sensor and biosensor systems. Owing to the discriminating catalytic action, solidity and biocompatibility for designing sensing system, nanoscale materials empowered electrochemical detection systems are accomplished of being entrenched into/combined with portable or miniaturized devices for specific applications. In this review, the advance development of portable and smart sensing/biosensing systems derived from nanoscale materials for clinical and biomedical applications is described.

Keywords: Portable sensor, Smart sensor, Electrochemical sensor, Nanomaterials, Clinical diagnostics, Biomedical applications

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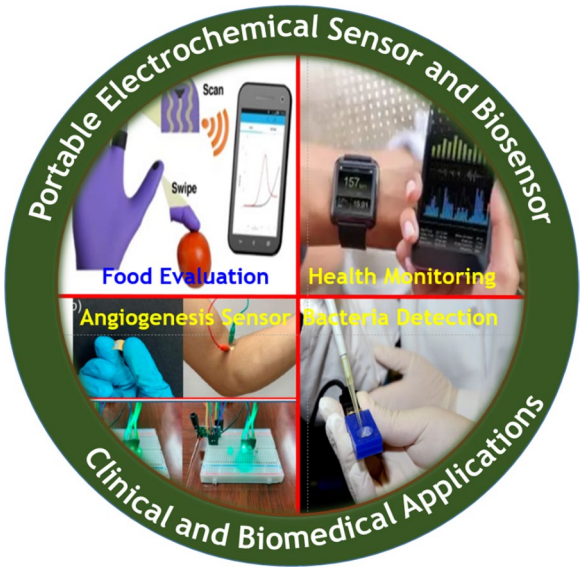
Graphical Abstract



Introduction

Point-of-care (POC) diagnostics and in vitro diagnostic (IVD) tests usually do not include the utilization of laboratory technical person and the ability to deliver the results. In general, the emergent biomarkers are included such as proteins, nucleic acids, metabolites, drugs, ions and gaseous species, human/cancer cells, and microbes (Qin et al. 2022; Totoricaguena-Gorrino et al. 2022; Yang et al. 2022a, b, c). The analytical samples such as blood, saliva, urine or other bodily fluids may be employed in whether near patient in a hospital and clinical laboratories (Pourang et al. 2022; Qin et al. 2022). These examinations generally admit a small sample and almost not at all pre-preparation and deal a consequence in few seconds to few hours. The analytical assessments need basic teaching to practice and certain sending single or multiple targets markers/biomarkers (He et al. 2022; Hendricks-Leukes et al. 2022; Jankelow et al. 2022). Importantly, the understanding of the results may be as humble as inspecting a stripe or spot of color on a strip of polymer that executes the analytical procedure (Jovic et al. 2022; Kumar et al. 2022).

Electrochemical sensor systems own an extensive and ironic past in the area of analytical chemistry and causative to numerous medical industries (Barreiros Dos Santos et al. 2022; Beck et al. 2022; Maduraiveeran et al. 2018a, b). Electro-analytical detection methods have possessed strong attention in the numerous research fields as they have the volume to oblige as perfect sensing entrants, partaking such characteristics as fast response, stoutness, high sensitivity and selectivity, less price, ease of miniaturization, and the possible for online detection (Arivazhagan et al. 2020; Maduraiveeran et al. 2018a, b; Xue et al. 2018). The electroanalytical technology-based sensing devices are employed in day-to-day uses in several areas, starting from public health to scientific applications (Qin et al. 2022; Ahmad et al. 2019). The sensor systems provide the results quickly and frequently with saving time. The analytical samples may not transit to a laboratory or expect the consideration of a technician. The outcomes may not interval to be communicated. Rather, the results can easily be provided on the spot to patient. Certainly, this protects time, but speediness must not be operated for accuracy or reliability (Hassanzadeh et al. 2022; He et al. 2022; Kannan and Maduraiveeran 2022; Maduraiveeran 2022).

Moreover, the parameters of price may vary from those of conventional laboratory measurements. The sensor device price is fewer but does only one or a few dissimilar examinations due to the sensor systems usually slighter and more dedicated than laboratory structures. In particular, the analyte molecules do not straightly interact with the reader; henceforth, self-cleaning subsystem is not required (Pankratova et al. 2021; Ruan et al. 2021; Samper et al. 2021). A variety of POC chips or strip-based disposable sensors are effectively employed for numerous on-board reagents. The POC system has superior complication in relation to a blood-draw tube, and

functionality sorts it more pricey, so examinations traded in great capacity stem most of their income from the useable (Sinha et al. 2022). The POC experiments may circuitously, occasionally extremely, inferior medical prices, which lead sample mislabeling and mishandling, along with misdirection of results. The fallouts are delivered more speedily, allowing more operative action of swiftly continuing conditions, even building a life-or-death variance with certain contaminations. In the present review, we highlight the advance design and development of portable and smart sensing/biosensing systems based on nanoscale materials for clinical and biomedical applications (Fig. 1).

Smart and portable sensor systems

Smart and portable sensor devices are being developed in the arena of sensor technology. Smart sensor typically is the grouping of a detecting materials with processing abilities delivered by a microprocessor (Rajendran et al. 2021). In general, smart sensor is a digital transducer combined with signal processing unit and a communication interface (Zhou et al. 2022). Smart sensor system is usually embedded with a digital motion processor (DMP), which can easily receive input from external sources and use pre-built functions to detect a specific combination of inputs. This is the major difference between a normal portable sensors and smart sensors. The enhancement of sensing abilities of such sensor devices in relations of sensitivity, discrimination ability and steadiness over the integration of both new sensitive nanomaterials and design of sensor strategies are evidenced (Meng et al. 2022). It is understood that as the mandate for sensitive, speedy, discriminating and multiple detection of various biomarkers endures to produce, it prepares the value of electrochemical sensor systems. Electrochemical sensor platforms are eagerly improved for sensing a wide range of chemical and biological markers, which may be combined into strong, portable and miniaturized systems using nanostructures while residual comparatively cheap, in contrast to spectroscopic and chromatographic instrumentation (Hendricks-Leukes et al. 2022). A wide variety of nanostructured materials have been employed to construct a various series of electrochemical detection systems, usually based on their unique catalytic and sensing characteristics (da Silva et al. 2022; Franco et al. 2022; Gevaerd et al. 2021; Karbelkar and Furst 2020; Nie et al. 2010). Current developments in the preparation of nanostructured materials and analytical approaches offer a robust and encouraging forthcoming toward the understanding of analytical systems (Fig. 1).

Fig. 1 Portable electrochemical sensors and biosensors for various applications

The construction and commercialization of less price nanoscale material-based smart detection elements continue important subjects in the expansion of analytical systems for clinical and biomedical sectors (Karbelkar and Furst 2020; Nie et al. 2010). One of the essential problems that needs instantaneous determination toward the progress of imminent very discerning and precise, portable/miniaturized, swift, and simultaneous multiple sensors is the important holdup that leftovers between laboratory archetypes and their extensive profitable tenders (Govindhan et al. 2014; Maduraiveeran and Ramaraj 2007; Zhao et al. 2021). A broad cooperative labors among multidisciplinary scientific disciplines and manufacturing sectors may be indispensable, and certainly, are acceptable for the efficacious enterprise, progress, and employment of improved, "*market ready*" sensors.

Smart and/or portable sensor devices potentially signify an innovative group of detecting competence, and self-awareness which are highly crucial machineries of imminent intellectual devices. The dynamic intellect depressed to the constituent equal via the strategy of smart sensor devices may have a thoughtful influence on claims in environmental safety, health monitoring and medical diagnostics both nearby and on a world-wide measure (Qin et al. 2022; Raymond et al. 2022). Owing to more quick, trustworthy, full-bodied, inexpensive and well-organized way with a unified interface, the new cohort of smart detection systems may retain implanted aptitude to deliver the end user. Though, in order to spread the potential of detection devices, additional progresses in both micro-technology/nano-technology and software algorithms are necessary. Recent literatures show that contemporary development of electrochemical detection

platforms majorly concentrations on the combination of both micro- and nano-fabrication to enterprise sensors with reduced dimension and energy burdens with enhanced portability (Montes-Cebrian et al. 2019; Poenar 2019; Wen et al. 2019). The combination and interaction of unique materials may be expected to endure as the construction of sensor systems with amplified selectivity.

Significant investigation attention near miniaturization of sensing devices from the ultimatum for extra sensitive capacities for arena and POC exercise is interested. It is understood that miniaturization of sensing tools that deals the outlook of incorporation of numerous phases in multifaceted diagnostic events into a solitary convenient expedient. Such designed systems may allow inexpert end-users to accomplish exceedingly composite clinical trials (Gaikwad et al. 2015; He et al. 2022; Jankelow et al. 2022; Karsten et al. 2015; Kumar et al. 2022). A segment of this development is usually engaged near reduction in the dimension of sensing parts to the nano-dimension and incorporated with electronics. Single-molecule determination is the central boundary for detecting the quantity of precise low-concentration assays pertinent, called premature period discovery of disease. The vital significance is a simplistic miniaturization, comfort of incorporation with devices, direct signal transduction and economic price for practical real-world applications (Pumford et al. 2020; Qin et al. 2020).

In addition, smart watches have numerous sensors suitable for receiving physical activity and monitoring illness. These mobile healthcare or mHealth contexts trust on communication means to get vibrant information from patients in real time. In recent years, a disposable freestanding electrochemical sensing system (FESS) is developed for simultaneously enables sensing and out-of-plane signal interconnection with the aid of double-sided adhesion. Generally, the flexible and thin film contains multiple vertically stacked films such as adhesive anisotropic conductive film (ACF), a noble metal electrode array film, a biochemical film, a microfluidic film, and a skin adhesive film (Zhao et al. 2020). The flexibility of the FESS in terms of its core capabilities is established by the deposition of numerous patterns of different noble metals such as gold (Au) and platinum (Pt) as well as different sensing layers to target a panel of physiologically relevant biomarker molecules in sweat.

Electrochemical glucose sensing system

Detection of level of glucose in blood is a severe for regulatory diabetes and the encounter of offering such fitted and dependable glycemic regulator ruins the topic of vast quantity of research (Arivazhagan and Maduraiveeran 2020; Arivazhagan et al. 2020; Kannan and Maduraiveeran 2021). It is anticipated that ~48.3 million people will have diabetes by 2050 in the US. Current research study assessed that the world diabetes occurrence among adults may be significantly increased to 6.4–9.5% by 2030. An inactive existence joint with deviations in eating behaviors and the growing incidence of fatness is supposed to be the chief reasons of for increasing rates. Glucose levels in blood are observed with a diversity of sensing systems in ex vivo or in vivo structures. Glucose biosensor systems employ a subsection of this family, viz. bioelectrodes and biosensors platforms for showing blood glucose a foremost character in this track (Izadyar et al. 2022; Ravariu and Arora 2021). In general, enzyme-based sensing electrodes like glucose oxidase (GO_x) that bind to transducers have thus been the aim of considerable exploration (Murugan et al. 2022; Tang et al. 2022). In 1962, Clark and Lyons developed the perception of glucose enzyme electrodes, which showed momentous movement to the expansion of dependable strategies for self-observing and continuous diabetes resistor (Moody et al. 1987; Sun and Tachikawa 1992; von Woedtke et al. 1994). A diversity of approaches has been discovered in the process of glucose enzyme electrodes. It is surprised that the current biosensor market is occupied by glucose biosensors. Glucose biosensors have been accounted for about 85% of the ecosphere market, calculating to be ~$5 billion USD and the glucose biosensor device market evolution is rushing and industrialists are involved in aggressive antagonism.

Nanostructured transition metal oxides (TMOs) materials have been employed as a significant class of sensing elements for enzyme free glucose sensor due to the multiple electrochemical redox pairs promote the glucose oxidation reaction (GOR) (Arivazhagan and Maduraiveeran 2022; Arivazhagan et al. 2020; Xue et al. 2018). For instance, Zhao et al. developed portable and enzyme-free electrochemical glucose sensor based on nanostructured gold nanoparticles dispersed on CuO nanowires on copper foam electrode (Zhao et al. 2021) (Fig. 2). The as-developed sensor exhibited high sensitivity of ~1.6 μA/μM/cm with a detection limit of ~0.9 μM. Conferring to the topical shot by *Global Industry Analysts, Inc*., the global marketplace for glucose biosensors and strips reached ~$11.5 billion USD in 2012. The same company is selling the blood glucose monitoring (BGM) by several segments such as *Blood Glucose Strips, Blood Glucose Meters and Lancets*. Global Industry Analysts, Inc., (GIA) publicizes the announcement of an inclusive global explosion on the biosensor systems in medical devices marketplaces. The worldwide ultimatum for biosensing systems in medical devices is conjecture to be extended $16.5 billion USD in 2017.

Medtronic Minimed Inc. offers the Continuous Glucose Monitoring (CGM), getting a more comprehensive

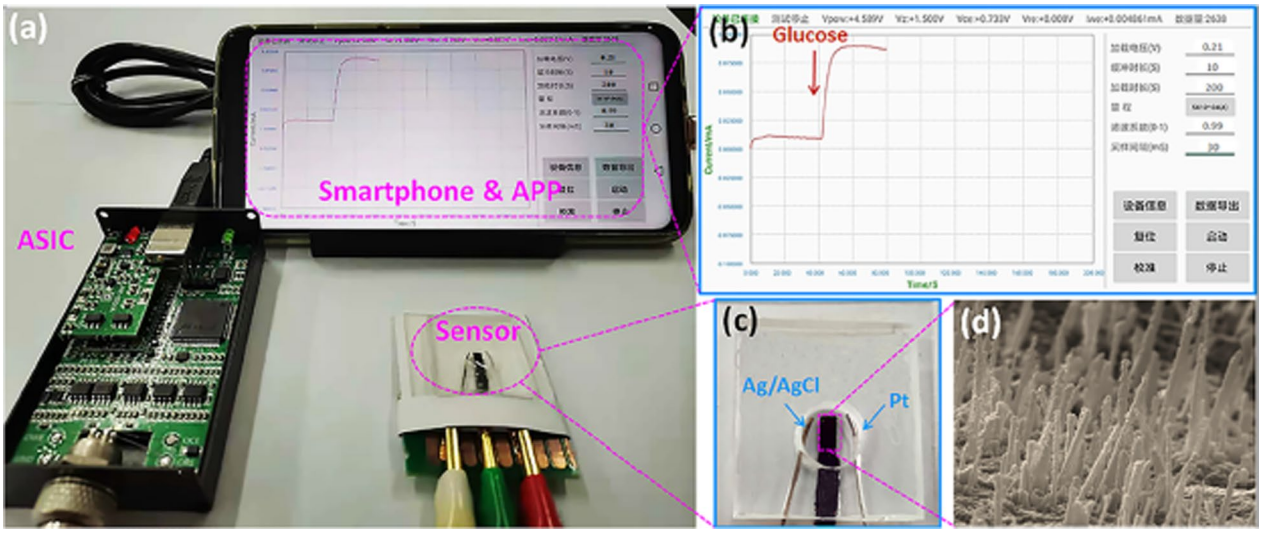


Fig. 2 Picture of the portable electrochemical detection of glucose incorporating with smartphone (**a**); Software interface of APP (**b**); Electrodes setup (**c**); FESEM image of the sensing element gold nanoparticles dispersed on CuO nanowires (**d**) (Zhao et al. 2021)

depiction of body glucose altitudes, which may clue to healthier action choices and improved glucose regulator. This is the most common glucose nursing resolutions are blood glucose meters and CGM devices in real-time during the day and night. A miniature electrode, termed a glucose detector, is implanted underneath the skin to quantity the level of glucose in tissue fluid, and it is associated with a transmitter that directs the info via wireless radio frequency to a observing and show device. This system could sense and inform when glucose is attaining a boundary. The modern Medtronic CGM systems can essentially attentive you before you extent your glucose confines.

Abbott Inc is currently being developed a similar sensor system, created on the wired enzyme technology of Heller's group, which includes supplement of a small pointer hooked on the skin and produces an interpretation each minute. The entrenched component, intended to utility for ~4 days between substitutes, is minor sufficient to be painlessly substituted by the consumer. *Cygnus Inc*. developed a watch-like glucose monitor system based on the coupling of reverse iontophoretic gathering of glucose through the skin with the biosensor role. The wearable *GlucoWatch device*, which is now available from *Animas Technologies Inc*. It comprises together the abstraction and the sensing purposes beside with the functioning and data-storage motherboard. An alarm capability is included to aware the distinct of very low or high glucose levels. Further directions for gathering glucose via skin and for noninvasive glucose trying are presently existence inspected with numerous clusters and businesses. Those global companies on biosensors market is being motivated by the upsurge in R&D events for emerging biosensors, offering extremely precise real-time diagnosis in medical opinion. The increasing medical uses, upsurge in R&D actions and the advent of new know-hows, such as microfluidics and noninvasive biosensing substitutions, establish the extra market drivers.

Recent years, wearable electrochemical glucose sensor systems for health monitoring and fitness management have expected a swiftly growing market, particularly those for noninvasive and incessant measurements with real-time display. They have offered various practical convenience and free of safety/infection risks (Chang et al. 2022). Park co-workers demonstrated a wearable electrochemical glucose sensor using of Au and Pt alloy nanoparticles dispersed on a reduced graphene oxide (rGO)-based nanostructured composite electrode, which was successfully micro-fabricated and micro-patterned on a flexible polyimide substrate (Xuan et al. 2018). The developed wearable sensor exhibited the limit of detection of ~5 μM, linear range of 0–2 mM and sensitivity of 48 μA $mM^{-1}cm^{2}$. Javey co-workers reported a self-powered and fully integrated smartwatch for the continuous detection of glucose in sweat (Zhao et al. 2019). The working function of the smartwatch is detection of glucose in sweat, process the signal and display which can be reinforced with the harvested/converted solar energy without external charging devices. The Zn-MnO_2-derived batteries work as intermediate energy storage units and the employment of aqueous electrolytes. Recently, Chang co-workers developed a smartwatch-based glucose sensor, comprising of glucose oxidase (GOx), carbon nanotubes, and Nafion composites electrodes (Chang et al.

2022). The established smartwatch sensor was successfully real-life tested on 23 volunteers, exposed 84.34% clinical accuracy of blood glucose extents for commercialization. Smartwatch-based wearable sensor devices realize the incorporation of energy modules with self-powered ability, electroanalytical sensors for noninvasive glucose monitoring, and in situ and real-time signal processing/display in a single platform, offering an emerging strategy for clinical investigation over conventional glucometer.

DNA-based electrochemical biosensing system

Microarrays of DNA are a significant implement for a diversity of uses in the field of gene expression, genotyping, drug discovery, molecular diagnostics, etc. (Zhang et al. 2022; Zhao et al. 2022; Zheng et al. 2022). They possessed a robust consequence in medical diagnostics for cancer, toxicology and infectious disease uses (Alonso et al. 2004; Alvarado-Ramirez et al. 2021; Anderson et al. 2013). Initially, Fodor co-workers (Chee et al. 1996) and Brown co-workers (DeRisi et al. 1997) have developed a sensor platform based on DNA microarrays for measuring mRNA or miRNA expression, from portray single nucleotide polymorphisms (SNPs) to recognize in vivo transcription factor (TF) binding locations. In addition, it can be acted as a diagnostic device for the detection of chromosome removal or intensification. DNA biosensor systems own the possible to overwhelmed the restrictions of DNA microarrays by offering swift and high sensitive utensils for genetic sensing, including: (i) the incorporation of microelectronics to microchip-derived nucleic acid tools in a great accessible procedure; (ii) the automation of the sensing step; and (iii) the capability to accomplish straight signal transduction evading the images treating and analysis of statistical methods, essential in canonical DNA microarray workflow. The applications of DNA-based biosensors contain molecular diagnostics, pharmacogenomics, drug airing, clinical analysis (Gaiani et al. 2022; Hanpanich et al. 2022; Li et al. 2022).

In recent years, novel peers of chips which may operate the sequencing of DNA for quickening clinical, biomedical and biological research in the area of genetics (Feng et al. 2019; Santos et al. 2019; Wu et al. 2017). These innovative machineries are majorly based on the sequencing of cyclic-array and comprise the subsequent profitable produces: the 454 Genome Sequencer based on Roche Applied Science, the Solexa from Illumina, the SOLiD platform derived from Applied Biosystems, the Polonator produced by Dover/Harvard and the HeliScope Single Molecule Sequencer from Helicos. Microarray-based sequencing empowers a much advanced grade of parallelism than that of conservative capillary-based sequencing, then offerings difficulties with elongated sequencing innings and precise data consistency. In addition, *CombiMatrix* developed an electrochemical DNA microarray system accomplished of sensing the existence and quantifying the profusion of thousands of diverse genes. *CombiMatrix* involvement substances when it originates to diagnostic challenging and they specify in the analysis of microarrayanalysis, aiding the clinical diagnostic essentials of the medical public from the time when 2005. The *CombiMatrix 12 K ElectraSense*® microarray usually is a chip of silicon with balancing semiconductor of metal oxide motherboard. This motherboard is communicated over pogo pin connectors to13 pads based on metal on electrode arena. This microarray establishes an extremely multiplexed electrodes system where signals majorly initiative chemical reactions that generate electrical signals at every electrode substrate (Mahmoodi et al. 2019; Song et al. 2020; Zhao et al. 2020). Biodevice Technology Ltd. developed a DNA stick on electrodes fabricate into the reaction tube (DNA stick), and it could be mixed using an electrochemical indicator after the amplification of PCR amplification. In addition, they established a DNA tester, which incorporates a temperature heater toward DNA intensification (Fig. 3) (Tamiya 2022). The selectivity of the ElectraSense microarray is considered as a multiplex sensor via the seizure molecules at apiece electrode. The gorgeous belongings of the electrochemical systems are immensely for enlightening the efficacy of diagnostic examining and monitoring of therapy.

Electrochemical bacterial sensing system

Detection of microbial infection relics a great contest (da Silva et al. 2022; Gevaerd et al. 2021; Scott et al. 1997). The preliminary loading of microbial cell of the analyte is relatively squat, thus requiring the culturing of the microorganisms to allow sensing and inventory with present approaches. In general, this strategy is intrinsically sluggish, captivating numerous times and postponing the discharge of yields to the marketplace or subsequent in tackle down-time (Zhao et al. 2022; Zheng et al. 2022; Zhu et al. 2022). The development of modern sensing system comes with any solutions to this tricky necessity be capable to sense microbiological pollution at the altitudes contemporary, through or soon afterward, specimen (Karbelkar and Furst 2020). Any analytical strategy must partake modest taster grounding actions and must not necessitate multifaceted and luxurious equipment (McEachern et al. 2020; Vilaplana and Marco 2020; Yeor-Davidi et al. 2020). Those characteristics sensing method to be absolutely appropriate for a characteristic eminence regulator laboratories. In general, electrochemical biosensors platforms may be characterized based on the electrical input such as direct current (DC) and alternating current (AC) as shown

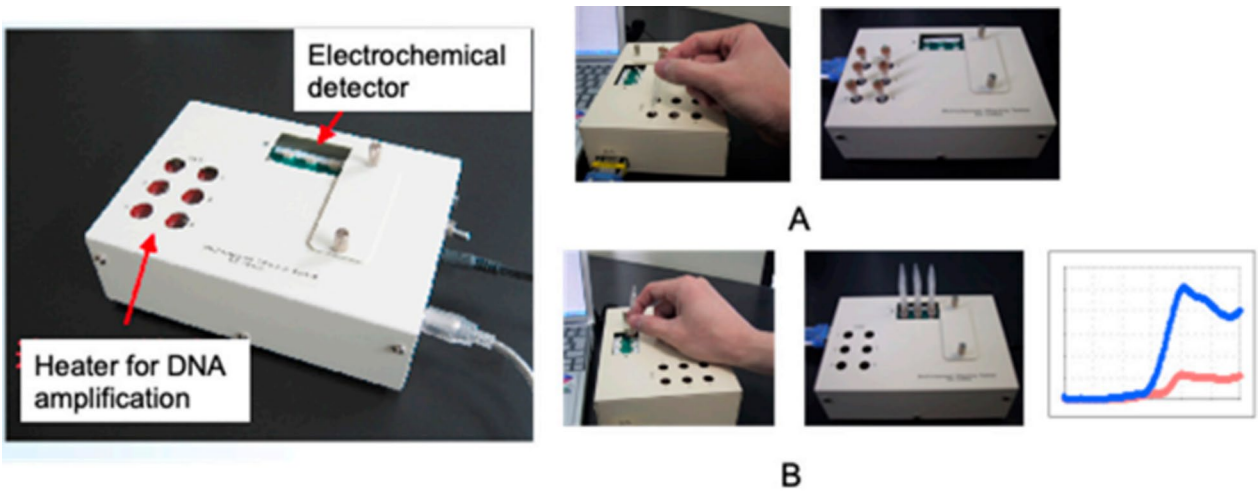


Fig. 3 Schematic illustration of the electrochemical DNA detector with heater (**A**); Sensing DNA after operation of DNA stick (**B**) (Tamiya 2022)

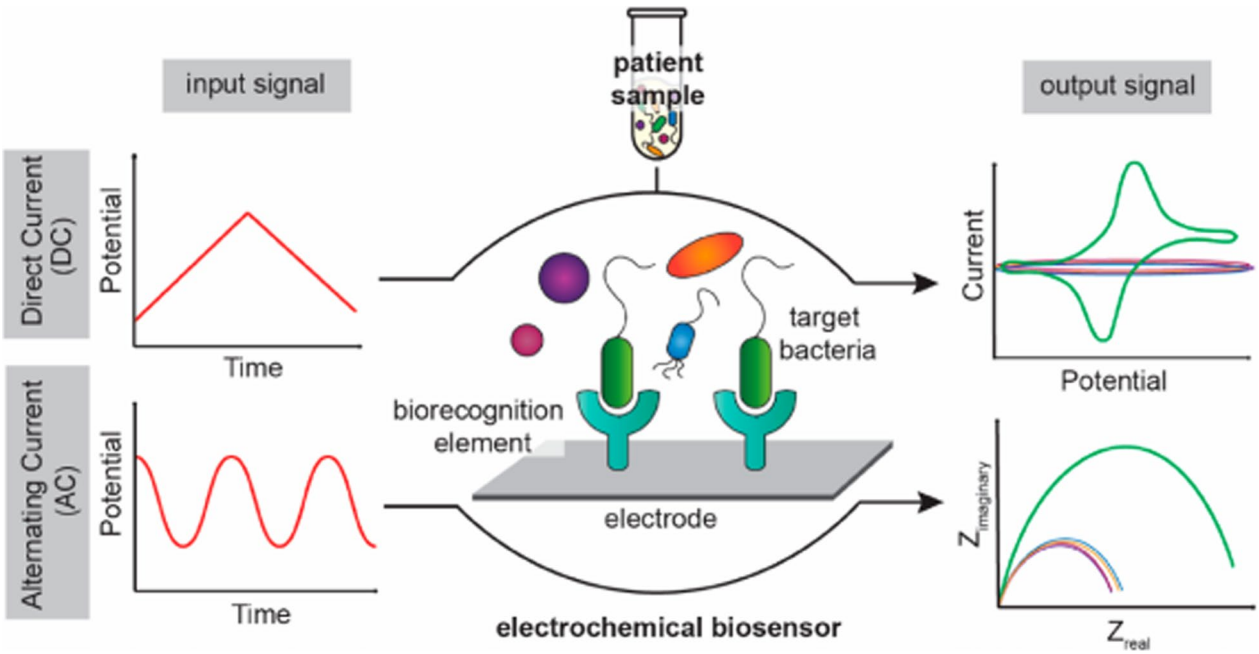


Fig. 4 Direct and AC current-derived electrochemical biosensors for bacterial detection (Karbelkar and Furst 2020)

in Fig. 4 (Karbelkar and Furst 2020). For the production of current at the interfacial electrochemical reactions, a constant polarity voltage usually is employed at zero-frequency with DC input. On the other hand, the voltage polarity may be oscillated at nonzero frequency for AC input. Figure 5 depicts the electrochemical sensor system with microfluidic chips for the detection of bacteria (Jing Jiang 2014). MICROPRINT, a technological gateway developed a sensor device based on cell imprinted electrochemical sensors, which provides the probable for expansion of fast and extremely sensitive cell sensing assays. BIO-CARD and a convenient electronic reader that processes containers and gathers data on definite microorganisms. BIO-CARD system includes new cell-capture membranes combined with detectors which counts electrons resulting from allocated reactions of cellular enzyme.

The contemporary portable sensor system for bacterial contamination has several merits, including of (i) User training is not required; (ii) Sample preparation is

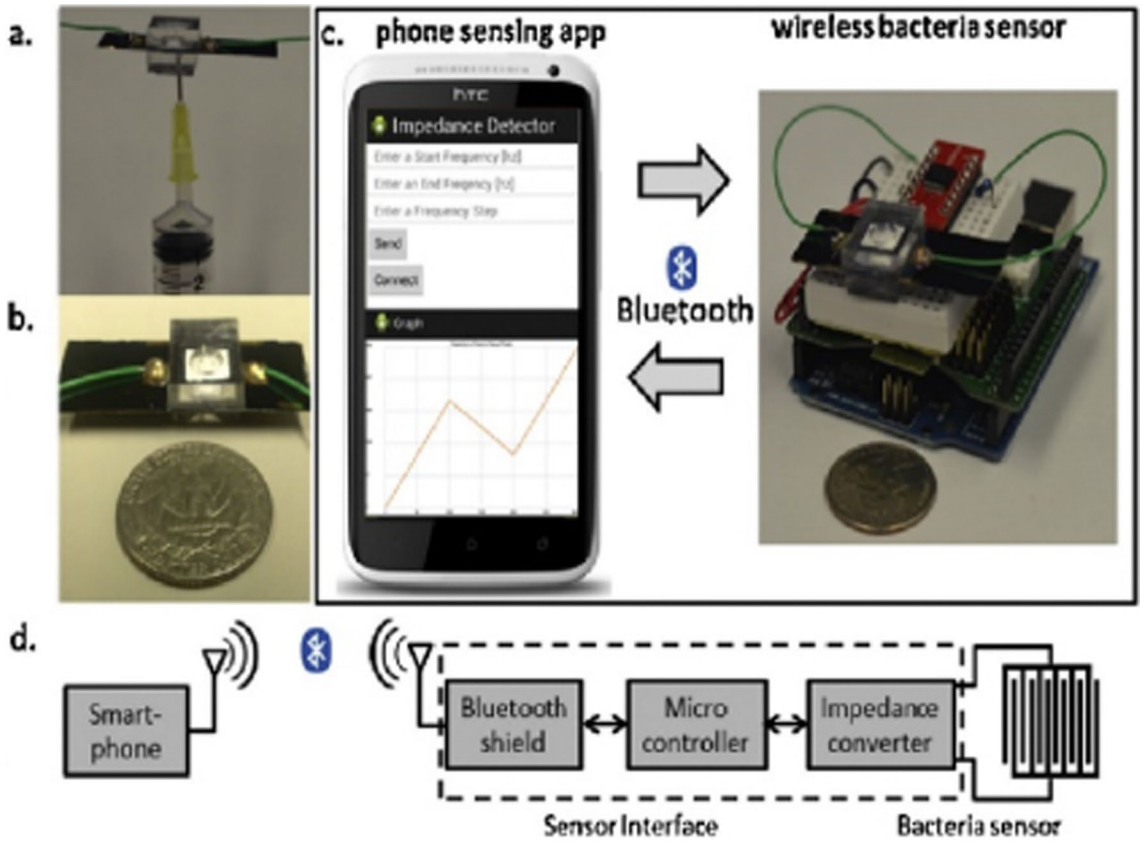


Fig. 5 Electrochemical detection of bacteria using of wireless cell phones (Jing Jiang 2014)

not required; (iii) It is a less price (reader €500 and < €1 per analysis); (iv) There is no outward reagents essential (Self-contained); (v) (< 8 h, outcomes obtainable inside same swing; (vi) Germ-free and non-obligatory sterile yields; (vii) Enable express go/no-go choices inside industrial setting; (viii) Sensitive (~ 1 cfu/mL) and many, precise organism examinations into single card (Jiang et al. 2020; Joshi and Kim 2020; Savas and Altintas 2019). This electro-analytical devices grades to substitute present exercise for counting of total bio-distinct types which is together employment exhaustive and laborious, characteristically necessitate 18–24 h for an assenting consequence. The MiCRA team established sensor for the recognition of bacteria. This model expedient intellects the attendance of enzymes ascending from microbial metabolic pathways. For example, a sensor for Escherichia coli may perceive β-galactosidase activity, and an enzyme convoluted in lactose fermentation. The device exhibits the detection limit of < 10 *E. coli* cells per 100 mL in a water solution (~ 7 h). Even the sensor is furthermore accomplished of determining 10^5 cfu/mL within 2 h.

Electrochemical Hy-GENSOR

For healthcare professionals, a hand hygiene valuation sensor system is a mobile, self-detecting hand-hygiene equipment (Bandodkar and Wang 2014), which is especially made for busy healthcare employees, marked by MiCRA-Biodiagnostics. This Hy-Gensor system inspects hand-hygiene position, presenting a measureable infection-risk valuation in immediate (Kim et al. 2013). In general, microbiological methods are influential but essential hours, or even days, to approve consequences (Zhou et al. 2017). MERCK marketed swab-type colorimetric tests, but these examinations provide qualitative "state-of-cleanliness" approximations, which are mainly employed with the food business. This device emphasizes on the speedy valuation of hand hygiene, where an alpha-numeric show signals the operator to finger or hand bacterial cell numbers, or delivers a response report on cleanliness grade. It is envisioned that the expertise will spread to higher excellence evidence of analyte documentation. It is mainly self-possessed of a micro-porous membrane owning a hydrophilic gel sub-layer with disposable reagents (Kim et al. 2013).

The enzymatic reactions thrive which are enumerated by a coulometric electrode system (Tahernia et al. 2020). This electronic indication is standardized in various methods (cell-count density, cfu/sq.mm, and data displayed/stored/Wi-Fi) and transferred with a concise measure (Jiang et al. 2020). This present machinery is envisioned for smear all over the healthcare business such as hospital wards, general patient (GP) surgeries, clinics, dentists, etc. (Savas and Altintas 2019; Yang et al. 2019). The sensor system can also be employed in handwash protocols and spot-test assessments. SM tests are high-quantity disposable substances, and it is essential to be valued consequently (<€0.2 per test). In UK, with 200 or hence huge NHS hospitals and 1000 s of healthcare workers, the bottom marketplace magnitude is over €20 m (everyday examining/year) in disposables.

Smartphone-based sensing system

Owing to the portability and ubiquitous availability of smartphone, it is extensively combined with sensor systems, including of examination strips, detection chips, and handgrip detectors for the detection of chemical and biological targets (Xue et al. 2022; Yang et al. 2022a, b, c). Employing built-in-function components, smartphones are frequently engaged as organizer, analyzer and displayer for fast, immediate, and POC observing, which would expressively streamline enterprise and decrease the price sensing devices (Song et al. 2022; Tehrani et al. 2022; Vila-Vicosa et al. 2022). Sensor methods, accessories of detectors, and combination approaches are emphasized to display schemes of the compacted, frothy, and less-price sensors and their successful employment in healthcare diagnosis (Lee et al. 2022; Liu et al. 2022; Pungjunun et al. 2022). Smartphone can be employed to carry out the biochemical sensing as collective and suitable as microelectronic tab info in conceivable forthcoming with the developments in micro-manufacturing, detection knowledge, miniaturized electronics and biosensing/electronic systems. Figure 6 presents the pictorial representation of smartphone-aided electrochemical detection of miR-21 (Shin Low et al. 2020). This electrochemical biosensing platform exhibited linear range of 1×10^{-4} M to 1×10^{-12} M ($R^2 = 0.99$) toward the sensing miR-21, and the results are analogous with the potentiostat/galvanostat.

Ho co-workers demonstrated a squeezed mobile phone platform for swift, quantifiable sensor for *Plasmodium falciparum* histidine-rich protein 2 (*Pf*HRP2) (Lillehoj et al. 2013). This smartphone-based sensor system contains of an entrenched circuit for dispensation signal and

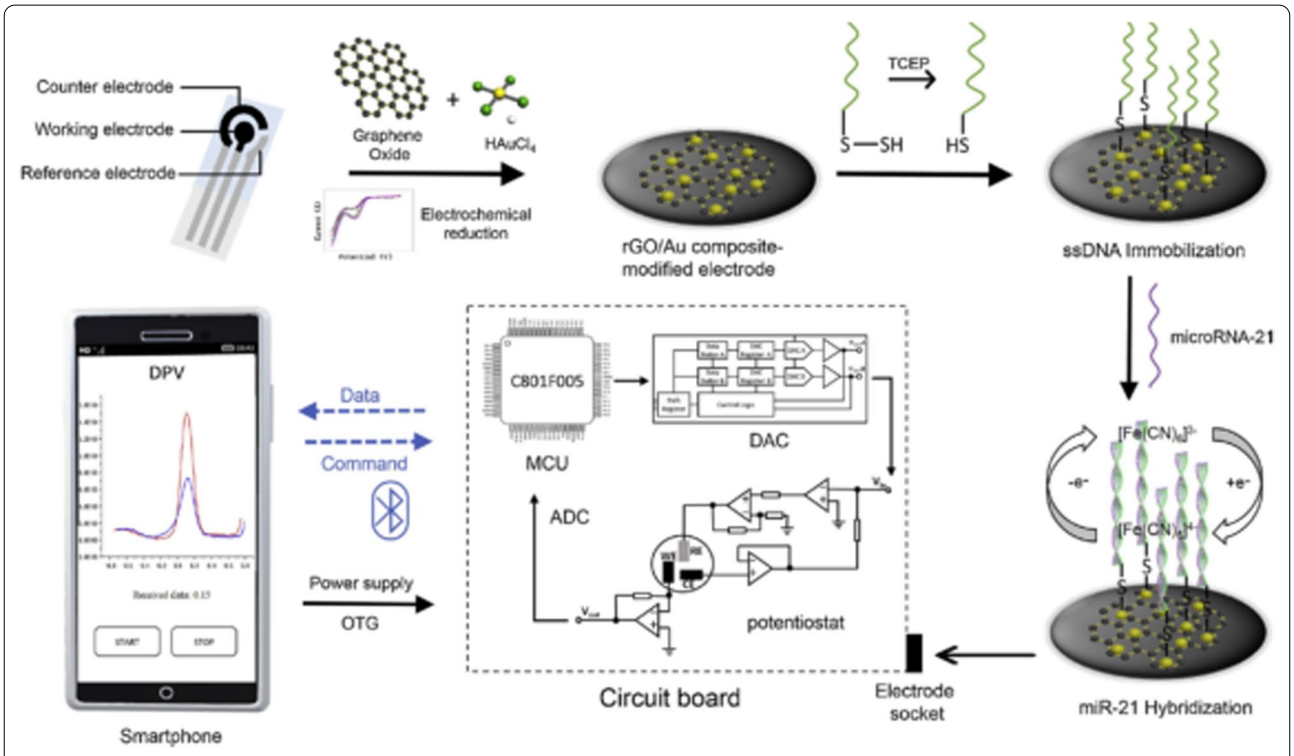


Fig. 6 Pictorial illustration of smartphone-based electrochemical biosensor platform. It contains of the composite of graphene/gold-modified sensing electrode, circuit board and smartphone with operating system of Android application for sensing miR-21 (Shin Low et al. 2020)

analysis of data, and throwaway microfluidic chips for fluidic treatment and bio-detection. The capillary flow is involved for stocking sample, handling, and pushing to improve functioning compactness and ease, and the schematically step-by-step directions displayed on the phone helps the operator via progression of sensing. Consequences are presented on the monitor for instant valuation afterward the accomplishment of every quantity, and the data are spontaneously protected to the memory of the smartphone for imminent examination and spread. The justification of this system was performed for sensing *Pf*HRP2, which is a vital biomarker for malaria, exhibited LOD of ~16 ng mL^{-1} in practical human serum (Lillehoj et al. 2013). This sensor device provides massive probable as an extensively reachable, POC system, particularly in distant and country parts due to its compact size and high performance.

Another mobile phone-based electrochemical sensing platform was developed using *MoboSens*, with combined plug-n-play microelectronic ionic device that executes sensing study through smartphone's audio jack (Wang 2015). This sensor system was applied to detect nitrate level. This compacted MoboSens sensing system, an approximate weight of 65 g, based on smartphone is clever to sense the level of nitrate in aqueous solution with a LOD of 0.2 ppm. The sensing nitrate ion using MoboSens was carried out by a microfabricated microfluidic sensor employing cyclic voltammetric technique. The strength of the capacities was proved with executing the experimentations underneath variable temperature, pH and ion interferences circumstances. The outcomes can be spontaneously protected on safe cloud waitrons. Moreover, the tested sensor performance by this lab-on-a-chip mobile detection system for field water excellence quantity and long-established this mobile detecting consequences with former remaining analytical analysis approaches (Yang et al. 2022a, b, c; Yang et al. 2022a, b, c; Yeon et al. 2022). These detection devices can deliver outstanding mobile boards to mechanism, execute, analyze and exhibition detection procedure for various uses extending from basic scientific researches to applied POC sensing, including cell and DNA imaging, analysis of human serum and biological measurements using influential computational capability and easy-to-operate verge of smartphone.

Conclusion and outlook

The design of electrochemical sensing and biosensing systems based on the functional nanomaterials toward the miniaturization and maintain the portability as the healthcare fashion is shifting to be additional patient-oriented. The patient-centered care can minimize needless measures, honors patient preferences, and progresses patient health. The employment of portable biosensors is growing rapidly due to the competitive research and fabulous commercial openings in the worldwide market for remote patient monitoring and reduce healthcare costs. In healthcare diagnostics, smartphones with outstanding built-in kit include multicore processor, high-resolve camera, global positioning system (GPS), ability of internet connection and effectual operating system are highly proper, performing as portable systems for point-of-care testing (POCT). Thus, the combination of smartphone-aided healthcare for bio-molecular diagnostics is of substantial prominence. The smartphone-based electrochemical sensor and biosensor system is portable, and simple, which is highly appropriate to be effectively practical in resource-limited and non-clinical environments.

With rapid advances in materials, mechanical and electronic processes, flexible and wearable electrochemical biosensors systems (wristbands, watches, deformable tattoos and stretchable patches) have broadly been established increasingly for in situ sensing of biomarkers for biological, clinical diagnosis and biomedical applications. The near field communication (NFC) based sensing systems offer wireless energy supply besides wireless data transmission among other detection devices. This system can be intended into a fully flexible structure, which requests a small-dimension NFC chip and couple antenna in its place of batteries or wires. The flexible structured sensors possess the potential to be effortlessly smeared to soft and erratically designed surfaces, including the human skin or textile fabrics for measuring specific biomarkers. In consequent, the dimension and consumption of power of the flexible systems could be significantly condensed, attaining skinned detecting with flexible biochemical sensing devices. Owing to advances of microelectronic technologies, the development of microfluidic systems couples with electroanalytical approach could be an innovative grouping. The combination of NFC-empowered smartphone and electrochemical sensing strategies, flexible epidermal biochemical sensing device may effortlessly be assembled to detect biomarkers, targeting successful POC-type system for mental health management.

In conclusion, the effective design of smart and portable miniaturized electrochemical sensing systems for online monitoring of in vivo and in vitro detection of emerging biomarkers is a stimulating mission. The advance development of portable and smart sensing/biosensing systems derived from nanoscale materials for clinical and biomedical applications is reviewed, including electrochemical glucose sensing system, DNA-based electrochemical biosensing system, electrochemical bacterial sensing system, electrochemical hy-gensor and smartphone/smartwatch-based sensing

system. It is highly understood that the miniaturized smart and portable electrochemical sensing and biosensing systems embrace a solid prospective through the merits low cost, rapid analytical efficacy, flexible design, facile miniaturized systems and smart monitoring. Furthermore, advances on nanoscale functional materials, miniaturization process, in situ and simultaneous detections, NFC interface will indeed stimulate toward biological, clinical and biomedical applications.

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Declarations

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