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Biotechnological Applications of Electrochemical Biosensors: A Review.

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ABSTRACT

Biosensors are analytical devices used for analysing and detecting a chemical substance by combining a biological component with a physicochemical detector. This arduous task is simplified by the inception of an electrochemical biosensor which has gained traction over the years, due to the direct conversion of a biochemical process to an electronic signal. This review highlights features like sensitivity, practicality, portability, fast response, and cost-effective that entails its incorporation as an important bioanalytical tool for medical, disease diagnoses, food industry, and environmental monitoring applications. The concept of basic elements for its design and the whole detection process is also described. Furthermore, an overview of materials used for the production of an electrode, prominently the metal nanoparticles-based fabrication is described. This review gives a comprehensive description of the sorting of electrochemical biosensor based on biological recognition elements and transducer acknowledging both pros and cons. Finally, it summarises the dire need for further perusal on the biosensor and its prospects.

Keywords: Electrochemical biosensor; environmental monitoring; disease monitoring; nanoparticle-based electrodes.

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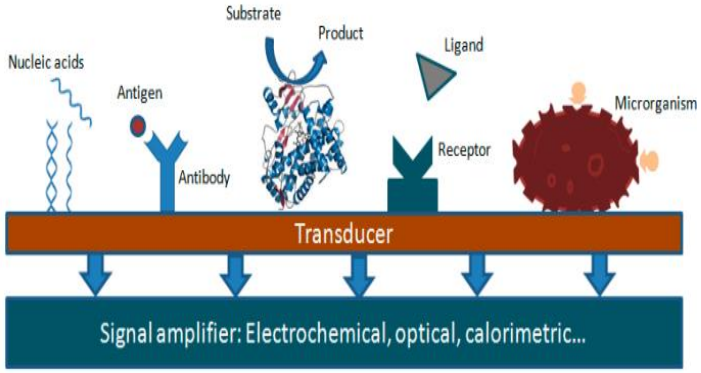
INTRODUCTION

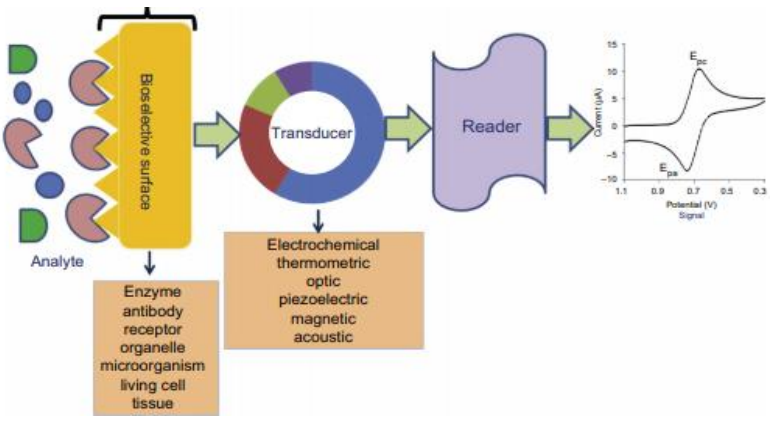
It is important to detect the diseases at the early stage for both patient health and reduction of treatment expenses. It is crucial to have a highly delicate and diverse procedure that can be effective in the early stages of diseases. Economic, miniaturized devices that can substitute time-consuming laboratory analyses are instantly essential for diagnostic purposes. In this context, a biosensor is one of the devices that fulfil these needs. Cammann coined the term "biosensor". Biosensors are specific, portable, and fast.[1,2] Based on the types of bioreceptors, biosensors can be classified into immune-biosensor, enzymatic biosensor (enzyme as a bioreceptor), etc as illustrated in **Fig. 1** and based on the form of transducer, it can be classified into an optical, colorimetric, electrochemical biosensor, etc. Onto the surface of the transducer, enzymes are immobilized via different immobilization methods such as covalent binding, physical adsorption, cross-linking, and entrapment. The receptor molecules interact with the analytes, which causes a biochemical transformation. This results in the generation of an analytical signal and the transducer sends this signal to an electronic system.[3]

Figure 1: **Different biosensors with various biorecognition elements [3]**



The biosensors that alter biochemical data like analyte concentrations into an analytical signal such as voltage or current is called an electrochemical biosensor. Voltage, current or resistance signal are analytical signals and enzyme or antibody are biochemical information which is generally in the form of analyte concentrations. Even minor levels of given analyses in body fluids i.e., blood, urine, or saliva can easily be detected. The basic principle of biosensors involves three key elements, that are required to design an electrochemical biosensor. These elements include: (i) biological recognition element which is highly specific towards biological material analytes, integrated or connected to the physio-chemical transducer (ii) transducer-transduces signal from biological target to electrical signal (iii) amplification and detection-produces an electrical signal that is used to analyze, manage and display the data derived [4,5] as shown in **Fig. 2.**

Figure 2 (a): Representation of working of biosensor [2]



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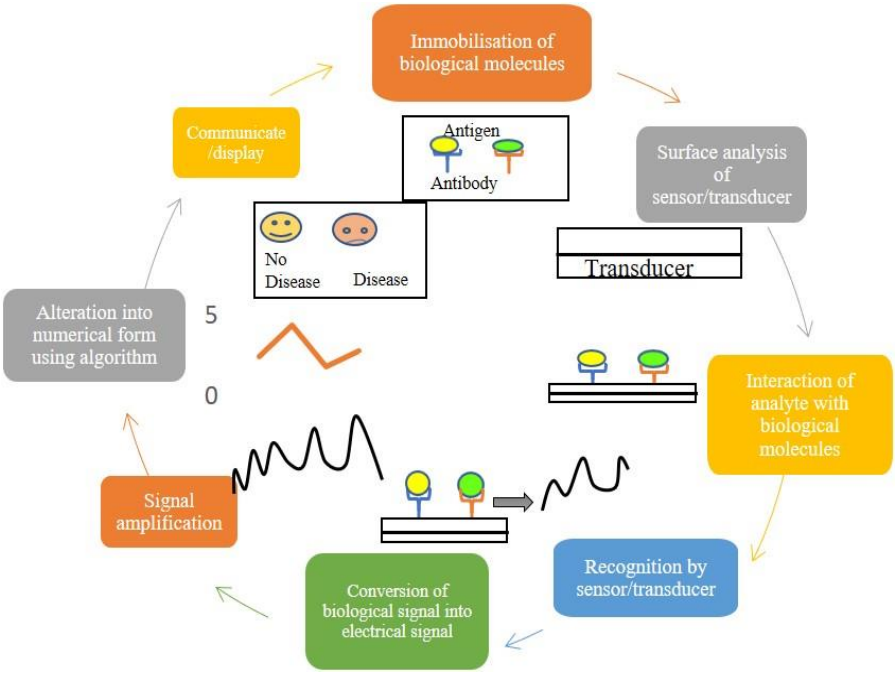
(a)

Fig 2 (b): Detection process of biosensor [2]



(b)

MATERIALS USED TO MAKE ELECTRODES FOR BIOSENSOR

The working of the biosensor is exclusively dependent on the resources used for the manufacture and production of the electrode. Solid, noble metal electrodes are the most preferred ones, like gold, platinum, and carbon. While selecting the materials, various factors like toxicity, cost, mechanical properties, conductivity, electrical conductivity, surface reproducibility, and potential range need to be taken into consideration. [6,7]

Because of excellent features, metal nanoparticles-based fabrications of sensors are currently being largely analyzed in the various fields of science.[8] Some of the materials are explained as follows:

1) **Silver nanomaterials**: These are exceptionally valuable equipment in biosensing technology. They comprise prospective applications in diagnostic fields for detecting infectious organisms, biomarkers, and other physiological threats. [6,9]
2) **Carbon nanomaterials**: Due to their low residual current, chemically stable, highly sensitive, readily renewable surface, robust mechanical strength, and high-reliability features, carbon nanomaterials are preferred for the design of electrochemical biosensor. [10,11,12] Carbon-based nanostructures exhibit one of its kind properties and morphological flexibility creating them multifunctional. A very small concentration of analytes can easily be recognized by carbon nanotubes. [13,14] AS graphene has an uncommon property of 2D- material and therefore proves to be a novel material for biosensor fabrication. Features like a higher catalytic activity than any other material, low atomic thickness, hardness (harder than diamond, electric conductivity at 25°, and flexibility make graphene attractive for the design of the electrodes. [12,15] The structure of graphene in different forms is shown in **Fig. 3.**

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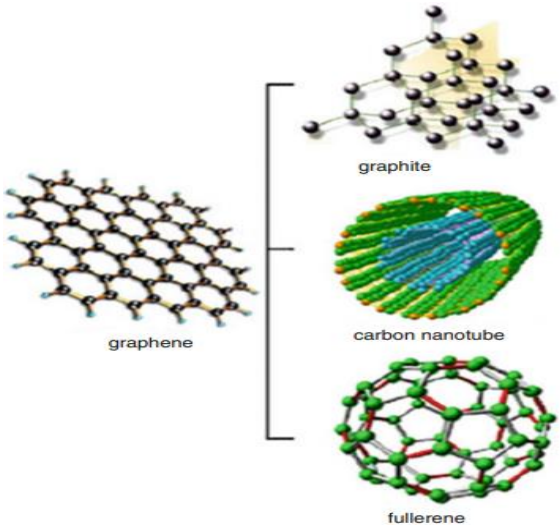
Fig 3: Structure of graphene, carbon nanotube, fullerene and graphite [12]



3) **Gold nanomaterials**: Due to their electronic and optical features, biocompatibility, and relatively simple modification and production, gold nanoparticles are mostly used for biosensor applications. Because of their low toxicity properties and no interaction with the bio components, they are largely used in the biomedical area. They are also known as noble materials having features like very good biocompatibility, surface-to-volume ratio, can easily be synthesized and very high stability. [16,17]
4) **Noble nanomaterials**: Due to unique thermal, electronic, and optical properties, gold and silver nanoparticles have attracted intense scientific and technical interest and they have a good optoelectronics property that makes them highly useful in biomedical applications. For drug delivery, molecular diagnostics and imaging, therapeutics, and biomolecule recognition purposes gold, silver, and platinum are used. [18,19]

TRANSDUCTION OF ELECTROCHEMICAL BIOSENSOR

Analytical information is obtained by connecting sensors to electrochemical transducers. The main principle behind the detection technique is that the oxidation-reduction reactions of the analyte instigate cause changes in the properties of the emulsion by the intake or generation of electron species. This change is measured by the working electrode after referring to the reference electrode. Such sensors measure the parameters like impedance, capacitance, or resistance. A few examples of such interactions include ligand-receptor, enzyme-substrate, antigen-antibody, reactions, and others. [20]

1) **Potentiometric detection**: These biosensors are based on ion-sensitive field-effect transistors (ISFET) and ion-selective electrodes (ISE). In this form of sensor, the measured constraint is a reduction/oxidation potential of an electrochemical reaction. The working principle depends on the circumstance that when a voltage is applied to an electrode in a solution, a current movement arises because of the electrochemical reaction. The voltage at which these reactions happen shows a specific reaction and certain species. [21] Interaction of the biomolecules gives rise to potential difference and for analyzing this, the Nernst equation is used. As the concentration-response is logarithmic, detection at minute changes is possible. [22,23] The selective membrane is used to cover the gate surface of a transistor in ISFET, that could be made up of tantalum oxide, silicon nitride, zirconium oxide, and alumina. [24,25,26] The working principle of a potentiometric biosensor is represented in **Fig. 4**.

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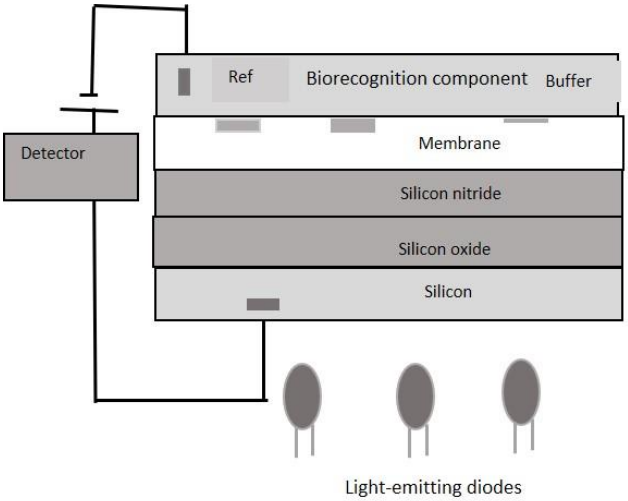
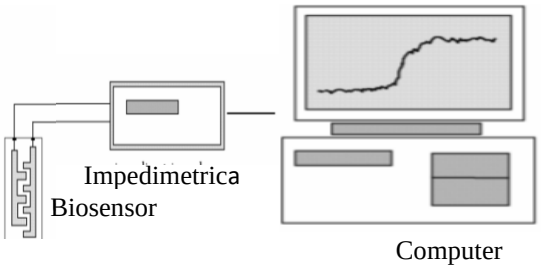
Fig 4: **Block diagram of potentiometric biosensor [26]**



2) **Amperometric detection**: Compared to potentiometric ones, amperometric are rather susceptible and extra suitable for mass production. Screen printed layer or noble metal is used as a working electrode that is covered by a biorecognition component. [25] Biolayer produces current by redox reaction which is measured directly and the redox reactions at the immobilized electrode surfaces help to measure the currents. So, the product must be electroactive and undergo the redox process. [27] The glucose meter is the best example of a successful amperometric biosensor, which has a rapid analysis feature. This portable and effective biosensor helps diabetic patients to easily check their glucose levels in the blood. [28,29]
3) **Impedimetric detection**: The surface of the electrodes is immobilized by different biolayers and the impedance of the system is deliberate. The electrochemical impedance spectroscopy (EIS) method is used to analyze the surface of the electrode which is modified by biological components and the function and structure of the electrodes. [30] Impedimetric methods are employed for forming a typical biosensor and these methods help to monitor the biochemical reactions like enzyme-substrate reactions, protein-ligand binding, antigen-antibody interactions, etc. The wide variation of physical and chemical properties is displayed by EIS. [31] The scheme of impedimetric detection is represented in **Fig. 5.**

Fig 5: **Simplified scheme of impedimetric biosensor [26]**



4) **Voltammetric detection**: It is an electro-analytical technique and gives information about an analyte. The quantity of current is measured by fluctuating the voltage. The alteration in the current with changing voltage gives the plot known as a voltammogram. There is a minutest potential essential to recruit an oxidation or reduction reaction at an electrode. There are many forms of voltammetry such as linear sweep, polarography (DC Voltage), normal pulse, differential staircase, and more. The only change among these methods lies in the way the potential is used. One of the most widely used methods is cyclic voltammetry and it is beneficial to acquire data about the electrochemical reaction rates (e.g. the chemical rate constant) and redox potential of analyte solutions. [23]

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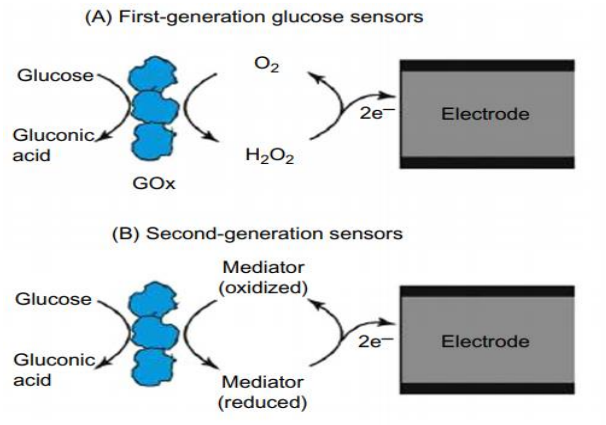
TYPES OF ELECTROCHEMICAL BIOSENSOR BASED ON BIOLOGICAL RECOGNITION ELEMENTS

1) **Enzymatic electrochemical biosensor***:* Enzymes are biological catalysts, which are produced in the living organism. They are specific to a particular type of substrates. The biological reaction is sped up by reducing the activation energy. For an enzyme-catalyzed reaction, the enzyme-substrate complex should be formed in which the enzyme binds to the substrate. [32,33] An advisable enzyme has to be immobilized onto the electrode surface, to achieve an enzymatic electrochemical biosensor. [34] Enzymes are immobilized onto the electrode by various methods like (1) entrapment- for trapping the enzyme, a combination of an enzyme with the monomer solution is polymerized to a gel. (2) Adsorption- chemical adsorption is stronger compared to physical adsorption. Chemical adsorption involves the formation of covalent bonds whereas physical adsorption ensues mainly by Vander Waals interaction. (3) Covalent bonding – bonding occurs between the transducer, a functional group, and substance. (4) Cross-linking- a biomaterial is chemically allied to another supporting material. The next-generation biosensors were established by linking enzymes with redox mediators (micro/nanomaterials, dye molecules, quantum dots, biomolecules) and their mixtures to improve the electron transfer characteristics associated with the nanomaterials. [35]Then the current change is monitored by the reduction and oxidation of specific analyte. Glucose biosensor is one of the significant enzymatic biosensors. Clark and Lyons invented the glucose meter in 1962, which began the epoch of biosensors, and from then onwards, the development in these fields accelerated at an uncontrollable rate. [2,28] The following reaction shows the amperometric detection of hydrogen peroxide:

$$\text{Glucose} + O_2 \xrightarrow{\text{Gox}} \text{Gluconolactone} + H_2O_2$$

To anticipate glucose in the blood, enzyme glucose oxidase (Gox) is impaired onto the membrane and connected on the Clark electrode surface. [2] Nanomaterials have exclusive advantages in immobilizing enzyme and could hold its bioactivity due to direct electron transfer between the enzyme's active sites and the electrode. [36] Biosensors, in particular, glucose biosensors, making usage of ZrO2/chitosan composite film [37], carbon nanotubes [38], TiO2 nanoporous film, Au nanoparticles [39], and titania sol-gel membrane [40] to immobilize enzyme. A representation of different types of sensors classified into different generations based on the sensing device in **Fig. 6**.

Fig 6: **Different sensor based on the material used [34]**



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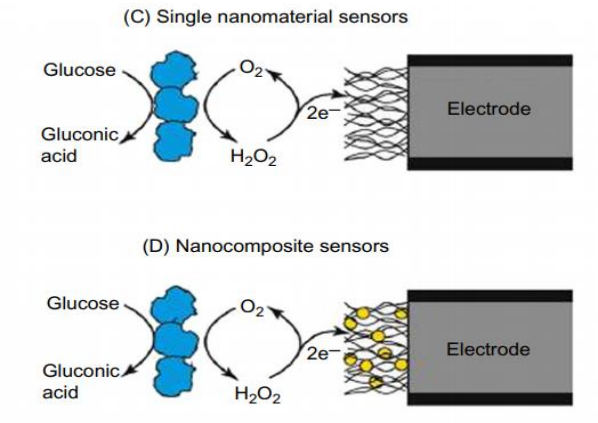


For cholesterol biosensor, cholesterol oxidase (ChOx) enzyme is used. Cholesterol oxidase is a flavin-enzyme (flavin-adenine-dinucleotide) that produces hydrogen peroxide. The following reaction shows the conversion of cholesterol and the liberation of H_2O_2.

Cholesterol + O_2 → 4-Cholesten-3-one + H_2O_2

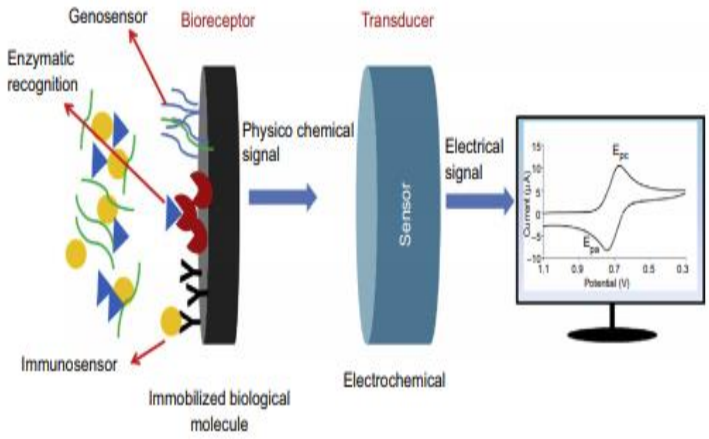
The total or free cholesterol present in the serum is detected using cholesterol oxidase, as this helps in bioconversion reactions. It is hence, a commercially and industrially important compound, as it is used in clinical diagnostics. [33,41]

An enzymatic biosensor is also used for urea sensing which mainly immobilises the urease enzyme by using zinc nanoparticles incorporated in chitosan solution. Enzyme-based biosensors have arisen as the most auspicious field for monitoring choline from the given serum sample. Choline is present in peripheral and central nervous systems of mammals. For the synthesis of the neurotransmitter acetylcholine precursor, choline is required. For choline determination, the enzyme electrode is immobilized with ChOx by releasing H_2O_2. The following reaction is for a single enzyme system

Choline + O_2 → Betaine aldehyde + H_2O_2

Choline is changed by ChOx, in the existence of oxygen by releasing H_2O_2. With the help of conducting material electrodes, H_2O_2 is detected. [33]A schematic of the electrochemical affinity sensor is represented in **Fig. 7**.

Fig 7: **Electrochemical affinity biosensors [2]**



2) **Bioaffinity based electrochemical biosensor***:* When compared to electrochemical enzymatic detection, affinity-based interaction alleviates us to overseer assays that are additional complex. [2,42] Illustration of the principle behind bioaffinity biosensor is shown in **Fig. 8.**

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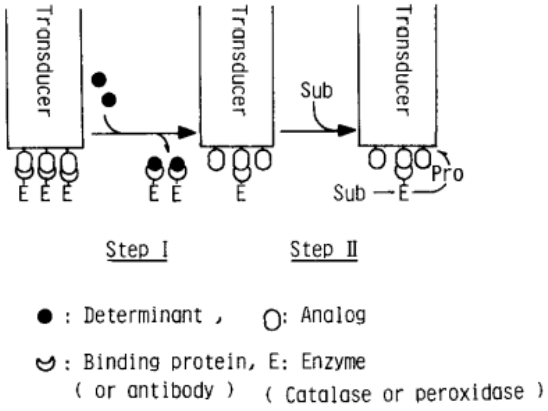
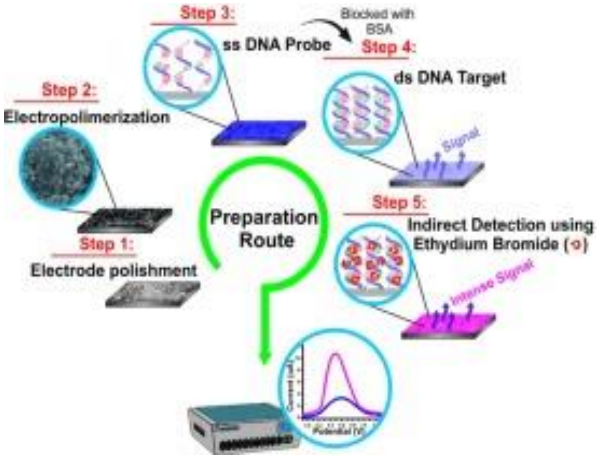
Fig 8: **Representation of a bioaffinity biosensor [42]**



The different types of affinity-based biosensors are:

a) Genosensors*:* a single-stranded oligonucleotide probe is immobilized on the electrode surface and for the detection purpose, the hybridization of two DNA sequences is monitored. [43,44] The nucleic acid part hybridizes with its homologous DNA and the transducer change hybridization into frequency signal or photoelectrical. The signal is then augmented and measured so that the DNA can be quantitated and qualified. [45] For point-of-care diagnostic, genosensor has been a promising device. Because of simple, fast, and inexpensive nucleic acid analysis features of genosensor, it has a multiplexed platform. MicroRNA (miRNA), degradation of messenger RNA, is supposed to be significant for the diagnosis of cancer and prognosis for reliable molecular biomarkers. [46] MiRNA plays important roles in several disease process, developmental and metabolic and have been observed as a therapeutic agent and as in cancer diagnosis. [47] The high sequence, low expression and short length of miRNA provoke the conception of efficient tools for their rapid, specific, and sensitive detection in multifaceted samples. Electrochemical genosensors can offer high sensitivity at low charge. [48] The approaches currently used for miRNA recognition are polymerase chain reaction (PCR), microarrays, and Northern blotting, which are generally less sensitive, require fluorescent/ radiolabelling, complicated instrumentation and time-consuming. Therefore, it is serious to advance robust detection approaches for miRNAs with simplicity, selectivity, and high sensitivity. [49] Preparation of electrochemical genosensor is illustrated in **Fig. 9**.

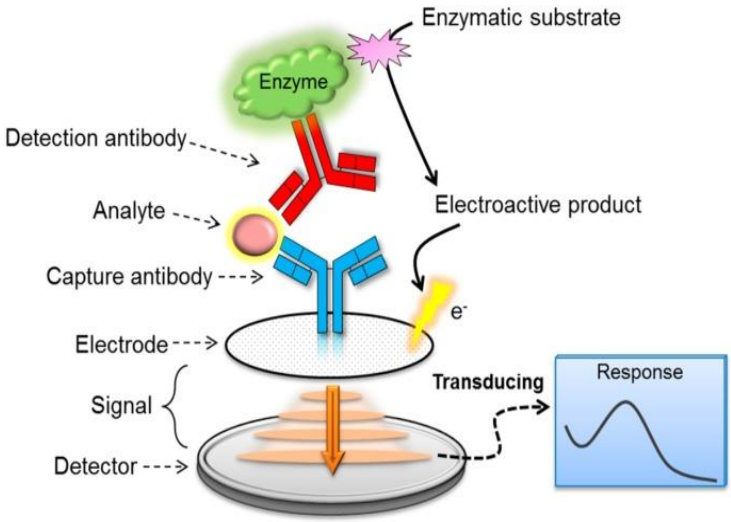
Fig 9: The following steps are engaged for detection method- electrode modification, hybridization, washing and electrochemical transducer [43]



b) Immunosensors: a solid-state device in which immunochemical reaction is coupled to a transducer. An electrochemically measurable signal is produced when a substrate is labeled with an antibody or

antigen, usually with an enzyme. [2,50] The highly precise reaction between the epitopes of an antigen and the variable regions of an antibody comprises of different sorts of bonding, mostly electrostatic interactions, hydrogen bonding, and van der Waals force. The immunosensors are usually easy to realize automation, simple to operate, digitization, and miniaturization. [51] The electrochemical immunosensor, employs the antibody as a capture agent and quantitatively measures the electrical signal ensuing from the binding occurrence between the antibody and target molecule (the analyte) as shown in **Fig.10. [**52]

Fig 10: **Schematic representation of immunosensor [52]**



The electrode offers solid support for the immobilization of antibody as well as a sensing means for the electron formed from the biological reaction in electrochemical immunosensor. [53] Nanomaterials are used as electrodes for suitable electron transfer ability and enhance the electrical signal. Nanomaterials have vast surface areas, which improves the mass passage of reactive molecules and loading capacity, resulting in a synergic role in signal amplification. [54] Immunosensors have been used for the detection of biomarkers, pathogens, toxins, antibodies, among other analytes. We have tabulated different analytes detected by immunosensor [55-69] in **Table 1**. Also, the sandwich assay scheme is represented in **Fig. 11**.

Fig 11: **Scheme of the sandwich assay [50]**

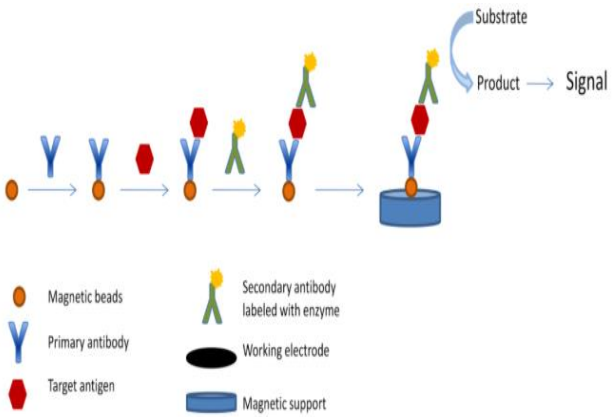


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Table 1: **Some examples of analytes detected with immunoassays and immunosensors [55-69]**

Analyte	Transducing method	Reference
Escherichia coli O157: H7		55
	Surface plasmon resonance	56
	Piezoelectric	57
	Electrochemical	58
	Fluorescence	59
Antibodies		
Antibody aimed at the foot and mouth disease	Electrochemical	60
Various antibodies aimed at Chagas disease	Electrochemical and fluorescence	61
Tumoral markers		62
Prostate-specific antigen (PSA)	Amperometric	63
PSA	Amperometric	64
PSA, C-reactive protein	Cantilevers	65
CA 125, CA 153, CA 199	Chemiluminescence	66
Toxins and pollutants		
Aflatoxins	Electrochemical	67
TNT	Fluorescence	68
Clostridium botulinum toxin A	Fluorescence	69

c) Cytosensor: a biosensor that evaluates the cells. To acquire information about the cells, the change in the impedance, current, and capacitance has to be measured. It is widely used for the detection of cancer cells. [2,70] The similarity in cancer cells and normal cells leads to trouble in the treatment and diagnosis of cancer. In the body, cancer cells are surrounded by normal cells. [71] Diagnosis of breast cancer is achieved using numerous approaches such as biopsy [72], computerized tomography (CT) [73], positron emission tomography (PET) [74], flow cytometry [75] and magnetic resonance imaging (MRI). Overall, these approaches have partial success over the long term. They are often tedious, time-consuming, costly, and may lead to false-positive or negative results [76]. Discovery of circulating tumor cells (CTCs) by electrochemical cytosensors has gained implausible status in cancer diagnosis and treatment due to cost-effectiveness, non-invasiveness, portability, and high sensitivity. Biorecognition elements and transducer are the two main units of a cytosensor. The biorecognition element (an aptamer/antibody) primarily senses the target cells and the transducer functions to convert these biorecognition interactions into signals. Preferably, a robust cytosensor is expected to permit selective detection of 1 to 200 cancer cell/mL in a typical blood sample. [77] Electrochemical cytosensors translate the interface between biorecognition elements and living cells into electrical data for quantitative examination of the cell. [78] The common type of cytosensors is fabricated based on sandwich assays. The sandwich assembly consists of cancer cells sandwiched amid different or same biorecognition elements. Sandwich assays are considered an approach for signal amplification as well as refining the specificity of cell detection. [79]

d) Aptasensor: aptamers are short and single-stranded oligonucleic acid, a molecule that is highly specific to various ligands (amino acids, proteins, and drugs). The biological surface which acts as a platform and electrochemical current alteration is monitored. [2,80] For aptasensing, aptamers should be immobilized onto the electrode surface. For sensing platforms, numerous electrode materials are used in aptasensors such as gold, carbon nanotubes, glassy carbon, graphite composites, graphene, carbon paste, and graphite. [81] We have tabulated immobilization methods used in the preparation electrochemical aptasensors with advantages and disadvantages [82-88]in **Table 2**. The generic principle of Aptasensor based on the impedimetric measure, before the interaction with analyte and sensing occurred, is shown in **Fig. 12.**

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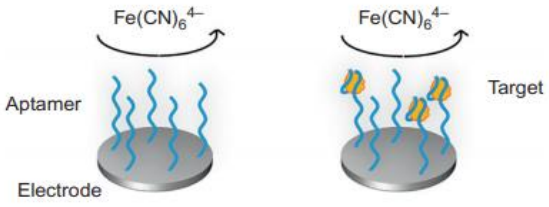
Table 2: **Summary of immobilization methods used in the preparation electrochemical aptasensors [82-88]**

Immobilization methods	Advantages	Disadvantages	Reference
Physical adsorption	Simple, fast, low cost, direct method	Desorption by a change of ionic strength, pH	82,83
Covalent binding	Good stability, high binding strength	Use of linker molecules, slow irreversible, expensive	83,84,85
Avidin-biotin affinity	Good orientation, high specificity, well-controlled	Expensive, use of a biocompatible linker	83,86
Self-assembled monolayers (SAM)	Good orientation, high sensitivity	Use of linker molecules, expensive	87,88

Fig 12: **Principle of Faradaic Aptasensor [81]**



THE APPLICATIONS OF ELECTROCHEMICAL BIOSENSORS

Relative simplicity is the central leadership of the electrochemical biosensors and they, therefore, obtain applications in numerous fields like disease diagnosis, biomedical, environmental monitoring of hazards, drug formulation and discovery, telemedicine, and food quality. [89]

1) **Biomedical**: Due to high sensitivity, selectivity and simple operation electrochemical biosensor have become an essential biomedical research weapon. At this time DNA sensor is generally used for rapidly and directly diagnose a specific sequence of DNA. The largest benefit of the DNA sensor is to identify clinical disease, which facilitates doctors to identify and analyze disease timely for understanding the function of diseases and their improvement. Even drug testing can

be done by DNA biosensor. We have tabulated the advantages and disadvantages of DNA biosensors [90] in **Table 3**.

Table 3: **Different types of DNA biosensors [90]**

Sensor type	Advantages	Disadvantages
Direct DNA electrochemical	High sensitivity, no mark, a wide range of electrodes application	High background signal, simple, easily damage the samples
Indirect DNA electrochemical	High sensitivity, without standard procedure, multiple targets detected by an electrode	Difficult preparation of the probe layer, damaged specimen
DNA-mediated electron transforms	High sensitivity, no mark, only for mismatch detection with independent sequence, appropriate for DNA protein	Biochemical treatment for a target sample
Electrochemical nano-particles enlarge	Particularly sensitive, applied to different nanoparticles for the detection of multiple targets	More detection step and uncertain of surface structure reliability and strength, often damage the samples
DNA-specific instructions detection of redox	Medium sensitivity used to detect multiple targets, the same samples	Possible of sequence changes

2) **Environmental monitoring***:* A lot of biosensors have been established for the detection of a variety of pollutants such as phenols, polluting gases, heavy metals, surfactants, and pesticides. Most of the biosensor used for environment monitoring is based on enzyme inhibition. Some common enzymes are urease, horseradish peroxidase, cholinesterase, and tyrosinase. [91]
   a) For pesticide determination: Pesticides are widely used in the industrial and agricultural fields due to their pesticidal activity. They are generally used to increase crop production. However, extensive use of pesticide contaminates the soil, water, and food. [92] Based on their persistence, polarity and volatility pesticides can be classified into fungicides, insecticides, and herbicides. [93] Acetylcholine esterase (AChE) has been extensively used in emerging biosensor for the detection of pesticides (carbamate and organophosphorus). AChE detects numerous pesticides like diisopropyl fluorophosphate, carbaryl, paraoxon, aldicarb, and chlorpyrifos ethyl oxon. [94] We have tabulated the biosensor for pesticide determination [95-99]in **Table 4.**

Table 4: **Biosensor for pesticide detection [95-99]**

Pesticide	Enzyme	Transducer	Reference
Paraoxon	AChE	Amperometric	96
Carbaryl	AChE	Amperometric	97
Carbofuran	AChE	Amperometric	97
Chlorpyrifos ethyl oxon	AChE	Amperometric	96
Triazine	Tyr	Amperometric	98
Paraoxon	OPH	Optical	99

AChE (acetylcholinesterase), Tyr (tyrosinase), OPH (organophosphorus hydrolase)

b) For heavy metal determination*:* High toxicity metals like mercury, copper, zinc, and cadmium impose a risk to the environment. [100] For the detection of metals, a heavy metal biosensor is used with immobilized glucose oxide and urease. For mercury detection, an amperometric biosensor was developed by immobilizing urease in the poly film. [101] We have tabulated the biosensor for different heavy metal detection [95,102-105] in **Table 5**. Currently, heavy metals are one of the serious causes of pollution. Heavy metals are non-biodegradable and a low concentration of metal is a danger to health and the environment. Several of the bacterial biosensor established for the study of heavy metal in environmental samples, it makes usage of definite genes responsible to these elements such as biological receptors. Bacterial strains unaffected to several metals such as tin, cobalt, silver, copper, and mercury have been isolated as likely biological receptors. [90, 106]

Table 5: **Biosensors for heavy metals detection [101-105]**

Heavy metals	Biorecognition elements	Transducer	References
Cu (II) Cd (II)	Urease	Optical	102
Hg (II)	Urease	Potentiometric	103
Cu (II) Cd (II) Pb (II)	Urease	Conductometric	104
Hg (II)	Urease	Amperometric	101
Hg (II) Ag (I) Cu (II) Cd (II)	Glucose oxidase	Amperometric	105

c) BOD determination: The quantity of biodegradable organic material in water is specified by the biochemical oxygen demand (BOD) parameter. Monitoring of air, soil, and water can be done by environmental biosensing products and detection of river water contamination, pesticides are monitored. A quick determination of BOD could be accomplished with a biosensor-based technique. [107] BOD biosensors usually comprise of an oxygen electrode, a biomembrane (mostly microbes), and measures the respiration activity of cells. The first microbial biosensor for BOD valuation was stated by Karube et al. (1977). After that, several biosensors have been established with improved features. [108]

3) **Food industry**: In the modern diet, high sugar consumption has been allied with chronic health issues including risk of fatty liver disease, diabetes, obesity, and cardiovascular disease. [109] To ensure food quality and safety, sophisticated quality control approaches are desired in the food

industry. Analytes like alcohol, oligonucleotides, and phenols need to measure at various phases. amperometric glucose biosensors propose great potential for their use in the processing industry and food production. [110]

Biosensors address three groups of food examination prospects: quality, authenticity, and safety. Food safety focuses on the recognition of unwanted impurities in food like pathogenic microbes [111], allergens [112], pesticides, antibiotic residues [113], and biological toxins. [114] It is also used to check the nutritional value of a food product. Authenticity analysis checks the production procedure of food material and provides information about the forging of food. [115]

In fermentation, process starch is the most frequently used raw material. Detection of starch can easily be done by enzyme electrode biosensor. Rennerberg promotes an ingenious method in which glucoamylase and glucose oxidase will be impaired and the electrode measured hydrogen peroxide biosensor electrode amylase. [90]

In the food industry, the quantity of glucose can be used as the main indicator in the storage life of fruit reliability. Glucose content among jam, wine, apple juice, and honey are measured by enzyme electrode-based biosensor. Niculescu developed amperometric biosensor which is used to detect the presence of ethanol in the beverages. [106,107] Electrochemical biosensors are used in food safety rather than authenticity analysis and quality. Conventional analysis for sensing harmful microorganisms (aflatoxin [116], Escherichia and Salmonella [117]) and pesticide (carbamates and organophosphates [118]) is expensive and time-consuming. The limitation is overcome by using biosensor which permits food products to be tested at all stages of production. Advanced technologies are in demand to certify the security of food from farm to plate [119]. Nanomaterials unified into various sensors play a vital role in promising food safety by producing a sensitive and rapid detection process due to their exceptional features. Therefore, the applications of a nanosensor for food hazards should be further discovered. [120]

CONCLUSION

The advance and study of a biosensor are becoming one of the most popular scientific areas at the collaboration of the engineering sciences and biological. The main aspect of biosensor developments is typically specificity, cost-effective, and sensitivity detection. Electrochemical biosensor proves the best alternative to time-consuming conventional methods. Currently, electrochemical nano biosensor being developed with enormously low levels of detection with the astonishing features of nanomaterials such as graphene and carbon nanotube. To acquire an exceptional point of care (POC) analytical stages, labs on chips (LOCs) can be combined with electrochemical biosensor to deliver sensitivity, practicality, and fast response. Electrodes are used for the conversion of chemical signals into electrical signals for analysis. Biosensors can sense many biomolecules in the human body like DNA, blood ketones, glucose, uric acid, lactate, cholesterol, and other biomolecules which have made an enormous contribution to the medical fields. The electrochemical biosensor has great application in disease diagnose, food industry, environmental monitoring, and medicine. It not only detects the disease at an early period but also to deliver and administer instant therapeutics so that the disease can be treated efficiently.

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