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A REVIEW ON BIOSENSORS AND RECENT DEVELOPMENT

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ABSTRACT

A biosensor is a device that combines a receptor and a transducer to transform a biological reaction into an electrical signal. Because of the broad variety of biosensor applications, such as health care and illness diagnostics, environmental monitoring, water and food quality monitoring, and medication delivery, the design and development of biosensors has taken center stage for researchers and scientists in the last decade. The main challenges in biosensor development are I efficient biorecognition signal capture and transformation into electrochemical, electrical, optical, gravimetric, or acoustic signals (transduction process), and (ii) improving transducer performance (i.e., increasing sensitivity, shorter response time, reproducibility, and low detection limits even to detect biorecognition signals). These problems may be solved by combining sensing technologies with nanomaterials that vary in size from zero to three dimensional, have a high surface-to-volume ratio, excellent conductivities, shock-bearing properties, and color tunability. Nanoparticles (NPs) (high stability and carrier capacity), nanowires (NWs) and nanorods (NRs) (high detection sensitivity), carbon nanotubes (CNTs) (large surface area, high electrical and thermal conductivity), and quantum dots (QDs) are some of the nanomaterials (NMs) used in the fabrication of nanobiosensors (color tunability). Furthermore, these nanomaterials may function as transduction elements in and of themselves. This review summarizes the evolution of biosensors, the different types of biosensors based on their receptors and transducers, and modern biosensor approaches that use nanomaterials such as NPs (e.g., noble metal NPs and metal oxide NPs), NWs, NRs, CNTs, QDs, *and dendrimers, as well as their recent advancement in biosensing technology with the expansion.*

KEYWORDS: *Biosensors, Carbon Nanotubes, Gold Nanoparticles, Nanomaterials, Nanobiosensing.*

1. INTRODUCTION

Nowadays, we take pleasure in the benefits of science and technology in our day-to-day life. We frequently use various types of appliances or gadgets to interact with the physical environment, such as computers, copy machines, mobile phones, microwave ovens, refrigerators, air conditioning and television remotes, smoke detectors, infrared (IR) thermometers, turning on and off lamps and fans. Many of these applications rely on sensors to function. A sensor is a device or module that detects changes in physical quantities such as pressure, heat, humidity, movement, force, and electrical quantities such as current and transforms them into signals that can be monitored and analyzed. A device that can transfer energy from one form to another is known as a transducer. A measuring system's heart is the sensor. Range, drift, calibration, sensitivity, selectivity, linearity, high resolution, reproducibility, repeatability, and reaction time are all qualities that an ideal sensor should have. Sensor technology has grown in importance as a result of a variety of applications, including environmental and food quality monitoring, medical diagnosis and health care, automotive and industrial production, and space, military, and security[1], [2].

1.1. BioSensor Classification:

Sensors are divided into many groups based on the physical amount (substance) or analyte to be measured, such as[3]–[5]

1. Source of energy (active and passive sensors),
2. Direct physical contact (contact and non-contact sensors),
3. compare-and-containment (absolute and relative sensors),
4. Sensors, both analog and digital, and
5. Detection of signals (physical, chemical, thermal, and biological)

1.1.1. Active and Passive Sensors:

Active sensors, such as microphones, thermistors, strain gauges, and capacitive and inductive sensors, need an external energy source to function. Parametric sensors are the name for these kinds of sensors (output is a function of the parameter). Thermocouples, piezoelectric sensors, and photodiodes are examples of passive sensors that produce signals without requiring external energy. Self-generating sensors are the name for these kinds of sensors.

1.1.2. Contact and noncontact sensors:

Touch sensors, such as temperature sensors, need physical contact with a stimulus, while non-contact sensors, such as optical and magnetic sensors and infrared thermometers, do not.

1.1.3. Absolute and relative sensors:

Absolute sensors, such as the thermistor and strain gauge, respond to stimuli on a scale of one to one thousand. Relative sensors detect stimuli in relation to a fixed or changeable reference, such as a thermocouple that detects temperature differences and a pressure gauge that measures pressure in relation to atmospheric pressure.

1.1.4. Analog and Digital Sensors:

An analog sensor converts a physical amount measured into an analog representation (continuous in time). This category of analog sensors includes thermocouples, resistance temperature detectors (RTD), and strain gauges. The output of a digital sensor is in the form of a pulse. The digital sensor category includes encoders.

1.1.5. Detection of signals:

Sensors are classified as physical, chemical, thermal, or biological depending on how they detect signals.

1. *Physical Sensors:* Physical sensors take physical measurements and transform them into a signal that the user can recognize. Environmental changes such as force, acceleration, velocity of flow, mass, volume, density, and pressure may be detected by these sensors. Physical sensors have been widely used in the biomedical sector, especially as microelectromechanical system (MEMS) technology has advanced, allowing for the creation of more accurate and smaller sensors, as well as the development of new measurement technologies.
2. *Chemical Sensors:* A chemical sensor is defined as "a device that converts chemical information into an analytically useful signal ranging from the concentration of a particular sample component to total composition analysis," according to the International Union of Pure and Applied Chemistry (IUPAC). Chemical sensors are used to monitor the activity or concentration of chemical species in the gaseous or liquid phases. They're also utilized in environmental pollution monitoring, food and pharmaceuticals analysis, and organophosphorus chemical assay monitoring. They may also be utilized to make clinical diagnoses.
3. *Thermal Sensors:* A thermal sensor is a device that measures the temperature of an environment and converts the input data into electrical data so that temperature changes may be recorded or monitored. Thermocouples, thermistors, and RTDs are examples of temperature sensors.
4. *Biological Sensors:* Biomolecular activities such as antibody/antigen contacts, DNA connections, enzymatic interactions, and cellular communication processes are all monitored by biological sensors. In brief, biological sensors are referred to as biosensors.

2. BIOSENSOR

2.1. Principle and Design:

A biosensor is a device or probe that combines a biological element like an enzyme or an antibody with an electrical component to produce a quantifiable signal. The electronic component detects, records, and sends data on physiological changes as well as the presence of different chemical or biological elements in the environment. Biosensors are available in a variety of sizes and forms, and they can detect and measure even low amounts of infections, hazardous chemicals, and pH values. An analyte, bioreceptor, transducer, electronics, and display are all components of a conventional biosensor[6], [7].

1. Analyte: An interesting material whose components are being identified or discovered (e.g., glucose, ammonia, alcohol, and lactose).
2. Bioreceptor: A biomolecule (molecule) or a biological element (e.g., enzymes, cells, aptamers, deoxyribonucleic acid (DNA or RNA), and antibodies) that can detect the target substrate (i.e., an analyte) is known as a bioreceptor. During the interaction between bioreceptor and analyte, signal generation (in the form of light, heat, pH, charge or mass change, plant or animal tissue, and microbial products) is termed biorecognition.
3. A device that converts energy from one form to another is known as a transducer. A biosensor's transducer is an important component. It transforms a biorecognition event into an electrical signal that corresponds to a quantity or the presence of a chemical or biological target. Signalization is the name for this energy conversion process. The number of analyte–bioreceptor interactions is proportional to the number of optical or electrical signals generated by transducers. Transducers are classified as electrochemical, optical, thermal, electronic, or gravimetric transducers based on their working mechanism.
4. Electronics: The signal is transduced and processed before being displayed. The transducer's electrical impulses are amplified and transformed to digital form. The display unit quantifies the processed signals.
5. Display: The display unit consists of a user interpretation system, such as a computer or printer,that produces output so that the user may read and comprehend the appropriate answer. The output may be in the form of a numerical, graphical, or tabular value, or a figure, depending on the end-user need.

2.2. Biosensor Evolution:

The development of biosensors has been divided into three generations depending on component attachment, i.e., the technique of integrating the bio-recognition element (bioreceptor) with the transducer. The biosensors of the first generation (Ist gen) detect the concentration of analytes and products of bioreceptor reactions that diffuse to the transducer's surface and generate an electric response. Mediators-less amperometric biosensors are another name for this kind of sensor. In his initial paper, the founder of biosensors, Leland Charles Clark Jr., outlined the components of a biosensor. An electrode that can monitor the oxygen content in blood was the subject of this 1956 report. Clark reported the use of an amperometric enzyme electrode for glucose detection in an experiment in 1962. Updike and Hicks improved Clark's work in 1967, creating the first functioning enzyme electrode based on glucose oxidase mounted on an oxygen sensor[8], [9].

2.3. Biosensor Characteristics:

Certain static and dynamic criteria are required to create a highly effective and competent biosensor system. The performance of biosensors may be adjusted for commercial usage based on these criteria.

1. *Selectivity:* When choosing a bioreceptor for a biosensor, selectivity is an important characteristic to consider. In a sample including mixed spices and undesirable impurities, a bioreceptor may identify a certain target analyte molecule.
2. *Sensitivity:* The smallest quantity of analyte that can be properly detected/identified in a few steps and at low concentrations (ng/mL or fg/mL) to confirm the presence of analyte traces in a sample.
3. *Linearity:* Linearity helps to ensure that the measured findings are accurate. The greater the linearity (straight line), the more accurate the detection of substrate concentration.
4. *Response time:* The amount of time it takes to get 95% of the results. (e) Reproducibility: Precision (similar result when the sample is tested more than once) and accuracy are two characteristics of reproducibility (capability of a sensor to generate a mean value closer to the actual value when the sample is measured every time). It refers to the biosensor's ability repeatability provide similar findings when the same sample is tested several times.
5. *Stability:* One of the most important qualities in biosensor applications that need continuous monitoring is stability. The degree of susceptibility to environmental perturbations both within and outside the biosensing equipment is referred to as stability. The affinity of the bioreceptor (the degree of the analyte's binding to the bioreceptor) and the bioreceptor's degradation with time are two variables that influence stability.

2.4. Biosensor classification:

Biosensor classification is a broad and interdisciplinary subject. Bioreceptors are the main component in biosensor fabrication, as previously stated. Enzymatic biosensors (the most common biosensor class), immunosensors (high specificity and sensitivity and are specifically useful in diagnosis), aptamer or nucleic acid-based biosensors (high specificity for microbial strains and nucleic acid-containing analyte), and microbial or whole-cell biosensors are the different types of biosensors. The second categorization is based on the transducer, with electrochemical (potentiometric, amperometric, impedance, and conductometric) biosensors, electronic biosensors, thermal biosensors, optical, and mass-based or gravimetric sensors being the most common. Bioreceptor analyte combinations, which are restricted, are another categorization. Detection systems (optical, electrical, electronic, thermal, mechanical, and magnetic) and technology (nano, surface plasmon resonance (SPR), biosensors-on-chip (lab-on-chip), electrometers, and deployable) are divided into categories.

2.5. Biosensor classification:

Bioreceptors-based Biosensors are categorized as catalytic, affinity, or non-catalytic biosensors based on the biorecognition principle. The interaction of analyte bioreceptors in a catalytic biosensor leads to the creation of a novel biochemical reaction product. Enzymes, bacteria, tissues, and entire cells are all included in this biosensor. The analyte is permanently attached to the receptor in an affinity (non-catalytic) biosensor, and no new biological reaction product is produced during the contact. Antibodies, cell receptors, and nucleic acids are among the targets for detection in this kind of sensor.

3. NANOMATERIAL-BASED BIOSENSORS (Nanobiosensors)

Biosensor research and development has grown more open and interdisciplinary as a result of advancements in nanotechnology. Exploring NMs for various features, such as NPs (metal and oxide-based), NWs, NRs, CNTs, QDs, and nanocomposites (dendrimers), offers the potential of enhancing biosensor performance and increasing detection power via size and shape management.

Nanobiosensors have the same fundamental operating principle as their macro- and micro-counterparts, but they are built with nanoscale components for signal or data processing. Because of their dimensionality, nanobiosensors offer an advantage over their traditional macro- and micro-counterparts in terms of interdisciplinary applications[10], [11]. Nanobiosensors are useful in the field of nanotechnology for:

1. Biochemical detection in cellular organelles and medical diagnostics
2. Detecting nanoscopic particles in industrial and environmental settings, and
3. Identifying very low levels of potentially hazardous chemicals.

The role of NMs in the improvement of biosensing systems has been extensively researched based on their categorization. For example, NPs-based biosensors include all sensors that use metallic NPs as biochemical signal enhancers. Similarly, nanotube-based biosensors that use CNTs are utilized as enhancers of reaction specificity and efficiency, while NW biosensors use NWs as charge transport and carriers. QDs are also used as contrast agents in QD-based sensors to improve optical responses.

4. DISCUSSION

New methods to sensor technology have been used to satisfy the growing needs of different sectors. With advancements in nanotechnology and nanoscience, sensor technology has grown even more. Nanotechnology has spanned physics, chemistry, biotechnology, biology, bioinformatics, medical science, healthcare, food engineering or processing, aerospace, and electronics, as well as the energy sector and environmental research. The capacity to handle and control materials at the atomic and molecular level (nanometer range), as well as a subsequent knowledge of basic nanoscale phenomena, have opened up new possibilities for biosensor development. More significantly, dimensionality is a key factor in influencing the physical, chemical, biological, electrical, and optical properties of nanomaterials. Nanomaterials are divided into four categories depending on their nanoscopic dimensions: 0D, 1D, 2D, and 3D materials. A 0D NM (NPs and QDs) is a material with nanoscale dimensions in all three dimensions. It is 1D NM if two dimensions of a material are nanosized while the other dimension is considerably bigger (NWs, NRs, NTs, nanobelts, and nanoribbons). It's a 2D NM if just one dimension is nanosized (nanoprisms, nanoplates, nanocoatings, nanolayers, nanosheets, nanowalls, nanodisks, and CNTs). Bulk nanomaterials (also known as 3D NMs) are materials that are not limited to the nanoscale in any dimension (less than 100 nm) (nanoballs, dendritic structures, nanocoils, nanocones, nanopillars, multi-nanolayers, and nanoflowers). The ability to synthesize materials in the nanoscale range allows for unique physical, chemical, and biological characteristics, and is critical to nanotechnology's success. A top-down method (a bulk material is restructured to create nanosized materials) and a bottom-up approach (a bulk material is restructured to form nanosized materials) have both been used to synthesize NMs (materials of nanodimension are formed by assembling molecule by molecule or atom by atom). Lithography, laser ablation, ion milling, and chemical etching are some of the methods used in the top-down approach. Molecular beam epitaxy, physical or chemical vapor deposition and evaporation, and bio/chemical processes for the creation of supramolecular complexes, self-assembled monolayers, and protein-polymer nanocomposites are all popular methods in the bottom-up approach.

Biosensor research and development has grown more open and interdisciplinary as a result of advancements in nanotechnology. Exploring NMs for various features, such as NPs (metal and oxide-based), NWs, NRs, CNTs, QDs, and nanocomposites (dendrimers), offers the potential of enhancing biosensor performance and increasing detection power via size and shape management.

5. CONCLUSION

In this review article, we have discussed types and mechanisms of biosensors basedon receptors (enzymes, antibodies, whole-cell, and aptamers), transducers (electrochemical, electronic, optical, gravimetric, and acoustic), and nanomaterials (gold NPs, Ag NPs, Pt NPs, Pd NPs, NWs, NRs, CNTs, QDs, and dendrimers). Biosensors offer versatile applications in the fields of engineering and technology, medicine and biomedical, toxicology and ecotoxicology, food safety monitoring, drug delivery, and disease progression. With the application of NMs in biosensors, we have witnessed rapid growth in biosensing technology is witnessed in the recent decade. This is because of the employment of new biorecognition elements and transducers, progress in miniaturization, design, and manufacture of nanostructured devices at the micro-level, and new synthesis techniques of NMs, all ofwhich bring together the life and physical scientists and engineering and technology. The sensing technology has become more versatile, robust, and dynamic with the induction of nanomaterials. The transduction mechanism has been improved significantly (like greater sensitivity, faster detection, shorter response time, and reproducibility) by using different nanomaterials (such as NPs, NRs, NWs, CNTs, QDs, and dendrimers) that each has differ- ent characteristics within biosensors. Though there is considerable improvement in the use of nanostructured materials in biosensors applications, there are few limitations, which hinder these applications for the next level. For instance, lack of selectivity remains a setback for the CNT-based gas sensors, hampering its usage in CNT-based devices. However, this hurdle can be overcome by coupling CNTs with other materials. The other issues in these sensors include the sustainability of nanostructures in sensor applications, which have been insufficiently investigated, the fabrication of nanostructures, and the toxicity, which changes according to the physical properties of the material type. These issues should be investigated and addressed while expanding new nanostructured materials for their use in biosensors. Most nanobiosensor devices used in biomedical applications require a large sample for detection, which may lead to false-positive or false-negative results. Very few biosensors have attained commercial success at the global level, apart from electrochemical glucose sensors and lateral flow pregnancy tests. There is also a need for making nanostructure-based biosensors at an affordable cost that give rapid results with accuracy and are user-friendly. For example, nanomaterials should be integrated with a tiny biochip (lab-on-chip) for sample handling and analysis for multiplexed clinical diagnosis. More research should be done in this area and we expect the ongoing academic research to be realized into commercially viable prototypes by industries in near future.

REFERENCES

1. P. Mehrotra, "Biosensors and their applications - A review," *Journal of Oral Biology and Craniofacial Research*. 2016, doi: 10.1016/j.jobcr.2015.12.002.
2. N. Bhalla, P. Jolly, N. Formisano, and P. Estrela, "Introduction to biosensors," *Essays Biochem.*, 2016, doi: 10.1042/EBC20150001.
3. H. A. Alhadrami, "Biosensors: Classifications, medical applications, and future prospective," *Biotechnology and Applied Biochemistry*. 2018, doi: 10.1002/bab.1621.
4. R. Monošík, M. Streďanský, and E. Šturdík, "Biosensors - classification, characterization and new trends," *Acta Chim. Slovaca*, 2012, doi: 10.2478/v10188-012-0017-z.
5. H. Kaur, A. Bhosale, and S. Shrivastav, "Biosensors: Classification, Fundamental Characterization and New Trends: A Review," *Int. J. Heal. Sci. Res.*, 2018.
6. S. N. Botewad, D. K. Gaikwad, N. B. Girhe, H. N. Thorat, and P. P. Pawar, "Urea biosensors: A comprehensive review," *Biotechnology and Applied Biochemistry*. 2021, doi: 10.1002/bab.2168.
7. F. Yang, Y. Ma, S. G. Stanciu, and A. Wu, "Transduction Process-Based Classification of Biosensors," in *Nanobiosensors*, 2020.
8. R. Mahr, C. Gätgens, J. Gätgens, T. Polen, J. Kalinowski, and J. Frunzke, "Biosensor-driven adaptive laboratory evolution of l-valine production in Corynebacterium glutamicum," *Metab. Eng.*, 2015, doi: 10.1016/j.ymben.2015.09.017.
9. Y. Liu, Y. Zhuang, D. Ding, Y. Xu, J. Sun, and D. Zhang, "Biosensor-Based Evolution and Elucidation of a Biosynthetic Pathway in Escherichia coli," *ACS Synth. Biol.*, 2017, doi: 10.1021/acssynbio.6b00328.
10. W. Zhang, Y. Du, and M. L. Wang, "Noninvasive glucose monitoring using saliva nano-biosensor," *Sens. Bio-Sensing Res.*, 2015, doi: 10.1016/j.sbsr.2015.02.002.
11. Y. J. Teh, A. Bahari Jambek, and U. Hashim, "A study of nano-biosensors and their output amplitude analysis algorithms," *Journal of Medical Engineering and Technology*. 2017, doi: 10.1080/03091902.2016.1223195.