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Fundamentals of Biosensor - An Introduction with its Applications in the Engineering Perspective

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ABSTRACT: A biosensor is an analytical device that detects a chemical substance by combining a biological component with a physicochemical detector. Sensors are divided into many groups based on the material or analyte being tested, such as energy source, physical touch, comparability, analogue and digital sensors, and signal detection. The sensitive biological aspect, that could include tissue, microorganisms, organelles, cell receptors, enzymes, antibodies, nucleic acids, and other biomimetic components, is a biologically derived material or biomimetic element that interacts with, binds to, or identifies the analyte under analysis. Biosensor used to detect small molecules such as glucose, hydrogen peroxide and adenosines. Other than that biosensor also used as to detect functional protein molecules. With today's advanced technologies, the use and production of biosensors will be more advanced and practical in the future.

KEYWORDS:biosensor, biosensor historical perspective, biosensor parameters, biosensor application.

I. BIOSENSOR

Biosensors typically employ a biologically sensitive factor in conjunction with a physical transducer to translate biochemical events into physical signals in a selective and quantitative manner[1]. Generally, biosensor represent devices that convert a physical or biological event into a measurable signal. They identify analyte molecules using immobilised biomacromolecules and higher integrated systems [2].

II. ISTORICAL PERSPECTIVE ABOUT BIOSENSOR

Table 2.1 below illustrated that the historical perspective about biosensor from 1906 until 2018 [3]. The development that was highlighted in yellow is the addition of the biosensor perspective.

Table 1: Development of biosensors in different timelines.[3].

Year	Development of Biosensor
1906	M. Cramer observed electric potential arising between parts of the fluid
1909	Soren Sorensen developed the concept of pH and pH scale
1909-1922	Griffin and Nelson were the first to demonstrate the immobilization of the enzyme invertase on aluminum hydroxide and charcoal
1922	W.S. Hughes discovered a pH measurement electrode
1956	Leland C. Clark, Jr invented the first oxygen electrode
1962	Leland C. Clark, Jr et al. experimentally demonstrated an amperometric enzyme electrode for detecting glucose
1967	Updike and Hicks and realized the first functional enzyme electrode based on glucose oxidase immobilized onto an oxygen sensor
1969	Guilbault and Montalvo demonstrated and reported the first potentiometric

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	enzyme electrode-based sensor for the detecting urea
1970	Discovery of ion-sensitive field-effect transistor (ISFET) by Bergveld
1973	Guilbault and Lubrano defined glucose and a lactate enzyme sensor based on hydrogen peroxide detection at a platinum electrode
1974	K. Mosbach and B. Danielsson developed enzyme thermistor
1975	D.W. Lubbers and N. Opitz demonstrated fiber-optic biosensor for carbon dioxide and oxygen detection
1975	First commercial biosensor for glucose detection by YSI
1975	Suzuki et al. First demonstrated microbe-based immunosensor
1976	Clemens et al. demonstrated first bedside artificial pancreas
1980	Peterson demonstrated the first fiber-optic pH sensor for in vivo blood gases
1982	Fiber-optic biosensor for glucose detection by Schultz
1983	Liedberg et al. observed surface plasmon resonance (SPR) immunosensor
1983	Roederer and Bastiaans developed the first immunosensor based on piezoelectric detection
1984	First mediated amperometric biosensor: ferrocene used with a glucose oxidase for glucose detection
1985	The development and application of biosensing devices for bioreactor monitoring and control [4]
1990	SPR-based biosensor by Pharmacia Biacore
1992	Handheld blood biosensor by i-STAT
1999	Poncharal et al. demonstrated the first nanobiosensor
2004	The Micro-ElectroMechanical Diaphragm (MEMD) is introduced as a sensor platform to measure the mass load for developing high performance biosensor [5].
2005	Electrochemical impedance spectroscopy studies of polymer degradation: application to biosensor development [6]
2016	A physics-based compact model to characterize the dc, ac, transient and noise response of FET based pH sensors [7].
2018	S. Girbi et al. demonstrated nerve-on-chip type biosensor for assessment of nerve impulse conduction

III. THE ENGINEERING OVERVIEW OF BIOSENSOR

In general, biosensors use a biologically sensitive element in combination with a physical transducer to translate biochemical events into physical signals in a selective and quantitative manner. The biosensitive part is used for target recognition and/or signal generation, while the physical transducer is used for signal production or conversion. Biological probes consisting of molecular species such as antibodies or other proteins, aptamers, or nucleic acids for binding with target analytes such as antigens, ligands, and complementary nucleic acids are used in many cases [1].

The key problems that many biosensors face today are low sensitivity, poor specificity, and fouling. The emergence of nanotechnology offers some promising solutions to these problems. Improved sensitivity and antifouling capability of biosensors, for example, have been investigated by modification of the surfaces of biosensor electrodes, namely the incorporation of nanostructures into the electrode surfaces. Nanostructures such as gold nanotubes, carbon nanotubes, and gold nanoparticles have also been used to alter the surface of electrodes, resulting in enhanced sensing efficiency over traditional unmodified flat electrodes [1].

In addition to specificity, the molecular probes used in a biosensor must have long-lasting activity and antifouling action. The underlying signal transduction system used by the transducer does not interact with the analyte, resulting in false signals [1].

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Currently, antibodies, nucleotides, enzymes, cells, and synthetic molecules are the most widely used susceptible components. Biosensors that use antibodies as the sensitive factor work by binding an antigen to a particular antibody. Biosensors that use nucleotides as the sensitive element are widely used to target genetic materials like DNA. Biosensors that use enzymes as the sensitive element work by catalysing chemical reactions [1].

Cell-based biosensors are another significant class of sensors that has recently received a lot of attention. Since cells can provide highly selective and responsive receptors, channels, and enzymes, using whole cells as the sensitive element is very appealing. As the sensitive factor in synthetic molecule-based biosensors, synthetic polymers such as aptamers are frequently used. Aptamers are synthetic nucleic acids that can be combined (or fit) with amino acids, drugs, proteins, and other non-nucleic molecules. As a result, this class of biosensors can provide high affinity and specificity to a wide range of targets [1].

IV. THE DIFFERENT TYPE OF SENSOR AND TECHNOLOGY WITH RESPECT TO ITS APPLICATION OF FUNCTION

Biomedical applications [8]

The two most widely used enzymes for glucose detection are glucose oxidases (G-ox) and glucose dehydrogenases. Binesh and colleagues' example clearly shows how to use G-ox to its full potential. They identified a simple and one-step method for generating graphene-(G-ox) biocomposite with an excellent sensitivity of 1.85 $\mu AmM^{-1}cm^{-2}$over a glucose concentration range of 0.1-27 mM. A prototype show was also performed over human serum to research the possible bioapplication of the engineered biosensor, and findings were replicated with very high precision that had previously been observed using traditional methods of glucose level evaluation.

Nanoparticles (Nps) are used as a sensing tool. Zheng and colleagues suggested a more compatible method for measuring blood glucose levels. They obtained the same aforementioned aim by using immobilised gold Nps and G-ox composite. The membrane derived from chicken eggshells was used as the fabrication medium for the Nps, which was a much more environmentally friendly way of engineering this biosensor. After wrapping the membrane-based composite around the oxygen electrode, it was used as a biosensor.

G-dh (glucose dehydrogenase) may also be used for biosensing. Aside from these direct methodologies, Yan and his colleagues documented a fascinating indirect procedure in which they presented a prototype of a needle-biosensor that could be used to detect glucose in human tears. Since diabetic patients have a much higher concentration of glucose in their tears than the normal person, the glucose content in tears was discovered to be linked to the glucose level in blood serum. Table2 shows the types of the biosensor used for glucose detection that are from Jazib Ali and his other researchers [8].

Table 2: : Biosensor for glucose detection [8].

Biosensor	Linear range	Response time	Detection limit	Sensitivity $\mu AmM^{-1}cm^{-2}$	References
Graphene-(G-ox)	0.1-27 mM	<5 s	---	1.85	[44]
PB/MWNTs-(G-ox)-CS-ICPTES	0.25 μM-1.3 mM	<10 s	7.5 μM	5.94	[43]
AuNPs-(G-ox)-MWCNTs-PVA	0.5-8 mM	<10 s	0.2 mM	16.6	[45]
PdNPs/CS-GR-(C-ox)/GC	1 μM-1 mM	<10 s	0.2 μM	31.2	[48]
CS-Fc/GO/(G-ox)	0.02-6.78 mM	<5 s	7.6 μM	10	[49]
(G-ox)-AuNPs/ESM	8.3 μM-0.96 mM	<30 s	3.50 μM	9.421	[46]
Nafion/ZnO-HNSPs/(G-ox)/GCE	0.005-13.15 mM	<5 s	1.0 μM	65.82	[50]
(G-ox)/ (AuNPs/MWCNT)	20 μM-10 mM	<3 s	2.3 μM	19.27	[51]
(G-ox)-CS/AgNWs/GCE	10 μM-0.8 mM	<10 s	2.83 μM	---	[52]
(G-ox)/CeO_x NRs/ITO	2-26 mM	1-2 s	100 μM	0.165	[53]
PPF/(G-dh)/PT/CNT/PPF/Au	4.9-19 mM	5 ± 1 s	0.12 mM	5.1 ± 0.9	[54]
Nafion/(G-dh)-bacteria/CNT	50-800 μM	---	4 μM	---	[55]

Applications in tissue engineering [8]

DNA, nucleic acids, and genes: Many fundamental fields of study provide a clear connection to genetic diagnostics and DNA encoding. A DNA-specific sensor typically consists of three processes according to the researchers: the first one is the insertion of probes over the substrate film, while, the next one is the contact with the appropriate DNA sequence through analogue base pairing, and lastly, The chemical signal generated as a result of base interaction is read out in the form of an analytically useful signal. Li et al. announced the development of a highly sensitive DNA electrochemical biosensor using dendritic gold

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Nps. Under the concentration restriction of 1fM, this biosensor demonstrated DNA recognition ability up to 1fM. (1fM-1nM).

Chen et al. made a significant contribution to DNA biosensing by developing an ultra-sensitive sensor for the electrochemical detection of oral cancer from saliva secretions that is fundamentally dependent on nuclease-mediated highly targeted recycling of DNAzyme. With the aid of this sensor, the targeted DNA could be quantified to 0.02 fM.

Precision and reproducibility in measuring hydrogen peroxide (H2O2) content are important in both clinical and tissue engineering environments. Its concentration in humans is a direct predictor of oxidative stress or hypoxic conditions in tissues. Table 3 below illustrated the biosensor types that used to detect hydrogen peroxide.

Table3: Hydrogen peroxide detector biosensor[8].

Biosensor	Linear range	Response time	Detection limit	Sensitivity μAmM^{-1}	References
PANI/HRP/GE–CNT–Nafion/AuPt NPs	17 μM-0.1 mM	---	17 μM	3.7×10^2	[70]
Hb/AuNPS/ZnO/Gr/GCE	6.0-1130 μM	<2 s	0.8 μM	---	[71]
Hb-PpPDA@Fe_3O_4/GCE	0.5-400.0 μM	<4 s	0.21 μM	-0.076	[72]
Hb/3DOM GTD/ITO	5.0 μM-1.0 mM	---	0.6 μM	144.5	[76]
HRP–polyAuNPs–Au	5 μM-1.1 mM	8 s	1.5 μM	498	[77]

Applications in food industry [8]

Bacterial monitoring: E. coli strain 0157:H7, Listeria monocytogenes, campylobacter, and salmonella are common bacteria associated with food spoilage and health risks. The bacteria listed above are common problems in the food industry because they reduce consumer demand for food if the company's food becomes contaminated with these food spoiling biological entities. The authors also mentioned that while piezoelectric biosensors are commonly used for Salmonella monitoring because they can detect monoclonal antigen-antibody complexes quickly and easily, they are poor detectors of polyclonal antibody complexes, which is a significant limitation that needs to be addressed for potential improvements.

The cause of listeriosis, a common human disease. Listeriosis, like the common flu, causes miscarriage. According to Geng and Morgan, fiber-optic biosensors have been widely used to detect the existence of L. monocytogenes. Surface Plasmon Resonance (SPR) biosensors and fiber-optic biosensors have proved to be the most effective for detecting L. monocytogenes.

Detection of fungal pathogens: Fungi, including bacteria, are a common cause of food spoilage and severe health problems, which can be fatal in the majority of cases. Botrytis sp., Aspergillus, Colletotrichum, and a variety of other fungal species are commonly responsible for food contamination. Biosensors with detecting ranges for different types of bacteria [8] that degrade food and cause risk to human health were shown in table 4.

Table4: Biosensors for detection of various types of bacteria [8].

Bacteria	Types of biosensors	Found in foods	Detection range/limit	References
Salmonella	Piezoelectric	Eggs, meat, raw milk, meat and dairy products.	1.7×10^2 cells/mL	[88]
L.monocytogenes (pure culture)	Fibre-optic	Raw milk, meat, milk products.	10^7 to 10^8 CFU/mL	[85]
	SPR sensor		low concentrations upto 10^6 CFU/mL	[89]
C. jejuni (pure culture)	SPR sensor	Raw milk, uncooked chicken, contaminated water.	10^1 to 10^8 CFU/mL	[90]
E. coli O157:H7	Amperometric	Raw milk, milk products, juices, cheese etc.	1.0×10^7 cells/mL	[86]

Environmental applications of biosensors [8]

Heavy metals are the most dangerous to human health because they cannot be biodegraded. Heavy metal hyperaccumulation causes a variety of undesirable health conditions. Several forms of biosensors have also shown great success in detecting and tracking toxic levels of heavy metals that would otherwise cause adverse health effects, according to the authors. Heavy metal-resistant genes, such as copper, mercury, tin, and cobalt, are used in bacterial-based cell biosensors. They may, however, continue to work when heavy metals interact with their cytoplasm; their dependence is focused on the conjugation of specific luminescent proteins, such as luciferin, with specific genes that resist heavy metals.

Enzyme-based biosensors have also shown promising results in this regard, as have fibre-optic biosensors for detecting toxic levels of various heavy metals such as lead, cadmium, mercury, copper, nickel, cobalt, and so on. These biosensors work by inhibiting heavy metals on

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various types of enzymes with metal ions, and then tracking these inhibitions with different types of biosensors with high specificity. The use of amperometric biosensors to detect the inhibition of mercury ions (Hg+2) by urease enzyme action was effective. The detection of cobalt, nickel, mercury, gold, and lead by the same enzyme urease resulted in toxic levels being regulated using fiberoptic sensor technology.

Polychlorinated biphenyls (PCBs) are non-biodegradable pesticides and insecticides that, while successful for pest management, cause PCB concentration in the soil, which is then absorbed by crops and causes serious health problems, the majority of which are related to cancer. Immunological biosensors that use piezoelectric transducers to monitor antigen-antibo35dy interaction have been most effective in the precise detection of these organic compounds in foods and soils in recent years.

Microorganisms that live in sewers and waste waters normally break down organic compounds to produce poisonous substances. Biochemical oxygen demand (BOD) is the amount of molecular oxygen (O2) needed by microorganisms to live in wastewater. It is mainly required during the breakdown of organic compounds. As a result, chemical pollution of bodies of water is increasing. In 1983, the company Nisshin Denki Electric Co. Ltd. produced the first commercial biosensor for BOD level monitoring.

Organophosphates, which are often used as insecticides (pesticides), alter soil fertility, damaging many beneficial insects and microbes in the soil and contributing to biodiversity loss. Another kind of nanotechnological sensor has recently been used to measure toxic levels of these pesticides in soils and water to detect these pesticides. Nanotechnology has been used to upgrade enzymatic biosensors, allowing them to be immobilised. Acetylcholinesterase (enzyme) sensors, for example, detect organophosphates by inhibiting acetylcholinesterase activity, with acetylcholinesterase activity continuously monitored.

Authors stated that, the commercial biosensors for tracking dioxins, nitrates, E. coli, and dioxin-like compounds have also been developed and successfully used. Airborne toxins and pathogens can also be detected using microbe-based biosensors. Phage sensors can detect pathogenic bacteria in the air. Table 5 demonstrate that types of biosensor were used in the environmental pollutant detection [8].

Table 5: Biosensor that used to detect various environment pollutions[8].

Pollutants	Biosensors	Detectability source	References
Heavy metals (Hg, Cd, Ni, Co, Zn, Cu, Pb, Au, Pb, Cu)	Bacterial-based sensors	Soil, sewage water	[95]
	Amperometric (Ureases enzyme-based) for Hg		[97]
	Optical sensor		[98]
PCBs	Piezoelectric immuno-sensor	Soil, water and various foods (fruits, vegetables)	[99]
BODs	Optical sensor	Contaminated, waste waters	[100]
Nitrogenous Compounds	Ezyme-based conductimetric sensor	Natural water sources	[101]
Organophosphates (Pesticides)	Enzymatic sensors (Acetylcholinesterase based)	Soils, water sources	[102]

V. ENGINEERING PERSPECTIVE ABOUT BIOSENSOR

A biosensor is a system or sensor that mixes a biological element, such as an enzyme or antibody, with an electronic part to generate a detectable signal. The electronic device determines, monitors, and send data about physical effects or the existence of various biochemical materials in the environment. Biosensors come in a range of sizes and shapes, and they can identify and measure pathogens, toxic chemicals, and pH levels even at low concentrations. An analyte, bioreceptor, transducer, circuitry, and display are typical components of a biosensor.[3]

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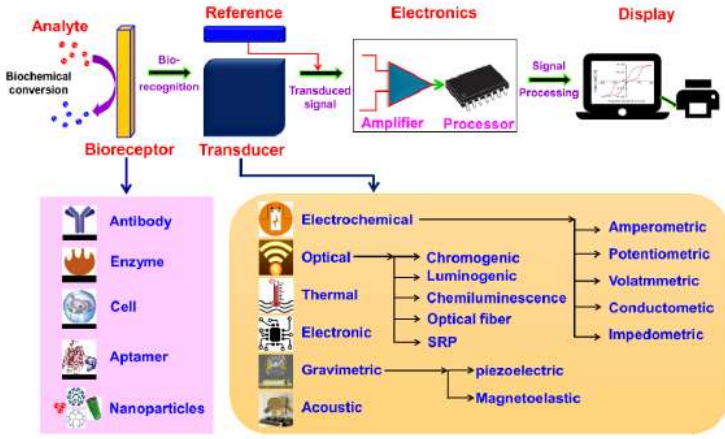

Figure 1: Schematic diagram of typical biosensor [3]

Figure 5.1 above proves that, how a biosensor work in an engineering perspective. In the bioreceptor also shows what type of bioreceptor is detect from the analyte. Also, the different types of transducer that can be used as a biosensor transducer.

Analyte [3]:
A substance of interest whose constituents, such as glucose, ammonia, alcohol, and lactose, are being identified or detected.

Bioreceptor [3]:
A bioreceptor is a molecule or biological element that can recognise the target substrate. Biorecognition refers to the process of signal formation that occurs during the interaction of a bioreceptor and an analyte.

Transducer [3]:
A device that converts energy from one form to another. The transducer in a biosensor is an important part. It converts the biorecognition event into an observable electrical signal that represents the amount or presence of a chemical or biological target. This process of energy transfer is known as signalization. Transducers produce optical or electrical outputs determines the number of analyte–bioreceptor connections. Based on their operating principles, transducers are classified as electrochemical, optical, thermal, electrical, or gravimetric.

Electronics [3]:
The signal that has been transduced is processed and prepared for view. The transducer's electrical signals are amplified and translated to digital form. The display unit quantifies the interpreted signals.

Display [3]:
The display unit consists of a user visualization device, such as a computer or a printer, that produces feedback so that the user can read and understand the prone to the effects. Depending on the end-user requirement, the output could be a numerical, graphical, or tabular value, or a number.

Detection of Small Molecules
Glucose [9]
In clinical applications, biosensor-based monitoring of blood glucose concentration has now become a significant diagnostic method for accurately tracing diabetes with elevated levels of glycated haemoglobin (HbA1c). Continuous glucose regulation in culture media, on the other hand, is used in tissue engineering applications to indicate cell metabolic activities. A variety of biosensors systems have been suggested for glucose regulation. This includes electrochemical biosensors, which are widely used to detect glucose oxidase or glucose dehydrogenase in interstitial fluids from blood. Despite some promising technical advances in recent years, there is currently no non-invasive method in clinical use.

A prominent glucose absorption band exists in the mid-infrared (MIR) region, providing an isolated band in human blood. The MIR method, on the other hand, is limited by high water absorption and background fluctuation, both of which frequently skew the results. The effects of photoacoustic and thermal radiation methods on water accumulation are also complex. The non-invasive and non-contact wavelength modulated

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differential laser photothermal radiometry (WM-DPTR) technique was recently developed for continuous or intermittent glucose monitoring in the MIR range. In vitro serum-glucose levels in human skin can be determined using this process.

Hydrogen Peroxide (H2O2) [9].

H2O2 (Hydrogen Peroxide) at high concentrations is cytotoxic to human cells as well as a variety of mammal, plant, and bacterial cells. A high concentration of H2O2 is highly harmful to biological systems. H2O2 detection methods based on fluorescence and electrochemistry have been widely used in tissue engineering applications. However, these approaches, such as the electrode-based approach, have disadvantages such as poor H2O2 specificity, low sensitivity, difficulty in applying to biological conditions, and invasiveness of measurement.

Because of their high expediency, selectivity, and sensitivity, amperometric enzyme-based biosensors have received a lot of attention. The efficient binding of enzyme to the solid electrode surface leads to the development of responsive and stable sensors. Because of this, the methods based on nanomaterials have received the most attention. Biosensors based on silver (Ag) nanoparticles (AgNPs), for example, can be used as an inevitable part of the electrode. Using direct electrochemistry of haemoglobin (Hb) in Hb-Ag sol on a glassy carbon (GC) electrode, Xu and colleagues developed an H2O2 biosensor.

Ex-vivo and in-vivo tissue engineering both benefit with the use of nanoprobes/sensors for H2O2 identification. In general, nanoprobes have a size range of 10–500 nm, which is much smaller than the size of biological cells, resulting in less physical damage to cells or tissues when performing measurements. Furthermore, by conjugating target-specific ligand moieties onto the nanoparticle decorated electrode surface, nanoprobes can be rendered tissue or cell specific.

Adenosines [9].

Essential multifunctional molecules found in the blood, heart, and liver are Adenosine diphosphate (ADP) and adenosine triphosphate (ATP). Luciferase-based methods have long been used to quantify adenosines; however, there in vivo use is limited due to their low sensitivity and resolution. As a result, alternative and more convenient ATP calculation methods are needed. Biosensors can be used to test extracellular ATP in situ as well as for sensitive in vivo applications.

In vivo extracellular ATP concentrations can exceed the hundred micromolar range due to hypoxia, trauma, ischemia, cancer, or inflammation. The normal bioluminescence luciferin/luciferase assay is used to measure extracellular ATP in cell supernatant. This method, however, does not allow for the measurement of extracellular ATP concentration in real time. Llaudet and associates developed a microelectrode recording system for in vivo ATP measurements; though, their method requires inserting the electrode into the tissue, which may interfere with the ATP analysis.

Schneider and co - workers developed a scanning tip treated with an ATPase-containing S1 myosin fragment in order to identify ATP release sources and quantify ATP concentration. This form, on the other hand, is much too complicated for clinical use. Hayashi and colleagues developed a biosensor that can be placed in close proximity to ATP-releasing target cells. This approach produces a consistent result for extracellular ATP concentration. Xie and fellow researchers proposes a new localised surface Plasmon resonance (LSPR) array chip for efficient, label-free, high throughput ATP sensing using a standard microplate. According to the paper, the developed LSPR sensor chip can be used for miniaturised and high throughput detection of biological samples in tissue engineering applications.

Detection of Functional Protein Molecules [9].

Lab-on-chip and visual biosensors have been used to identify epidermal growth factor receptor (EGFR) biomarkers for initial cancer diagnosis. Fluorescence-based biosensors are useful tools in engineered tumour models for detecting biomarkers early in clinical diagnostics, monitoring disease progression, and responding to treatment or therapeutics. Protein kinases are essential proteins in cell signalling pathways and disease progression, and they can function as real-time biomarkers in response to various therapeutics, which can be detected using biosensors.

Detection of Other Analytes [9].

Members of the Enterobacteriaceae family can be detected using piezoelectric immunosensors. Neisseria meningitidis and Brucella melitensis can be detected by a light addressable potentiometric sensor. Endotoxins are complex lipopolysaccharides (LPS) found in the outer cell wall of all Gram-negative bacteria that cause fever, multiorgan failure, septic shock, sepsis, meningococcemia, and severe morbidities like neurologic deficiency and hearing loss. Endotoxin detection is critical for quality control in biological

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products, recombinant therapeutic products, medical devices, serological products, food safety, and water security.

The biosensor detected E. coli endotoxin using the fluorescence method, with a lower limit of detection of 10 ng/mL and a detection time of 30 seconds. An amperometric biosensor detected endotoxin from Salmonella minnesota at 0.1 ng/mL and a piezoelectric biosensor detected it at 0.1 pg/mL. Virus identification and quantification are critical for a wide range of applications ranging from sanitation and food production to diagnostics and therapeutics. An optical biosensor was used to detect dengue virus, an SPR EIS biosensor was used to detect HIV, and an optical and quartz crystal microbalance (QCM) biosensor was used to detect Hepatitis C virus-induced liver inflammation.

VI. DESIGN CONSIDERATION OF THE BIOSENSOR DEVICES

Modelling and Fundamental Design Considerations for Portable, Wearable and Implantable Electronic Biosensors [7]. Chronic disorders, such as cancer, diabetes, acquired immune deficiency syndrome (AIDS), and others, are leading causes of death worldwide. Every year, nearly 36 million people die because of chronic diseases, with developed countries accounting for 80 percent of all deaths. Portable, wearable, and implantable biosensors can help avoid these preventable deaths by allowing for regular or continuous self-monitoring of vital health parameters.

The integration of various laboratory operations (conducted to perform biomedical testing) such as mixing, sorting, transport, and sensing onto a chip will enable the creation of portable hand-held diagnostic devices. Furthermore, whether these devices are versatile and/or bio-compatible, they may be worn as part of clothing or inserted into the body to provide continuous health monitoring.

Aside from portable lab-on-chip sensors for rapid testing, another recent trend in biosensor production over the last decade has been the development of wearable and implantable sensors to allow continuous monitoring of vital health parameters. This may allow for round-the-clock (24-hour) monitoring of the patient's health, allowing the patient to live a normal life. Wearable sensors require non-invasive tracking of health parameters by embedding the sensor into clothing fabric or wearing an independent wearable such as a smart watch. This entails tracking the body's electrical signals or assessing the concentration of a biomolecule (for example, glucose) in body fluid.

The physics and interpret experiments were designed to: 1) manipulate small droplets for lab-on-chip portable sensors, 2) enhance the sensing efficiency of transition-metal dichalcogenides-based flexible wearable sensors, 3) evaluate the performance trade-off in hydrogel-based implantable biochemical sensors, and 4) create compact models for device level integration of biosensors [7].

VII. CONCLUSION

As a conclusion, biosensor is a big scope of biology and sensor that have been developed by people even from 1906. Biosensors have a wide range of applications in engineering and technology, medicine and biomedicine, toxicology and ecotoxicology, food safety control, drug distribution, and disease progression. With the evolved technology nowadays the usage and development of biosensor will be more advance and realistic to be use in the future. Biosensors are used in the different applications such as to increase surface plasmon resonance in the sensing devices [10], likewise in the process of increasing the seeding time [11] and also in migratory phenotype [12].

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