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Upgradation of Biosensor: An Emerging Paradigm for Advanced Biomedical Application

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ABSTRACT

Recent developments in the creation of inexpensive, extremely effective, very sensitive, and particular biosensors have created new opportunities for the detection of samples, such as medications, tainted bioagents, metabolites, air pollutants, microbial load, etc., by converting biochemical signals into quantifiable physiochemical signals that allow the sample amount to be determined. In recent years, integrated biosensors, implanted biosensors, and nano-biosensors have become increasingly important in current research and development methodologies. Numerous biosensor types, including enzyme-based, tissue-based, immunosensors, DNA biosensors, thermal, and piezoelectric biosensors, have been examined here to demonstrate their numerous applications.To obtain new applications in a variety of disciplines, basic research is still needed to improve analytical tools and processes as well as sensing methodologies. The function of biosensors in medical science, including early rapid detection of the human papillomavirus and early identification of a variety of diseases, such as heart ailments caused by human interleukin-10, are important factors. Fluorescent biosensors are crucial for both cancer research and medication development. In order to test for viral and genetic disorders quickly, easily, and affordably, DNA biosensors based on nucleic acid recognition techniques are being developed. Furthermore, the identification of a particular DNA sequence is significant in a number of fields, such as food, environmental, and clinical study.

In the field of plant biology, biosensor applications are widely used to identify the missing pieces needed for metabolic processes. The fundamentals of biosensing devices are covered in this article, which might act as an introduction for individuals who are unfamiliar with this field.

Biosensors are particularly useful in the food, pharmaceutical, defence, and environmental and agricultural sectors, as well as in the early identification of diseases. For instance, biosensors are employed in electrochemical impedance spectroscopy for the treatment of cancer, in the identification of pesticides, one type of environmental contaminant, in the detection of dangerous chemicals and chemical warfare weapons, and in the potentiometric measurement of glutamate. Furthermore, it is anticipated that biosensors will find broader applications in the future, particularly in the early detection of illnesses. Scientists are now paying more attention to biosensors since their use has grown globally.

Keywords: Biosensor, Biomarkers, Transducer , Cancer , Covid-19 , Characterization of Biosensor , Diagnosis

1. Introduction

One of the recently defined groups of sensors are biosensors, which combine chemical and physical sensing techniques. The term "biosensors" was defined by IUPAC; in his opinion, biosensors are chemical sensing analytical instrument that transforms a reaction into electrical impulses which, apart from, are extremely precise physical characteristic such as temperature and pH. It was Cammann who coined the term "biosensor." Particularly, the biosensors are based on receptor-transducer technology, which can be used to clarify the medium's biochemical and biophysical characteristics. 1

The word "biosensor" describes a potent and cutting-edge analytical tool with a biological sensing element that has a variety of uses in biomedicine, drug development, diagnostics, food safety and processing, environmental monitoring, defence, and security.

In 1962, Leland C. Clark created an enzyme electrode, which marked the official origin of biosensor technology.2

Using the technique of electrochemical detection of oxygen or hydrogen peroxide, Clark and Lyons (1962) developed the first biosensor to assess glucose in biological samples with an electrode for immobilised glucose oxidase. Amazing progress has been made since then in biosensor technology and applications using cutting-edge methods ranging from electrochemistry and nanotechnology to bioelectronics.

Due to its high accuracy in measuring disease-specific blood glucose, the blood glucose monitoring biosensor device has become quite popular in the market both in vitro and in vivo biomarkers.3

The term "sensor" is derived from the Latin word "sentire," meaning "to identify," and thus Cammann was the first to use the word.The biosensor works on a receptor-transducer basis, which can decipher the molecular or biophysical characteristics of the medium. Its most alluring qualities are sensitivity and selectivity. characteristics that allow it to identify specific biological the medium's molecules.1

Utilising devices to process materials with dimensions less than 10 nanometres is a significant application of nanotechnology. The Greek word "dwarf" is the source of the suffix "nano," which joins the word "technology" to form nanotechnology. The term about 50 years ago, in 1974, Japanese researcher Norio Taguchi used nanotechnology for the first time. Long time ago Nanotechnology has advanced quickly since the 2000s in the areas of biosensors and at this moment, biosensors are being used widely.4

These days, sensors have properties that can be applied to a wide range of devices and are utilised in all fields of technology. For instance, sensors are used in a variety of big and small gadgets, including television remote controls, computers, and refrigerators. The importance of size and shape for the analyte to recognize the substrate is shown in Figure 1. 5

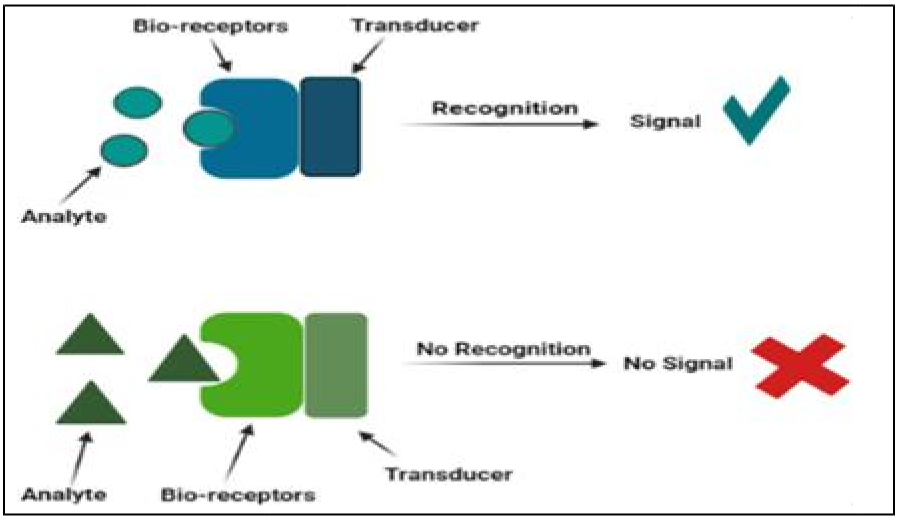

Figure 1. Importance of size and shape for the analyte to recognize the substrate

2. Types of Biosensor

The pioneers named Clarke and Lyons began Biosensor in late 1960s. Different kinds of biosensors being utilized based on two elements namely known as sensing element and transduction modes. Enzymes based biosensor, immunosensor which includes antibodies biosensor, DNA biosensor, Thermal and piezoelectric biosensor, biological tissues, organelles and microorganisms which can be detected with the help of whole cell biosensor comes under the category of sensing element.6

Transduction mode relies upon the physiochemical change coming about because of detecting component. Subsequently on the premise of various transducers biosensors can be electrochemical (amperometric, conductometric and potentiometric), optical (absorbance, fluorescence and chemiluminense), piezoelectric (acoustic and ultrasonic) what's more, calorimetric. 7

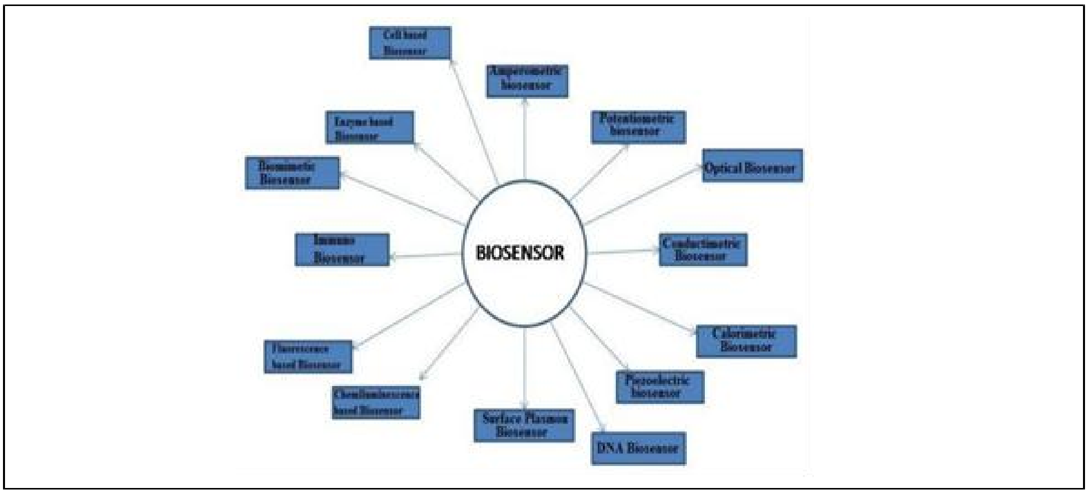

Figure 2. Types of biosensors applied invarious fields of engineering

1. Amperometric biosensor

High affectability biosensors can readily identify electroactive organisms found in natural test samples. The reduction or oxidation of electroactive species is calculated and associated with the analyte centralisation, such as glucose biosensors to detect diabetes, which generates current because of the potential two electrodes' differences.

These limit of anodes Finally, Tom's examining the plausible preparation of a contemporary perhaps connected to two cathodes, the extent to which contemporary consistently matching the substrate centralisation. The oxygen cathode of Clarke for the test's (analyte's) oxygen content.8 These use the result during reduction. Biosensors to make things easier.

The primary issue with these biosensors is that they rely on the segregated O2 fixation in the outcome of the analyte. This could be beaten. Finally, Tom is using go to examine these particles exchange electrons with one another. Stated in response to the obvious response to the cathode rather than lowering those O2 declined in the analyte result.9 Those in any event, modern anodes eliminate especially those electrons starting with the reduced proteins without the assistance of arbiters, in addition to needing assistance protected with electrically coordinated typical salts. Thus, the natural test specimen's catalysts are supposed to catalyse even if they may not be electrodynamicthe production of species that are radiodynamic. For in this case, the purposeful parameter is in the present.7

2. Potentiometric biosensor

This approach converts the biorecognition process into a potential source of scientific data. Flag that causes oxidation or decline the capacity for biological reactions. A permanent the conductive layer for selected particles is usually employed to determine the possible flag, this occurs when the atom of the analyte works in tandem with the surface, such as that of H+ particles, to discover penicillin. Using triacyl and penicillinase as chemicals glycerol via means of lipase.10 An elevated impedance.By using a voltmeter, the electrical possible certification or electromotive between two cathodes, or power (EMF). Among the terminals accumulate a modification in shift or fixation in the configuration and we refer to this cathode as the pointer anode or occasionally referred to as an ion selective electrode (ISE). 11

In actuality, billions of estimations are performed annually in practically every clinic worldwide all throughout the planet. This is shocking. Taking into account that these devices are exceptional for providing prompt, quick, maintain cost-free and free estimates.12

3. Optical biosensor

This kind of biosensor may be founded on the electrochemiluminescence or optical diffraction principles, where a protein covers the silicon wafer by via covalent bonds, which are subsequently exposed to ultraviolet radiation via a picture veil, while the antibodies remain dormant in the places that are not covered. When the nalyte is used to manufacture sliced wafer chips. The formation of antigen-counteracting agent connections consequently, in the dynamic localities creating a grinding diffraction. A light source and extra optical segments are used in optical biosensors to create a light bar with specific attributes and to expedite this light to an operator for balancing, an adjusted a photo detector in addition to a detecting head.13 Both reactants in more frequent slant reactions are measured by these biosensors. On the contrary, they assess an advance for fluorescence on absorbance that accelerates towards the results produced in relation to the reactant responses.14 However, they also measure certain motions that triggered the innate optical characteristics of the surface of the biosensor in view of the dielectric stacking on it protein particles, for instance (in situation from claiming a typical slant answers). A lot of assurance, biosensor coordination, particularly the use of brightness luciferase firefly impetus for identification secure evidence of minuscule life forms nearby sustenance, followed by clinical testing.The tiny life forms need assistance, particularly when they are lysed, as this causes them to release ATP, which is utilised to support the local luciferase. approximately 02 to plan light, which is the approximate tom is finally examining the biosensor.15

4. Conductometric biosensor

The electrical conductance/protection of the arrangement is the intentional parameter. Based on conductometrics biosensors support the link between conductivity and an instance of biorecognition. The majority of answers incorporate a modification in the focus on ionic species, which may lead to an modification to the electrical setup stream of current or conductivity. 16 A conductometric biosensor is essentially made up of two metal terminals, usually made of silver or platinum, that are separated by a certain separation. An AC is usually used for exchanging voltage (current) is linked across the terminals, resulting in a current stream being kept up between them. In the middle of a the ionic creation is triggered by biorecognition modifications as well as an Ohmmeter (multimeter) is employed to measure the change in conductivity between the cathodes of metal.10 Several recent studies have shown that this process is ready to perform fast differentiation (less than 10 minutes) various diseases carried by nourishment (i.e., Salmonella and Escherichia coli O157:H7.17 In the sandwich immunoassay plot, Alocilja and associates used a conductive polyaniline mark, which basically improved the affectability by creating a conducting scaffolding between the two subatomic cathodes. Unfortunately, this strategy's affectability is generally below par, which is one of its major problems compared to alternative electrochemical methods.18

5. Calorimetric biosensor

Many catalyst-catalyzed reactions are exothermic, producing heat, which is used to estimate the rate of reaction and, as a result, the emphasis of the analysis. The temperature variations are rectified by thermistors, such as biosensors for cholesterol

using oxidase of cholesterol (warm yield 53 KJmol-1). The strategy for the analyte is encountered a small, crowded bed area comprising a material that has been immobilised; the course of action's temperature is set right prior to the game plan's section into the fragment as well as as it exits the section utilising independent thermistors.19 These will be the ones who truly matter in every manner, with every consideration given to the appropriate sort of biosensor that uses a minimum of two proteins of the biosensor's passage on connect two or three answers that will expand those lights give in. contrast, multipurpose proteins might have an opportunity to be used. An the use of glucose oxidase is one example for glucose confirmation.7

6. Piezoelectric biosensor

Simply put, piezoelectricity is the direct collaboration of mechanical and electrical frameworks in non-driven gem or comparable structure that the Curie siblings discovered for the first time in 1880. 20

In essence, a piezoelectric biosensor operates by taking into account the crucial fact that a swaying the reverberating repetition of a gem is distinctive.21

A biosensor's transducer and biorecognition component are crucial parts. As a result, the transducer in a piezoelectric biosensor is composed of a piezoelectric material (such as quartz) and biosensing material that is fixed to the piezoelectric material, which vibrates at a fundamental frequency.22 The external electrical flag, which provides a precise current calculation, controls the repetition when the target analyte is presented to the substance being detected, the connection or response will result in a recurrence motion, which will alter current readings that can be analysed to determine the mass of the interesting analyte. Surface acoustic waves (SAW) and bulk waves (BW) are the two primary types of piezoelectric sensors. Writing suggests that piezoelectric sensors are not given much thought and are viewed as inferior in any event.23 In contrast to biosensing that is based on electrochemistry and optics. 24

7. DNA biosensor

Biodetectors are another name for the class of biosensors used in DNA detection. The goal is to identify and quantify the characteristics of single DNA–DNA or immune response antigen bonds, which consequently have any impact on identifying and representing single DNA or antigen particles. Since the middle of 1953, the usage of nucleic acid advancement for specialised diagnostic applications has been steadily increasing.25

The remarkably precise tendency that restricts the response between two single-strand DNA (ssDNA) chains to form double-stranded DNA (dsDNA) is used in biosensors based on nucleic acids, which identify the nucleic acids as a common affirmation segment.26 This method has improved the DNA-based sensor over traditional methods, such as coupling radioisotropic and electrophoretic detachments, which are expensive, risky, time-consuming, and so on.27

The primary mechanism by which this biosensor functions is the recognition of the matching strand by ssDNA to create dsDNA by forming a stable hydrogen bond between two nucleic acids. An immobilised bioreceptor whose base grouping is related to the goal of interest is used as a test in order to achieve this. Focussing on the test that causes the hybridisation of related ssDNA to become dsDNA will result in a biological reaction that enables the transducer to open the flag into an electrical one. In this way, writing illustrates how the push to immobilise the ssDNA onto the detecting surface requires the presence of some linker, such as thiol or biotin. 28

8. Surface Plasmon biosensor

Electromagnetic surface plasmon waves are used by surface plasmon reverberation (SPR) biosensors to identify shifts when the sensor's biorecognition section and the target analyte work together. Fundamentally, the refractive record that is used to detect or view the reaction will change when the SPR biosensor is exposed to any motions. The SPR transducer is joining forces with the biomolecule/biorecognition section that detects and gets ready to interact with a particular analyte.29

This movement conveys a variety in the surface plasmon wave's constant spread and

this collection is meant to facilitate examination. The maintenance scope of the test is examined using a spectrophotometer.30 Various biorecognition components, such as proteins, counteracting agents, antigens, nucleic acids, and compounds, have been fused with SPR biosensors. 29

9. Chemiluminescence based biosensor

Chemiluminescence is a method of delivering liveliness from a chemical response that produces an emission of light, or luminescence in general. 31

In essence, an atom or particle undergoes a reaction as it unwinds from its energised state to its ground state, after which the response produces a light as a byproduct. Therefore, chemiluminescence can be used to see specific biological reactions that take place.32 Additionally, this characteristic has aided in the advancement of chemiluminescence-based biosensors.9 The reaction between the analyte and the immobilised biomolecule that has been separated with chemiluminescence species in the chemiluminescence biosensor will result in the delayed biological response of light transmission. One tool for identifying this transmitted light is a Photo Multiplier Tube (PMT).

According to an audit conducted by Zhang et al. in 2005 and Dodeigne et al. in 2000, chemiluminescence is a creating diagnostic equipment with a high degree of affectability, simple instrumentation, fast, distinct reaction characteristics, and broad adjustment range. Chemiluminescence-based transduction has been widely understood and linked to immunosensing and nucleic corrosive hybridisation, but not with standings. 33

10. Fluorescence based biosensor

As seen above, luminescence is the result of particles or atoms unwinding from an energized state to it's the ground state. To obtain the energized state, the various forms of iridescence contrast with the source of vitality. Electromagnetic radiation (photoluminescence, also known as fluorescence or brightness), heat (pyroluminescence), frictional forces (triboluminescence), electron impact (cathodoluminescence), or crystallization (crystalloluminescence) can all contribute to this vitality. 34,35

Thus, for fluorescence to start the electrical advancements in particles or atoms, which by then convey brilliance, an external light source (short-wavelength light) is necessary. (Light with a longer wavelength). Over time, fluorochrome particles—which are utilized to transmit light during the biorecognition event—have joined the fluorescence-based biosensor.36

Given that the majority of analytes lack trademarks and a significant portion of the common identifying section frightening characteristics, by attaching fluorescent optically responsive agents to the recognizing segments, the biorecognition event is transferred to the optical banner.29

11. Immuno biosensor

In the 1950s, a biosensor based on antibodies was unexpectedly linked to recognition, providing access to the probability of immune-conclusion. 29

Since then, a great deal of work has been done to develop immunosensor, a clinical diagnostic tool composed of an antigen or immunomodulation as a bioreceptor. 37

An antagonist is 'Y' formed immunoglobin (Ig), which is made up of two significant chains (H) and two light chains (L). Nevertheless, some human antibodies use disulphide bonds and an extra protein known as the joining or J chain to form dimeric or pentameric structures.29

Each chain has a variable and a stable component. The variable component relates specifically to the antigen that is linked to related antigen, which is extremely specific and unique. As a result, an immunosensor that uses antigen as a bioreceptor makes advantage of immunological reaction to the comparison antigen, which is incredibly specific, stable, and flexible. One component of an immune response's amino acid composition is its selectivity towards the coupling side of its antigen. 38

12. Biomimetic biosensor

A biomimetic biosensor is a manufactured or counterfeit sensor that mimics the functionality of a typical biosensor. Aptasensors, which use aptamers as the biocomponent, can be incorporated into these. Aptamers were described as phoney nucleic corrosive ligands in the early 1990s, when they were first discovered. Therefore, aptamers were artificially detected by nucleic corrosive tests; yet, they continued to function more like immunisers and showed remarkable adaptability in comparison to other bio-acknowledgment segments. Aptamers are synthetic nucleic nucleotide strands that can be designed to detect oligosaccharides, amino acids, proteins and peptides.39 Compared to an immune response-based biosensor, an aptamer offers a few advantages, such as high restriction proficiency, avoiding using animals (i.e., a lower moral dilemma), being smaller and less confusing, and so on. However, the typical test that aptasensors face is that they have inherent nucleic acid characteristics, such as auxiliary pleomorphism and synthetic ease of use, which lowers test proficiency and increases fabrication costs. In order to overcome this obstacle, some effort has been coordinated towards the representation and development of aptamer.29

13. Enzyme based biosensor

Among the different types of biosensors, protein-based biosensors are the most accurate; these biosensors were initially introduced an amperometric chemical cathode for a glucose sensor that uses a "dissolvable" protein cathode was developed by Clark and Lyons in 1962. Since the first biosensor, protein-based biosensors have seen tremendous growth in use for many applications till their introduction. Proteins are incredibly effective biocatalysts, with the ability to specifically sense and catalyse changes in their substrates. These unique characteristics enable the chemicals to be used as tools to build rational devices.

14. Cell based biosensor

The type of biosensor known as a cell-based sensor uses living cells as the biospecific detecting element and relies on the ability of living cells to identify physiological parameters, internal and extracellular microenvironment conditions, and generate a response through cell-jolt cooperation.40

Microorganisms, such as parasites or microscopic organisms, can be used as biosensors to identify specific atoms or the overall "state" of the encompassing circumstance. Additionally, proteins that are present in cells can similarly function as bioreceptors to recognise a particular analyte. 29

3. Structural Analysis of Biosensor Designing / Mechanism of Biosensor Devices

Potentiometric enzyme-based electrodes are used for the first time as a biosensor device to measure and monitor blood glucose. In the most recent developments, increased energy and time- consuming for the creation of portable, multifaceted, and tiny biosensors. Different kinds of biosensing elements were used to complete this duty, such as enzymes, microorganisms, tissue, cells, or organelles. The sensitivity of these elements is based on catalytic reactions, or they may be affinity-based elements like antibodies, receptors, and nucleic acids. 14

The coupling process that underpins biosensors can be either physical adsorption or encapsulation, where biological or organic materials connect to element that uses physical intermolecular forces as a sensor or matrix immobilisation, in which a porous material, such as gel matrix, serves as a biological element's limiting medium and establishes a direct connection with the biosensor element. A physical organic molecule is trapped in a specific semi-permeable membrane (which serves as a separating phase between the organic element and analyte) that is directly in contact with the sensor element . Another mechanism involves biological elements directly linking to the sensor by forming covalent amalgamates, also known as covalent coupling. 41

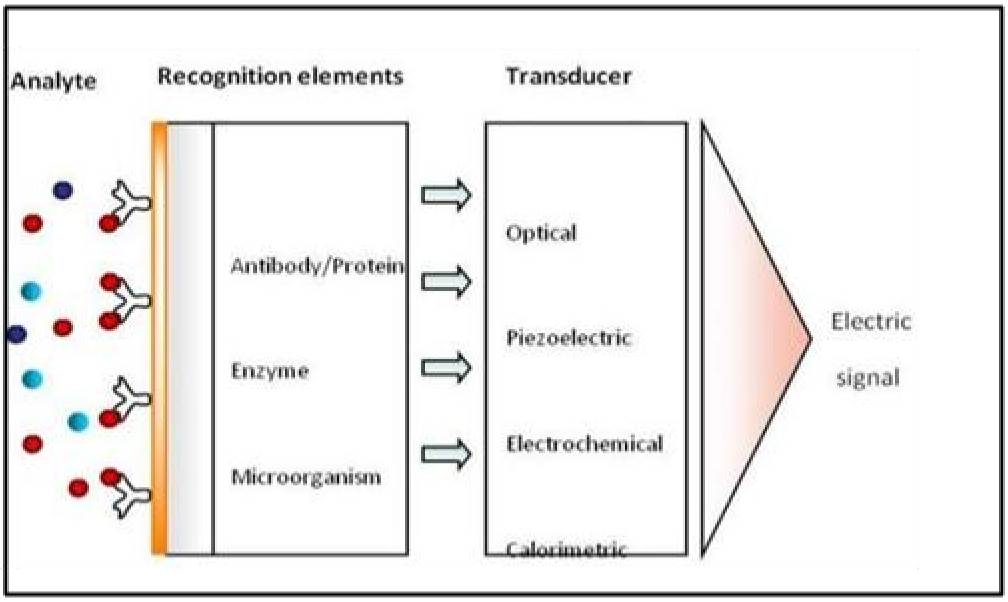

Figure 3. Schematic of a biosensor.

4. Biosensors used in Disease Diagnosis

4.1. Cancer

Cancer is defined as abnormal and uncontrolled cell growth due to an accumulation of specific genetic and epigenetic defects, both environmental and hereditary in origin.

Nearly 570,000 individuals are predicted to die from cancer in 2010, making it the second most common cause of death in the US (http://www.cancer.org/).

That's over 15,000 deaths every day. Men will be diagnosed in one out of two cases.

with cancer of some kind within the upcoming year, but women have a slightly higher chance of receiving a cancer diagnosis .

The most common type of cancer in men and women is prostate and breast cancer, respectively, with 192,000 new cases of each reported annually.42

Cancer Biomarkers

A biological molecule present in blood, other bodily fluids, or tissues that indicates a normal or aberrant condition is called a biomarker, according to the National Cancer Institute (NCI) procedure or of an illness or condition. A biomarker can be used to determine how successfully an illness or condition is treated by the body. DNA (specific mutation, translocation, amplification, and loss of heterozygosity), RNA, or proteins (hormone, antibody, oncogene, or tumour suppressor) are examples of molecular origins for biomarkers. One of the most useful techniques for early cancer identification, precise preoperative staging, assessing how well cancer responds to chemotherapy, and tracking the course of the disease may be cancer biomarkers. 43

1. **Prostate-specific antigen**

One of the earliest tumour biomarkers discovered and routinely used in clinical settings for prostate cancer screening and diagnosis was prostate-specific antigen (PSA). Research has indicated a significant correlation between elevated PSA levels and prostate cancer. PSA levels of

4.0 ng/mL are considered normal. About 30% of males with a PSA score between 4.1 and 9.9 ng/mL had prostate cancer, according to a research done by Smith. 43

suggest smaller tumours that do not turn out to be lethal, benign prostatic hyperplasia, or prostatitis (prostate inflammation). Therefore, there has been much debate regarding the fact that PSA levels are not invariably a sign of malignant tumours.

regarding the importance of regular PSA testing for prostate cancer . 44

2. **CA 15-3**

One significant biomarker that is examined in patients with breast cancer is CA 15-3. Additional biomarkers associated with breast cancer include BRCA1, BRCA2, carcinoembryonic antigen (CEA), and Clinically, CA 27.29.17,27 CA 15-3 is most frequently used to track patient treatment in situations of advanced breast cancer.

It has been demonstrated that in individuals with breast cancer, CA 15-3 concentrations rise by 10% in Stage I, 20% in Stage II, 40% in Stage III, and 75% in Stage IV. 45

3. Cancer Antigen 125

The most frequent cause of elevated cancer antigen (CA) 125 is ovarian cancer, however it is also connected to malignancies of the uterus, cervix, pancreas, liver, colon, breast, and lung and the digestive system. Pregnancy and menstruation are two nonpathological events that can also lead to increased CA 125.22 levels 90% of women with advanced ovarian cancer and 40% of those with intra-abdominal cancer had high CA 125. It should be mentioned, though, that 50% of individuals with Stage 1 ovarian cancer will have normal CA 125 results. 46

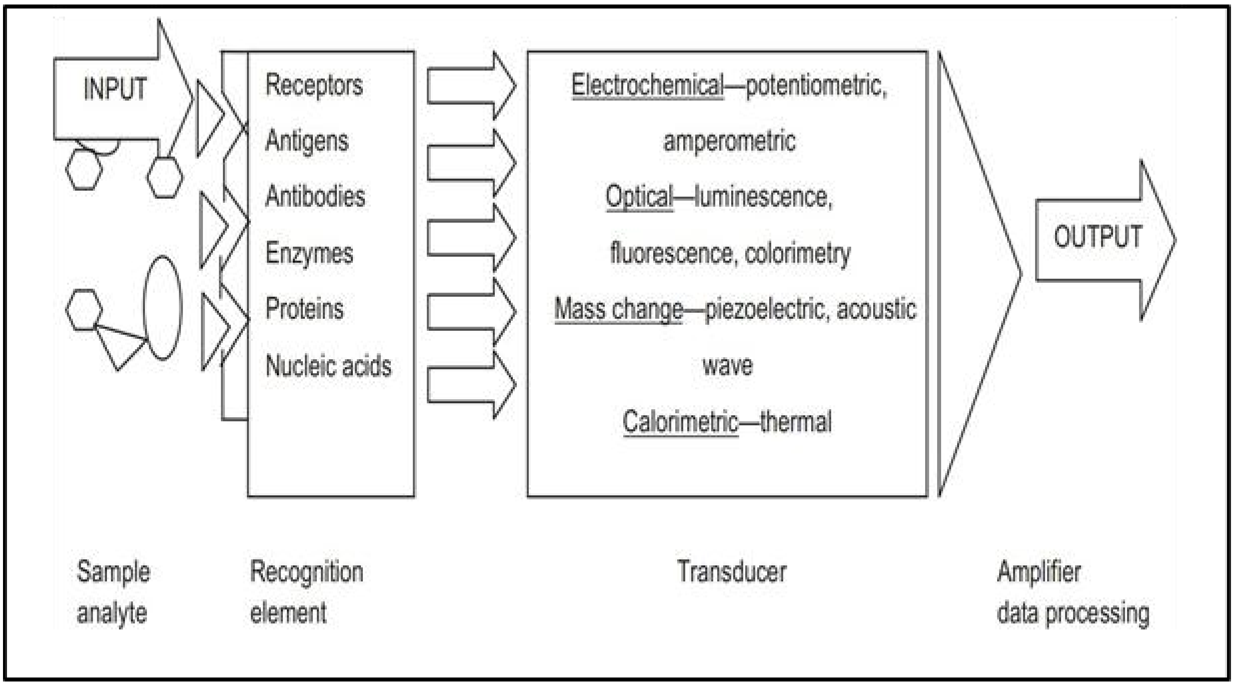

Figure 4. Illustration depicting the process by which biosensors function.

4..2 COVID-19

One of the deadliest and most contagious infections today is COVID-19, a b-coronavirus that is brought on by SARS-CoV-2.1–3. Those that are infected may or may not have symptoms, but they can spread to those who aren't afflicted.4. Large-scale SWI diagnostic testing is therefore essential for virus surveillance and detection. Currently, the medical experts involved in the diagnosis employ various diagnostic instruments for COVID-19 detection, including RT-PCR, enzyme-linked immunosorbent assay (ELISA), serological immunoassay, chest X-ray radiography, and computed tomography (CT) imaging.5. These traditional diagnostic methods necessitate highly skilled operators and advanced lab equipment.

Apart from intricate lab configurations, the discrepancies between diagnosis, sampling, and the reduction in viral load because of the development of quick and accurate diagnostic techniques for the extensive screening procedure of COVID-19 detection has been spurred by the natural immune system's responsiveness.

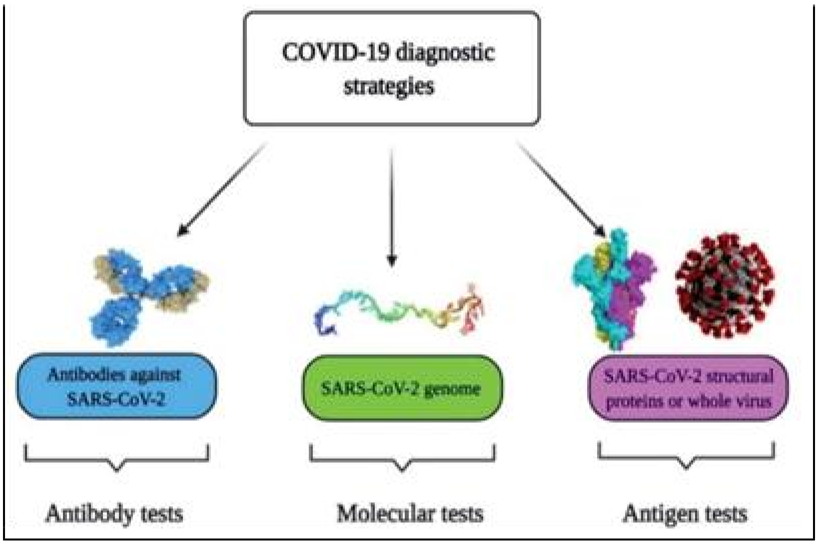

Figure 5. Commonly used methods for the spotting of SARS-CoV-2 and COVID-19 prognosis

Nano-biosensors as point-of-care diagnostic tools

Diagnostic tools for point-of-care spotting of SARS-CoV-2 and COVID-19 prognosis have found applications in many developing and underdeveloped countries. In association with pointof-care identifications, immunoassay methods have received more recognition than molecular diagnostic- based tools due to their better control and the generation of fewer false-positive cases.

Electrochemical nano-biosensors

Transistor-based instruments have recently been regarded as efficient platforms for the quick and affordable detection of a variety of species. Because of their capacity to conjugate with other substances, organic transistors have shown promise in this arena biological systems and identify COVID-19 (SARS-CoV-2).21–29 Seo's team created a graphene-oriented nanobiosensor to detect SARS-CoV-2 and for COVID-19 prognosis in order to increase the detection limit and address the aforementioned issue (shown in Fig. 3) for the SARS-CoV-2 viral identification platform.

Optical nano biosensor

Fluorescence, luminescence, surface plasmon, plasmon-enhanced fluorescence, surface-enhancing Raman scattering, colorimetry, reflectance, and absorbance are the alterations linked to the interactions between the bioreceptor and analyte in optical nano-biosensors. These are equivalent to the kinds of nanomaterials and the analyte concentration.41–44 Peng and associates have created a colloidal AuNPs-based chemiluminescence immunoassay that allows for the rapid and accurate identification of SARS-CoV-2 immunoglobulin-M (IgM) and immunoglobulin-G (IgG).

Magnetic biosensor

The advantage of chemical or optical nano-biosensors is that, because the biological environment is non-magnetic, they generate less background noise. A unique magnetic nanoparticle-based immunosensor has been demonstrated by Li and Lillehoj.51. The fact that using immunomagnetic signal amplification, the novel immunosensor can detect the viral protein with sensitivity and reproducibility .

Aptameric nano-biosensors

Aptamers can be added to nano-biosensors to improve their sensitivity and selectivity. Aptamers are small, single-stranded oligonucleotides that range in length from 25 to 90 bases. Aptamer spatial configurations in three dimensions are crucial for identifying viral components because of their great capacity for mixing.

For the detection of COVID-19, nano-biosensors coupled with aptamers offer a significant benefit. Aptameric nanobiosensors have the ability to function against many targets and conduct real-time analysis.

Some of the DNA aptamers, such as MSA1 and MSA5 possess high binding affinity (few nM range) to the spike protein (S1) subunit of the SARS-CoV-2.

Plasmonic nano-biosensor

When electromagnetic light waves contact with the free electrons present on the surface of metal nanoparticles, plasmons are created. The prism is coated with 50 nm metal nanoparticles to create a plasmonic metallic film.The running buffer for plasmonic sensors that are sold commercially makes up the specimen.47

4..3 Viral Infectious Disease

Throughout this millennium, a number of infectious diseases have been caused by viruses, such as Zika, the extremely dangerous Asian avian influenza (H5N1), Ebola ,

Hepatitis B as well as Hepatitis C, coronaviruses as well.

Biosensors for the Detection of Viral Infections

1. Biosensors for Direct Pathogen Detection

Direct pathogen measurement is performed exclusively through antibody–antigen interaction by targeting the virus-specific proteins (nucleocapsid, surface, or transmembrane proteins) of a target pathogen.

a) Aptasensors

Aptamers are oligonucleotides of single-stranded DNA or RNA that range in length from 20 to 100 nucleotides. They can be used to create synthetic bioreceptors. The aptamer sequence's elevated. A high-flux screening technique called "Systematic Evolution of Ligands by Exponential

Enrichment (SELEX)" selects molecules with affinity and specificity to the target of interest from a sequence pool comprising many nucleotide variations. Because of their interaction with the analytes, aptamers are commonly compared to antibodies; as a result, they are referred to as "chemical or artificial antibodies."

2. Indirect Methods for the Detection of Viral Genetic Material

b) Biosensors Combined with Isothermal Amplification

In order to achieve many temperature cycles during the nucleic acid amplification stage, typical PCR systems rely on temperature control devices. The use of isothermal amplification techniques later resolved this issue.

This made it possible for viral genes to replicate easily and affordably using a heating block or water bath at a steady temperature.

c) Nucleic-Acid Probe-Based Biosensing

Through hybridisation, peptide nucleic acids (PNAs), RNAs, or single-stranded DNAs (ssDNAs) function as molecular recognition elements. RNA is initially taken out of the virus in the case of viral infections. In order to identify viruses, this isolate is subjected to biosensors that have oligonucleotide probes immobilised on their surface. These probes are brief nucleic acid sequences that, depending on NA complementarity, can hybridise to target analyte single-stranded DNA or RNA and be labelled with synthetic target molecules in a variety of ways, including fluorescently and radioactively. Both sandwich and competitive assays could be implemented here, much like immunoassays.

d) CRISPR-Cas-Powered biosensor

In the past, a wide range of cell types and difficult-to-transform species have benefited from the rapid, easy, and effective transformation of endogenous genes using CRISPR and its produced customisable RNA guided nucleases, including Cas9

to use traditional methods for genetic manipulation. Additionally, a number of uses, such as gene editing and genome imaging, have been suggested utilising their capacity to identify and cleave particular DNA and RNA sequences. Their promise in nucleic acid-based diagnostics has been the focus of a lot of recent efforts. 48

4..4 Tuberculosis

Tuberculosis (TB) is a lethal infectious disease caused by Mycobacterium tuberculosis, which afects the lungs and the respiratory organs of patients.

It is an illness that spreads via the air when infected people cough, spit, or sneeze. It is one of the most deadly illnesses. It killed almost 1.6 million people worldwide in 2017, more than those killed by the human virus/acquired immune deficiency `syndrome (HIV/AIDS) that year. An estimated 1.7 billion individuals worldwide, or around 25% of the world's population, are infected with the M. TB bacteria. 49

Multiplex detection of TB biomarkers

A method called multiplex assay detection enables the simultaneous measurement of several analytes. When compared to many single target approaches, it has attracted a lot of interest recently because it is quick, easy, requires smaller sample quantities, and uses less reagents.50 Using a microbead-based multiplex test, they examined several biomarkers; among them, five chemokines/cytokines were they were IFN-γ, interferon-gamma-inducible protein-10 (IP-10), interferon-gamma-induced monokine (MIG), IL-2, and tumour necrosis factor-alpha (TNF-α), and they were able to differentiate between active pulmonary TB patients and healthy controls. They found that multiplex detection of IP-10, IL-2, and IFN-γ performed significantly better as a diagnostic tool for tuberculosis than individual detection. Won et al. conducted another investigation. 51

5. Technical Approaches for Bio-transducer Elements

The biosensor's primary approach depends on whether it uses labelled or label-free detection. The type of label has a significant impact on the labelled detection. Chemical to identify the target; hence, for more accurate detection, these labelled biosensors needed particular sensing components made with the target protein immobilised. In the case of the label-free method, non- labeled target molecules are detected even which are difficult to tag. Such an approach opens the gateway for interdisciplinary workup of biotechnology with electrical, bio-engineering and electronic engineering to develop label-free biosensors along with a wide range of applications in the environmental and medical sciences. 51

6. Application Areas of Biosensors

The first biosensor is L.C. It was used by Clark in 1950 to measure the amount of glucose in the blood. Given the outcomes of recent years, research on biosensors is becoming more and more important today.3 Because biosensors operate in a variety of fields. Generally speaking, the amount of glucose is used to identify illnesses, viruses, medications, etc. It is still widely used in a variety of application areas.52 Alongside these, it also works in industries like industry, animal husbandry, waste management, pharmaceuticals, food, medical, quality control, and military applications.

Furthermore, the following are additional potential areas of use for biosensors. diagnostic of bacteria and viruses, control of processes, control of industrial wastewater, analysis of toxic gases

in mines and businesses, biomedicine, field farming, Garden-vineyard veterinary, agricultural, etc. Despite the fact that there are currently 25 commercially available biosensors, biosensors for many more chemicals have been developed. This figure is known to be greater than 180, despite the fact that it is unclear.53 Silver nanoparticles have been employed in biosensors for bacterial and viral detection based on these uses.54 Figure 6 shows the application areas of biosensors.

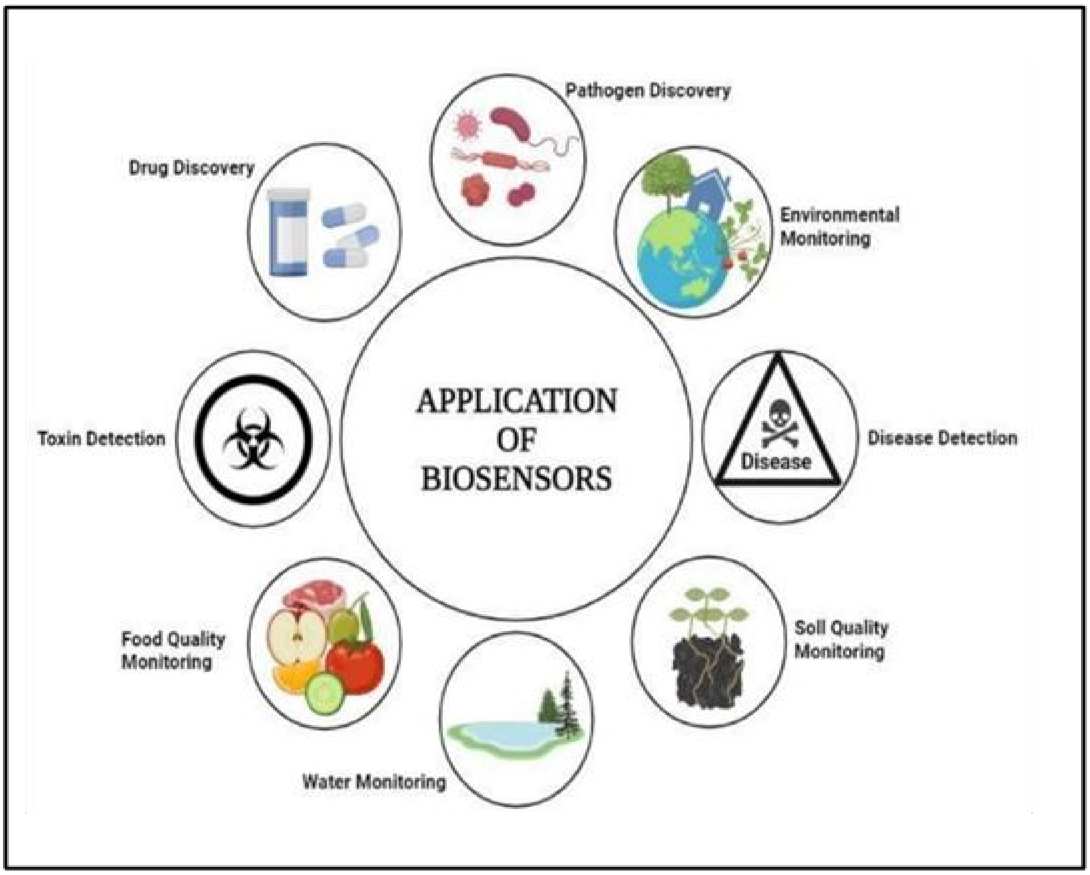

Figure 6. shows the application areas of biosensors.

7. Characterization of biosensor

Characterisation techniques are used to ascertain the features and behaviour of equipment. Characterisation investigations are initiated due to different stages once the biosensors immobilisation values and operating parameters are modified. Steps in the Characterisation Work: these includes linear measurement range, electrochemical impedance, repeatability, and reproducibility. Real sample trials and characterisation. 55

1. **Linear Measurement Range**

Biosensors are prepared under minimal conditions following the development of the biosensor and the modification of the components of the bioactive layer.56

Finding the values of the different concentrations of the material under study yields a conventional graph. The measuring range is defined as the range in which a linear rise is seen in the graphic interpretation. 57

2. **Repeatability**

New measurements are made using the biosensor developed in the concentration of several chemicals, such as tributyltin, within the ideal conditions indicated by the repeatability tests of the analysis results made using the biosensors created. Calculating the variation allows for the observation of repeatability. Standard deviations and coefficients of the values obtained.58

3. **Reproducibility**

To ascertain how distinct the outcomes attained throughout the biosensor preparation phases are from one another, reproducibility tests are conducted. A specific number of biosensors with the same composition are prepared under the same conditions in order to make standard graphs that show the outcome of this. Circumstance R2 and linear determination ranges these graphs values are interpreted. The suffix nano in the term nanotechnology. 59

4. **Electrochemical Impedance Characterization (EIS)**

EIS is used to carry out this characterisation approach. This structure can be used to identify variations in the quantity of systems' electrical resistance and surface sensitivity.

5. **Real Sample Trials**

The biosensor systems developed as a result of the research are used in actual cases. This application offers insight into whether the biosensor assembly can be manufactured and analysed again, as well as how its characteristics might be used in future research. 55

6. **Most Used Techniques in Characterization**

Transmission Electron Microscopes (TEMs) are used in characterisation to ascertain the characteristics of materials. Atomic force microscope (AFM), scanning tunnelling microscope (STM), X-ray photoelectron spectroscopy (XPS), X-ray diffraction (XRD), water contact angle, and environmental analysis with a scanning electron microscope (ESEM) is usually the preferable method. It is crucial to research the

materials' chemical and physical characteristics. In the course of the study, surface chemical analysis and surface hydrophobicity of the altered paper found in investigations like ESEM, surface morphology, Utilising the Washburn test, water contact opener, and XPS, the intracellular behaviour of channels. 31

8. Studies on the biosensor

Nowadays, biosensors; It has begun to be researched and applied in many fields such as medicine, animal husbandry, agriculture, quality control, and military applications. Because of this, researchers have resorted to biosensors, which are inexpensive, compact, quick, and sensitive data sources. 60 According to current research on these sensors, biosensors can be used to identify viruses. 40 Strong biosensing biosensors based on electrochemiluminescence essence were employed to identify viruses. 29 Moreover, genomic sensors, affinity sensors, and immunosensors are employed. In addition to viral testing, another study claims that biosensors can now be used to detect cancer.

X. Wei et al.'s research indicates that optical biosensors are employed in cancer detection. Here, optical biosensors are used because they make it easier to identify chemicals that cause cancer, such as tumour cells and deoxyribonucleic acid (DNA) proteins. Furthermore, an additional biosensor utilised as a the surface plasmon resonance biosensor is a cancer biomarker. Conversely, surface plasmon resonance biosensors are favoured due to their great selectivity, safety, and inclusion in research themes. 61 Biosensors offer a wide range of applications, as every review or article points out. Research and studies for the creation of biosensors are ongoing at the same time. It is currently anticipated that future decisions will be made more quickly and sensitively.

9. Future Advantages of Biosensor

Tools created to investigate the dynamic changes of biomolecules and bio-functions are collectively referred to as biosensors. It is now widely used in many different fields. Nonetheless, biosensors are instruments created in numerous domains that will be utilised for research in the future as well as now. The following benefits of biosensor technology will be used in a wide range of applications in the future.

These advantages are illustrated in Figure 7

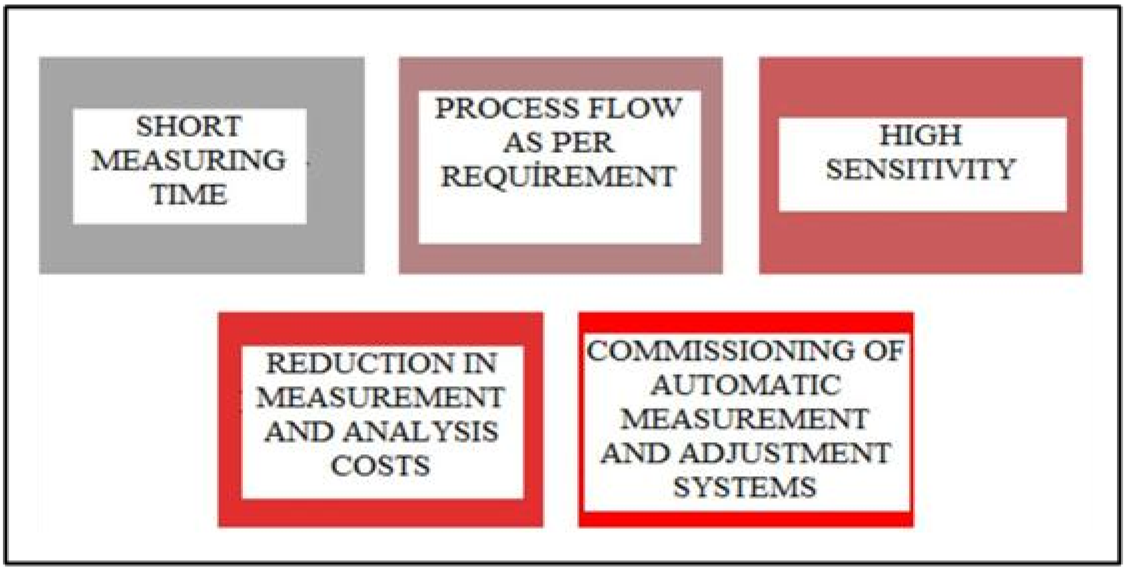

Figure 7. Biosensor usage advantages

Furthermore, biosensors are promising because they provide specific and dependable results, are reusable, can be mass produced in an inexpensive disposable manner, are practical and short-term, and don't require specialised knowledge to use. It's obvious

demonstrates that there are sensors, and as biochip technology advances, the range of applications for biosensors will grow in significance and weight daily. Additionally, nanotechnology has expanded the possibilities for biosensors and provided a benefit for a number of potential biosensor applications.

10. Conclusion

Biosensors present an intriguing substitute for conventional techniques that integrate biological components with physicochemical identifying component and enabling quick "realtime" and numerous analysis for estimations and diagnosis. The technology of biosensors has been created with a range of applications, with a primary focus on the creation of transducers and sensing elements that are now being researched. Important markers of tumour growth are cancer biomarkers.

They serve as a prognostic strategy to treatment in addition to being utilised for illness monitoring and diagnosis. Among POC cancer is the ultimate objective of biosensor technology. diagnosis. Diagnostic Point-of-Care Testing (POCT) On-site testing is one area where biosensors are used. might make a significant difference, giving the patient and medical personnel quick and simple access to results. Due to its extremely high sensitivity and selectivity, indirect virus detection—for instance, using commercial PCR-based devices—remains the gold standard in clinical settings today.

One of the most deadly illnesses in the world and a major global health concern is tuberculosis. Therefore, it is essential to discover and diagnose this disease as soon as possible. Above the Over the years, a variety of techniques have been employed to identify tuberculosis, including the PCR- based GeneXpert method and the Mantoux tuberculin skin test. In our analysis, we concentrated on the identification of the TB cytokine interferon-gamma biomarker. It is common practice to use ESEM, XPS, XRD, and other techniques to characterise these materials acquired for sensor applications. Methods are employed. The environmental scanning electron microscope's great sensitivity and application for in-depth material characterisation are its most crucial features.

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