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BIOSENSORS: WAY OF DIAGNOSIS

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ABSTRACT: Biosensors have revolutionized the way of diagnosis by allowing detection of diseases at earlier stage & detection of altered amount of biomarkers in the body. All biosensors usually involve minimal sample preparation as the biological sensing component is highly selective for the analyte concerned. There are numerous biosensors available now-a-days such as electrochemical biosensors, optical biosensors, DNA biosensors, microbial biosensors, mass based biosensors, calorimetric biosensors etc, which enable reliable & fast detection of analyte & provide accurate results at earliest. Biosensors have many uses in clinical analysis, general health care monitoring, veterinary and agricultural applications, industrial processing and monitoring, and environmental pollution control. Biosensor technology has the potential to provide fast and accurate detection, reliable imaging of cancer cells, and monitoring of angiogenesis and cancer metastasis, and the ability to determine the effectiveness of anticancer chemotherapy agents.

INTRODUCTION: A **biosensor** is an analytical device, used for the detection of an analyte that combines a biological component with a physicochemical detector. It consists of three parts.

A) Sensitive biological element (biological material (e.g. tissue, microorganisms, organelles, cell receptors, enzymes, antibodies, nucleic acids, etc.), a biologically derived material or biomimic component) that interacts (binds or recognizes) the analyte under study. The biologically sensitive elements can also be created by biological engineering.

B) The *transducer* or the *detector element* (works in a physicochemical way; optical, piezoelectric, electrochemical, etc.) that transforms the signal resulting from the interaction of the analyte with the biological element into another signal (i.e., transduces) that can be more easily measured and quantified.

C) Biosensor reader device with the associated electronics or signal processors that are primarily responsible for the display of the results in a user-friendly way¹.

A common example of a commercial biosensor is the blood glucose biosensor, which uses the enzyme glucose oxidase to break blood glucose down. In doing so it first oxidizes glucose and uses two electrons to reduce the FAD (a component of the enzyme) to FADH₂. This in turn is oxidized by the electrode (accepting two electrons from the electrode) in a number of steps.



The resulting current is a measure of the concentration of glucose. In this case, the electrode is the transducer and the enzyme is the biologically active component. Many of today's biosensor applications use organisms which respond to toxic substances at a much lower concentration than humans can detect to warn of their presence. Such devices can be used in environmental monitoring, trace gas detection and in water treatment facilities. Nanobiosensors use an immobilized bioreceptor probe that is selective for target analyte molecules. Nanomaterials are exquisitely sensitive chemical and biological sensors. Nanoscale materials demonstrate unique properties. Their large surface area to volume ratio can achieve rapid and low cost reactions, using a variety of designs.

Biological biosensors often incorporate a genetically modified form of a native protein or enzyme.

The protein is configured to detect a specific analyte and the ensuing signal is read by a detection instrument such as a fluorometer or luminometer. An example of a recently developed biosensor is one for detecting cytosolic concentration of the analyte cAMP (cyclic adenosine monophosphate), a second messenger involved in cellular signaling triggered by ligands interacting with receptors on the cell membrane².

Similar systems have been created to study cellular responses to native ligands or xenobiotics (toxins or small molecule inhibitors). Such "assays" are commonly used in drug discovery development by pharmaceutical and biotechnology companies. Most cAMP assays in current use require lysis of the cells prior to measurement of cAMP. A live-cell biosensor for cAMP can be used in non-lysed cells with the additional advantage of multiple reads to study the kinetics of receptor response.

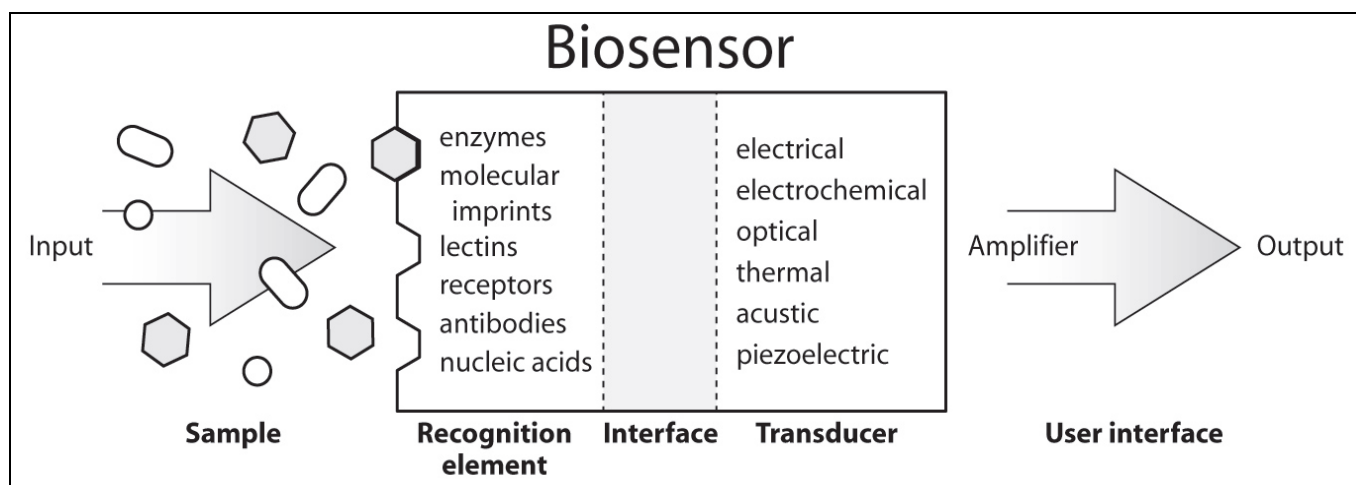


FIG. 1: CONFIGURATION OF A BIOSENSOR

Basic Characteristics of a Biosensor

1. **Linearity:** Maximum linear value of the sensor calibration curve. Linearity of the sensor must be high for the detection of high substrate concentration.
2. **Sensitivity:** The value of the electrode response per substrate concentration.
3. **Selectivity:** Interference of chemicals must be minimized for obtaining the correct result.
4. **Response Time:** The necessary time for having 95% of the response.

MATERIALS & METHODS:

Biosensor Recognition Elements: Initially, biosensor recognition elements were isolated from living systems. However, many biosensor recognition elements now available are not naturally occurring but have been synthesized in the laboratory. The sensing of targets, i.e. analytes of interest, is already being influenced by the emergence of engineered binding proteins³.

Employing the techniques of modern biotechnology, it is now possible to construct DNA polynucleotides at will, thus opening new paths for generation of biosensor recognition elements arising from paths not taken by nature⁴.

Enzyme based recognition: Catalytic enzyme based sensor recognition elements are very attractive for biosensor applications due to a variety of measurable reaction products arising from the catalytic process, which include protons, electrons, light, and heat. The enzyme urease has been widely used as a sensor biorecognition element due to a need for urea determination/monitoring for both medical and environmental applications⁵. The very apparent inherent, regulatory nature of allosteric enzymes affords great potential for use as biosensor recognition elements.

The regulatory subunit functions as the recognition element affecting, either in positive or negative fashion via conformational changes, the catalytic site serving as the transducing element⁶. In similar fashion, green fluorescent protein (GFP) is now used in many “allosteric-like” sensing element applications. Because the fluorophore is an intrinsic

part of the GFP polypeptide chain, no covalent modification of the protein is required. Numerous sensor applications involving use of GFP have been described⁷. Of all enzyme recognition element based biosensors, the glucose biosensor is the most widely studied and acclaimed sensor success story⁸.

Although a variety of glucose sensors are available, the glucose biosensor has changed little in principle over the years. As shown in **Fig. 2**, glucose encounters an immobilized enzyme and transduction is achieved amperometrically via an electrode. Currently, most glucose biosensors utilize glucose oxidase as their recognition element that catalyzes the oxidation of glucose to gluconolactone:



If oxidation is accomplished using glucose dehydrogenase (NAD⁺ prosthetic group), NADH is produced rather than H₂O₂.

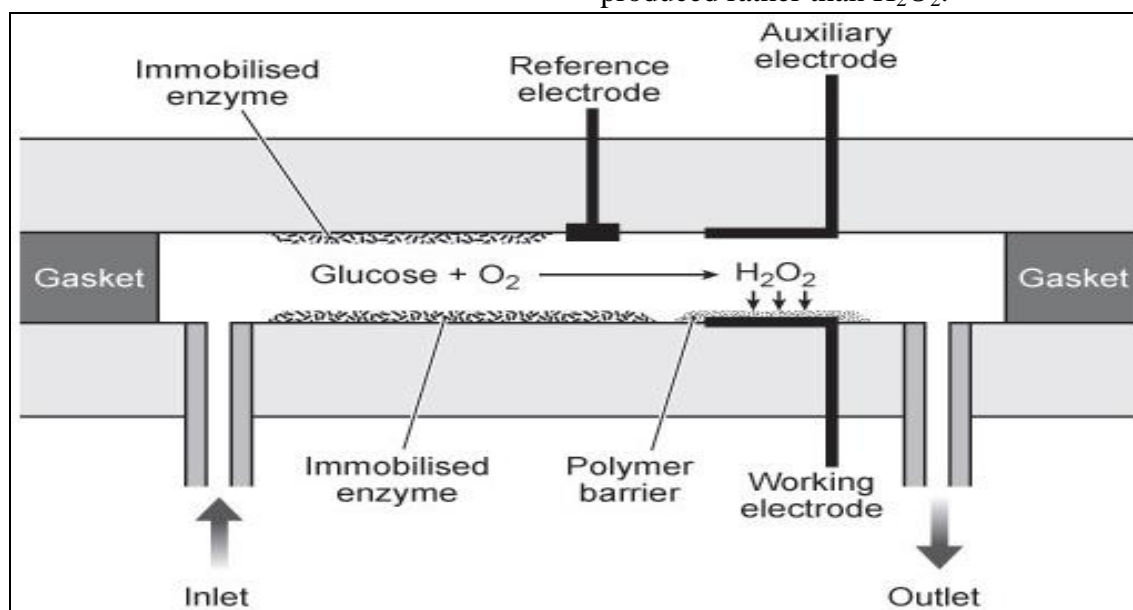


FIG. 2: DIAGRAM OF THE GLUCOSE SENSOR SHOWING THE ELECTRODE CONFIGURATION, THE POLYMER BARRIER DEPOSITED ONTO THE WORKING ELECTRODE AND THE SURFACE WHERE THE ENZYME (GLUCOSE OXIDASE) IS IMMOBILIZED

Antibody based recognition: With the notable exception of the glucose sensor, the majority of rapid detection systems employ antibodies for recognition, identification and quantitation of target analytes. Antibodies have been used extensively for detection purposes; however, their popularity increased significantly following Kohler and Milstein’s seminal work establishing monoclonal antibody (MoAb) technology⁹. Using cell clones that specifically produce MoAbs of choice, large quantities of antibody can now be produced.

Antibody recognition elements make use of the sensitivity and specificity of bimolecular antibody–antigen interactions. The major advantage of antibody sensor biorecognition elements is that the immunogen, i.e. target, need not be purified prior to detection. A variety of signal transduction (optical and electrochemical) techniques have been developed and the most useful has been enzyme-fluorescence based with catalytic turnover resulting in amplification of signal, thus increasing the sensitivity of the assay.

Like many routinely used diagnostic assays, the majority of current PSA (prostate-specific antigen) assays are variations of enzyme-linked immunosorbent assays (ELISA) reporting via the specific formation of PSA immune complex. Wu and coworkers¹⁰ observation of nanomechanical motion generated by protein ligand interactions on microcantilevers has led to immobilization of PSA antibody recognition element for detection of PSA in serum (**Fig. 3**).

Molecules adsorbed on a microcantilever cause vibrational frequency changes referred to as “curling” due to adsorption stress on one side of the cantilever. Surface plasmon resonance based optical transduction by noble metals has also been used as basis of antibody recognition element assays¹¹. Such technology readily lends itself to well established array microfabrication techniques, thereby offering the promising prospect of high throughput, biosensor based analysis of clinical samples.

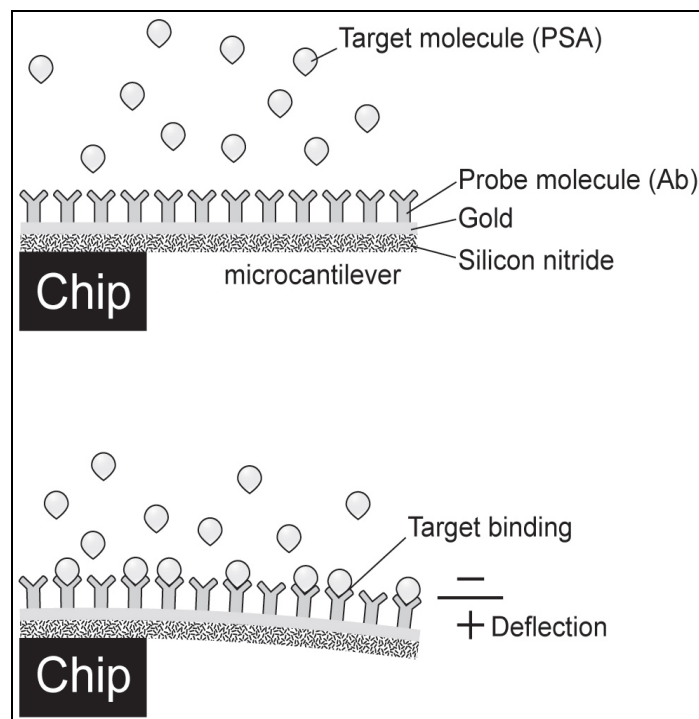


FIG. 3: DIAGRAM OF INTERACTIONS BETWEEN TARGET AND PROBE MOLECULES ON A MICROCANTILEVER BEAM¹⁰

Peptide nucleic acid based recognition: Peptide nucleic acids (PNA) are synthetic DNA analogues or mimics with a polyamide backbone instead of a sugar phosphate bone¹². Of significant importance to biosensing, PNAs exhibit superior hybridization characteristics and improved chemical and enzymatic stability compared to nucleic acids¹³.

Both double and triple stranded complexes are capable of being formed by PNA in association with nucleotides¹⁴. As shown in **Fig. 4**, the negatively charged ribosephosphate backbone of nucleic acids is replaced by an uncharged N-(2-aminoethyl)-glycine scaffold to which the nucleobases are attached via a methylene carbonyl linker.

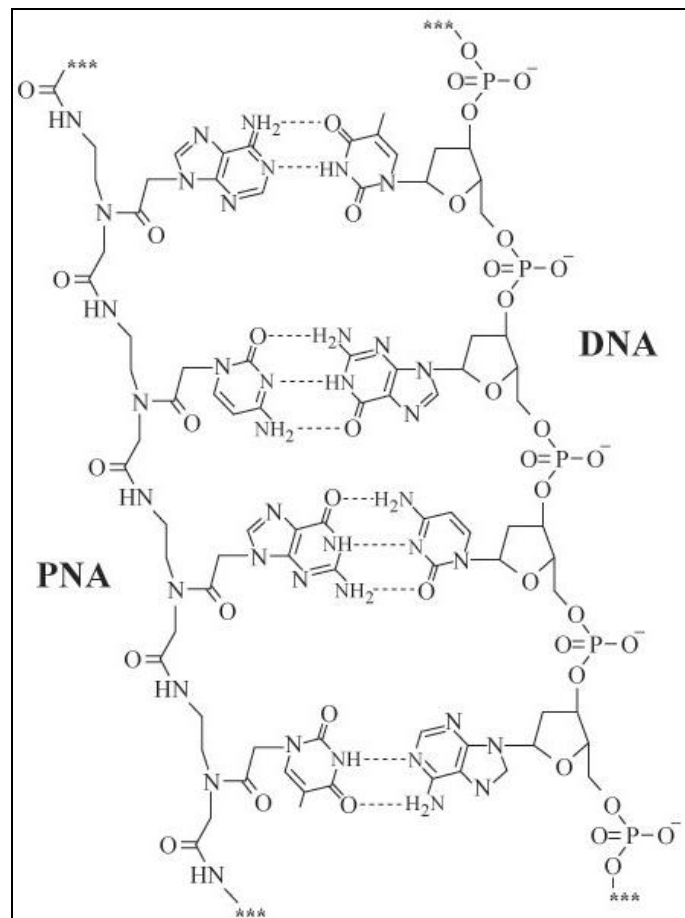


FIG. 4: COMPARISON OF THE STRUCTURES OF PEPTIDE NUCLEIC ACID (PNA) AND DNA¹⁴

Molecular imprint based recognition: Molecular imprinting is a method for making selective binding sites in synthetic polymers using molecular templates. Molecular imprinted polymers offer great promise for development of very stable “solid-state like” artificial biosensing elements. In recent years, the technology of molecular imprinting has proliferated as an inexpensive, accessible and effective strategy for developing sorbent materials exhibiting high specificity for selected substrate materials. Shown in **Fig. 5** is a generalized scheme describing synthesis of a molecular imprint receptor molecule. Although there are only a few examples of molecular imprint recognition element based biosensing, the possibility of imprinting against a wide range of analytes raises the possibility of

generation of robust, artificial biological receptors making possible multiple clinical sample analysis without pretreatment, effectively reagentless chemistries.

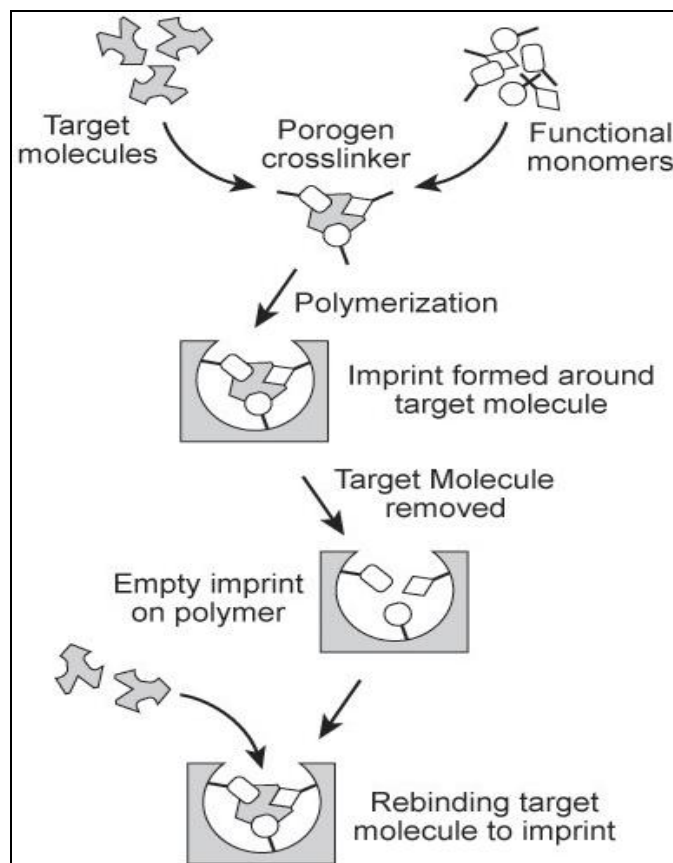


FIG. 5: SCHEMATIC REPRESENTATION OF THE PREPARATION OF MOLECULAR IMPRINTS

Lectin based recognition: Lectins constitute a broad family of proteins involved in diverse biological processes, occasionally having potent toxic properties. Lectins generally exhibit strong binding to specific carbohydrate moieties known as glycans, and this property has been extensively exploited as a basis for biosensor design¹⁵. Furthermore, particular structural profiles of glycans and their recognition by lectins have been attributed to disease progression, making analysis of saccharide–lectin binding processes important as a diagnostic tool.

Attachment of the biological elements: An important part in a biosensor is to attach the biological elements (small molecules/protein/cells) to the surface of the sensor (be it metal, polymer or glass). The simplest way is to functionalize the surface in order to coat it with the biological elements. This can be done by polylysine, aminosilane, epoxysilane or nitrocellulose in the case of silicon chips/silica glass.

Subsequently the bound biological agent may be for example fixed by Layer by layer deposition of alternatively charged polymer coatings¹⁶.

Alternatively three dimensional lattices (hydrogel/xerogel) can be used to chemically or physically entrap these (where by chemically entrapped it is meant that the biological element is kept in place by a strong bond, while physically they are kept in place being unable to pass through the pores of the gel matrix). The most commonly used hydrogel is sol-gel, glassy silica generated by polymerization of silicate monomers (added as tetra alkyl orthosilicates, such as TMOS or TEOS) in the presence of the biological elements (along with other stabilizing polymers, such as PEG) in the case of physical entrapment¹⁷.

Another group of hydrogels, which set under conditions suitable for cells or protein, are acrylate hydrogel, polymerize upon radical initiation. One type of radical initiator is a peroxide radical, typically generated by combining a persulfate with TEMED (Polyacrylamide gel are also commonly used for protein electrophoresis)¹⁸. Alternatively light can be used in combination with a photoinitiator, such as DMPA (2, 2-dimethoxy-2-phenylacetophenone). Smart materials that mimic the biological components of a sensor can also be classified as biosensors using only the active or catalytic site or analogous configurations of a biomolecule¹⁹.

Biosensing Method: The essence of the biosensor is matching the appropriate biological and electronic components to produce a relevant signal during analysis. Isolation of the biological component is necessary to ensure that only the molecule of interest is bound or immobilized on the electronic component or the transducer. The stability of the biological component is critical, since it is being used outside its normal biological environment. Attachment of the biological component to the electronic component is vital for the success of these devices. If the biological component is destroyed in the process of binding or if it binds with the active site unavailable to the analyte, the biosensor will not function. Attachment can be accomplished in a variety of ways, such as covalent binding of the molecule to the detector (usually through a molecular cross-bridge), adsorption onto the surface entrapment in porous material, or micro encapsulation.

Ultra-thin applications of biological material are usually deposited on transducers by using the Langmuir – Blodgett or molecular self-assembly technique.

Types of Biosensors:

1. **Electrochemical biosensors:** Electrochemical biosensors are normally based on enzymatic catalysis of a reaction that produces or consumes electrons. The sensor substrate usually contains three electrodes; a reference electrode, a working electrode and a counter electrode. The target analyte is involved in the reaction that takes place on the active electrode surface, and the reaction may cause either electron transfer across the double layer (producing a current) or can contribute to the double layer potential (producing a voltage). We can either measure the current (rate of flow of electrons is now proportional to the analyte concentration) at a fixed potential or the potential can be measured at zero current (this gives a logarithmic response).

Note that potential of the working or active electrode is space charge sensitive and this is often used (Biosensors Primer). Another example, the potentiometric biosensor, (potential produced at zero current) gives a logarithmic response with a high dynamic range. Such biosensors are often made by screen printing the electrode patterns on a plastic substrate, coated with a conducting polymer and then some protein (enzyme or antibody) is attached. They have only two electrodes and are extremely sensitive and robust. They enable the detection of analytes at levels previously only achievable by HPLC and LC/MS and without rigorous sample preparation.

All biosensors usually involve minimal sample preparation as the biological sensing component is highly selective for the analyte concerned. The signal is produced by electrochemical and physical changes in the conducting polymer layer due to changes occurring at the surface of the sensor. Such changes can be attributed to ionic strength, pH, hydration and redox reactions, and the latter due to the enzyme label turning over a substrate ¹.

2. **ICS biosensors:** An Ion Channel Switch (ICS) biosensor can be created using gramicidin, a dimeric peptide channel, in a tethered bilayer membrane ²⁰. One peptide of gramicidin, with attached antibody, is mobile and one is fixed. Breaking the dimer stops the ionic current through the membrane. The magnitude of the change in electrical signal is greatly increased by separating the membrane from the metal surface using a hydrophilic spacer. Quantitative detection of an extensive class of target species, including proteins, bacteria, drug and toxins has been demonstrated using different membrane and capture configurations ^{21, 22, 23, 24}.
3. **DNA Biosensors:** In the future, DNA will find use as a versatile material from which scientists can craft biosensors. DNA biosensors can theoretically be used for medical diagnostics, forensic science, agriculture, or even environmental clean-up efforts. No external monitoring is needed for DNA-based sensing devices. This is a significant advantage. DNA biosensors are complicated mini-machines-consisting of sensing elements, micro lasers, and a signal generator. At the heart of DNA biosensor function is the fact that two strands of DNA stick to each other by virtue of chemical attractive forces. On such a sensor, only an exact fit- that is, two strands that match up at every nucleotide position- gives rise to a fluorescent signal (a glow) that is then transmitted to a signal generator ²⁵.
4. **Microbial biosensors:** Using biological engineering researchers have created many microbial biosensors. An example is the arsenic biosensor. To detect arsenic they use the Ars operon ²⁶. Using bacteria, researcher can detect pollutants in samples. Microbial biosensors have many advantages:
 1. They can be implanted in the human body and are suitable for *in vivo* detection.
 2. They can be integrated on one chip and are useful for measuring various substrates in a small amount of sample solution simultaneously.
 3. Semiconductor fabrication technology can be applied to microbial biosensors. It is possible to develop disposable transducers for biosensors through mass production.

Biosensors in Food analysis: There are several applications of biosensors in food analysis. In food industry optic coated with antibodies are commonly used to detect pathogens and food toxins. The light system in these biosensors has been fluorescence, since this type of optical measurement can greatly amplify the signal²⁷. A range of immuno- and ligand-binding assays for the detection and measurement of small molecules such as water-soluble vitamins and chemical contaminants (drug residues) such as sulfonamides and Beta-agonists have been developed for use on SPR based sensor systems, often adapted from existing ELISA or other immunological assay. These are in widespread use across the food industry.

Biosensors and Cancer: In terms of cancer, the analyte being detected by the biosensor is a tumor biomarker. Thus, by measuring levels of certain proteins expressed and/or secreted by tumor cells, biosensors can detect whether a tumor is present, whether it is benign or cancerous, and whether treatment has been effective in reducing or eliminating cancerous cells²⁸. Biosensors that can detect multiple analytes may prove particularly useful in cancer diagnosis and monitoring, since most types of cancer involve multiple biomarkers²⁹. The ability of a biosensor to test for multiple markers at once not only helps with diagnosis, but also saves time and financial resources³⁰. A biosensor is made up of three components: a recognition element, a signal transducer, and a signal processor that relays and displays the results. The molecular recognition component detects a 'signal' from the environment in the form of an analyte, and the transducer then converts the biological signal to an electrical output³¹.

Optical Biosensors: Optical biosensors are light-based sensors that measure changes in specific wavelengths of light. The transducer can be luminescence, fluorescence, colorimetric, or interferometric based. Optical transducers convert changes in wavelengths or SPR in response to analyte recognition into an electrical/digital readout³⁰. Photonic crystal biosensors are a newly emerging class of biosensors that use an optical transducer. The photonic crystal sensor is designed to capture light from very small areas or volumes, allowing for greater sensitivity of measurement and then transmit that light into a high electromagnetic field for

display. By measuring the light reflected by the crystal, this technique can detect when and where cells or molecules bind to or are removed from the crystal surface. Another exciting example of this application of this type of technology to cancer detection is the oesophageal laser fluorescence-based optical biosensor for the diagnosis and monitoring of cancers of the throat. After being swallowed by the patient, the device directs a laser beam emitting a specific wavelength of light onto the surface of the oesophagus. The oesophageal wall reflects light at very specific wavelengths, based on whether the tissue contains cancerous cells or normal cells. This sensor has been tested on over 200 patients and found to accurately diagnose cancer over 98% of the time. By using this type of biosensor, surgical biopsies and the pain and recovery time associated with them could be avoided.

Mass-based biosensors: Piezoelectric and acoustic wave biosensors make up the class of mass-based biosensors. In terms of cancer detection, piezoelectric biosensors are more commonly used. Piezoelectric sensors are based on changes in the mass of quartz crystals when potential energy is applied to them. This change in mass generates a frequency, which can be converted into a signal. Immunosensors and microcantilever sensors that use piezoelectric technology have proven useful in the identification of cancer biomarkers³⁰.

Calorimetric biosensors: Calorimetric biosensors are less common than other biosensors for cancer diagnostics, but the introduction of nanotechnology to the field of biosensors has increased the range of applications for these types of biosensors. Calorimetric biosensors measure exothermic reactions. Many enzymatic reactions generate heat, and changes in heat can be used to measure analyte concentration. The reaction is monitored by measuring enthalpy changes, which indirectly provide information about substrate concentration³¹. Calorimetric biosensors are not commonly used for the diagnosis and prognosis of cancer, but some cancer detecting capabilities have been demonstrated.

Biosensors and Nanotechnology: Nanotechnology is a rapidly emerging field that is having an enormous impact on biosensors, and by extension, the diagnosis, prognosis, and monitoring of cancer. Most cancer is diagnosed only after it has

metastasized, making it much more deadly and difficult to treat. Roughly 60% of cancer cases are diagnosed in patients after the tumor has metastasized. The application of nanotechnology to biosensor development improves the chances of detecting cancer earlier, thus improving patient survival rates. One example of this is in the diagnosis of cancer by magnetic resonance imaging (MRI), one of the most common imaging technologies in use today for cancer diagnosis and monitoring. A major drawback of MRI is that it cannot detect entities that are smaller than a few centimeters. The use of nanomaterials as imaging agents allows for more sensitive and precise measurement of cancerous tissues.

Liposomes, dendrimers, buckyballs, and carbon nanotubes are all examples of nanomaterials that have been used to improve cancer imaging³². Additionally, the use of nanotechnology means smaller sensors, which translates into better access to and detection of cancer markers, as well as more powerful and specific signal enhancements, reduced cost, and high throughput detection. Nanoparticles are defined as particles on the scale of 1–100 nm in diameter. The small size of nanoparticles allows for a greater surface to volume ratio. This increase in ratio allows for better detection, imaging, and prognosis methods and improved drug delivery to tumor sites that were previously not accessible. Nanocantilevers, nanowires, and nanochannels are all examples of structures that have been exploited for the detection of cancer-specific molecular events and improved signal transduction³³.

Another major application of nanotechnology is the use of quantum dots. Quantum dots are luminescent nanocrystals that have many of the same properties as optical biosensors³⁰. Quantum dots can emit light of different wavelengths, intensity, and spectral width, allowing for the diagnosis and detection of multiple unique molecular elements³². They are able to track molecules and entire cells as they move through an environment. As such, they can be very important in monitoring cancer development by tracking the migration of cancer cells, cancer metastasis, and drug therapy effectiveness. The allure of quantum dots is their high stability, multimodality, and small size (~50–100 units in diameter for biological applications).

Quantum dots are also capable of delivering therapeutic agents to specific target sites to improve pharmaceutical effectiveness while minimizing side effects³⁴.

RESULTS & DISCUSSION: After more than 40 year of research in biosensors, a wide gap between research and application is evident. The lack of validation, standardization, and certification of biosensors has resulted in a very slow transfer of technology. With faster computers and automated systems, this process should accelerate in the future. There are number of biosensors available now-a-days. All have their specific purpose. Some of the biosensors of modern era are show in the **figure 6, 7, & 8**.



FIG. 6: BLOOD GLUCOSE BIOSENSOR (ONE TYPE)



FIG. 7: BLOOD GLUCOSE BIOSENSOR (ANOTHER TYPE)



FIG. 8: PREGNANCY TEST BIOSENSOR

TABLE 1: BIOLOGICAL ELEMENTS AND TRANSDUCERS COMMONLY USED IN THE FABRICATION OF BIOSENSORS

Biological elements	Transducers
Enzymes	Electrochemical
Antibodies	
Receptors	
Cells	Ion selective
Membranes	Field effect transistors
Tissues	Conductimetric
Organisms	Optical
Organelles	
Nucleic acids	
Organic molecules	Fiber optic SPR
	Calorimetric
	Acoustic

Applications: Biosensors have many uses in clinical analysis, general health care monitoring, veterinary and agricultural applications, industrial processing and monitoring, and environmental pollution control. The advantages are likely to include low cost, small size, quick and easy use, as well as a sensitivity and selectivity greater than the current instruments. The advent of cheap, user-friendly biosensors will revolutionize the practice of healthcare monitoring and enables more in-depth diagnosis on a metabolic basis. The introduction of suitable biosensors would have considerable impact in the following areas.

Clinical and Diagnostic Applications: Bench top biosensors of the electrochemical variety are used now in clinical biochemistry laboratories for measuring glucose and lactic acid³⁵. A key feature of this is the ability for direct measurement on undiluted blood samples. Consumer self-testing, especially self-monitoring of blood components is another important area of clinical medicine and healthcare to be impacted by commercial biosensors. Current methods are based on colorimetric dry reagent chemistry often in conjunction with a portable reflectance meter. Biosensors offer the potential of reusable systems and other advantages by employing electrochemical detection rather than colour changes to help alleviate the problems of those with poor eyesight (some of them diabetics who are often heavy users of biosensors for glucose determination).

Reusable sensors also permit calibration and quality control unlike the present disposable sticks where only one measurement can be carried out. Such testing will improve the efficiency of patient care, replacing the often slow and labour intensive present tests. It will bring clinical medicine closer to bedside, facilitating rapid clinical decision-making.

Industrial Applications: Along with conventional industrial fermentation producing materials, many new products are being produced by large-scale bacterial and eukaryotes cell culture. The monitoring of these delicate and expensive processes is essential for minimizing the costs of production; specific biosensors can be designed to measure the generation of a fermentation product³⁶.

Environmental Monitoring: Environmental water monitoring is an area in which whole cell biosensors may have substantial advantages for combating the increasing number of pollutants finding their way into the groundwater systems and hence into drinking water.

Important targets for pollution biosensors now include anionic pollutants such as nitrates and phosphates. The area of biosensor development is of great importance to military and defense applications such as detection of chemical and biological species used in weapons.

CONCLUSION: Biosensors have become the need of today. We should realize the importance of biosensors in many ways *viz* in clinical, industrial, environmental etc. In the present scenario, we have not completely understood the value of biosensors. After few years, we can be almost dependent on the use of biosensors in most of the areas. The major influences of nanotechnology on biosensor development involve nanomaterials, particularly quantum dots, as they cannot only facilitate diagnosis and tracking of cancer cells, but also can deliver drugs to target sites with precision and allow for more sensitive imaging systems that Biosensors can detect cancer at an earlier stage.

In the next 5-10 years, it is certain that nanotechnology will revolutionize cancer diagnosis and therapy. Integrating nanomaterials and biosensors will allow us to detect disease earlier, improve cancer imaging, and aid in diagnosis/prognosis and advance drug delivery while minimizing adverse reactions. The main requirements for a biosensor approach to be valuable in terms of research and commercial applications are the identification of a target molecule, availability of a suitable biological recognition element, and the potential for disposable portable detection systems to be preferred to sensitive laboratory-based techniques in some situations.

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