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A review on Biosensors and their applications in Human life and Agroecosystems

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Abstract: Enzyme-based, tissue-based, immunosensors, DNA biosensors, thermal, and piezoelectric biosensors have all been discussed here to illustrate their many uses. Biosensors are widely used in the food business to monitor quality and safety, to discriminate between natural and artificial ingredients, in fermentation and saccharification to detect exact glucose concentration, and in metabolic engineering to allow in vivo monitoring of cellular metabolism. Aspects of biosensors in medicine include early detection of human interleukin-10 causing cardiac problems, quick detection of human papilloma virus, etc. Drug discovery and cancer use fluorescent biosensors. Biosensors are widely used in plant biology to detect missing connections in metabolic pathways. Other uses include defense, medical, and marine. These procedures are costly, laborious, require complex equipment and specialized workers, and are now used to monitor agroecosystems. The development of small, fast, and economically feasible bio and nano sensors for detecting diverse organisms damaging natural agroecosystems has been greatly facilitated in recent decades. Thanks to the fast development of nanotechnology, bio and nano sensors for detecting various composites have been developed. So, this study focuses on diverse bio and nano sensors used to monitor agricultural ecosystems, and how they are implemented from proof-of-concept to commercialization.

Keywords: Agroecosystems, Nanoparticles, Nano sensors, Biosensors, Pesticides, Heavy metals, Pathogens, Agricultural production.

1. Introduction

Biosensors analyze biological responses and translate them to electrical signals. Biosensors must be very specific, independent of physical conditions like pH and temperature, and reusable. Cammann[1] created the term ‘‘biosensor,” and IUPAC defined it. [2] Material research, transducing devices, and immobilization procedures are required to fabricate biosensors. The materials utilized in biosensors are classified into three classes depending on their mechanisms: enzymes, antibodies and nucleic acids, and microbes. Challenges

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like persistent population stress, variable climate conditions, and increased resource competition have all presented a danger, necessitating the urgent need to ensure global food security. Existing agricultural practices include unrestrained resource consumption, advanced technology, and rising and indiscriminate use of agrochemicals. These activities have significantly harmed soil, air, and water resources, ultimately affecting human and animal health. Monitoring agroecosystems now includes gas chromatography, HPLC, mass spectroscopy, and more (Fig. 1). The sensitivity, specificity, and repeatability of such measures are undeniable, but their implementation is constrained by time, cost, and the need for specialized equipment and expert staff [3]. Thus, simple, rapid, and cost-effective approaches for monitoring agricultural pollutants are required [4]. Nano sensors are tiny element devices designed to detect molecules, biological components, or environmental conditions. These sensors are small, portable, and detect at a far lower level than their macroscale counterparts. [5]

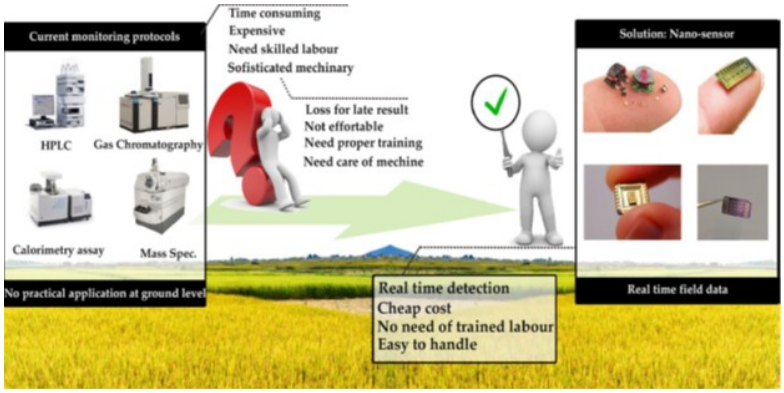

Fig. 1. Schematic representation of traditional and advanced monitoring technologies. [5]

2. Review of literature

2.1. Types of biosensors

Clark and Lyons developed biosensors in the 1960s. Enzyme-based, tissue-based, immunosensors, DNA-based, thermal, and piezoelectric biosensors are employed. Updike and Hicks reported the first enzyme sensor in 1967. The immobilization of enzymes via van der Waals forces, ionic bonding, or covalent bonding has been developed. These include oxidoreductases, polyphenol oxidases, peroxidases, and amino oxidases (Fig. 2). [6] Diviès created the first microbe or cell-based sensor. [7] Plant and animal tissues are used in tissue-based sensors. The analyte of interest might be either an inhibitor or a substrate. Rechnitz [8] created the first tissue-based arginine sensor. A membrane, chloroplast, mitochondrion, and micro-some-based sensor was developed. As a result, the detection time is prolonged, and the specificity is lowered. Antibodies have strong affinity for their antigens, i.e., they selectively attach to infections or poisons, or interact with immune system components. The DNA biosensors work by recognizing and binding

to the corresponding strand in a sample. The contact occurs when two nucleic acid strands create stable hydrogen bonds. [9] These miniature magnetic biosensors can detect magnetic micro- and nanoparticles in microfluidic channels via the magnetoresistance effect. [10] Thermal or calorimetric biosensors are created by combining biosensor components into a physical transducer. These include quartz crystal microbalances and surface acoustic wave devices. They monitor variations in a piezoelectric crystal's resonance frequency owing to mass changes. Optical biosensors include a light source, many optical components, a customized sensing head, and a photodetector. [11] Green fluorescent protein (GFP) and AFP variations and genetic fusion reporters have helped construct genetically encoded biosensors. [12] This form of biosensor is simple to design, control, and implant into cells. Another is a single-chain FRET biosensor. They are made up of two AFPs that may exchange fluorescence resonance energy when placed near together. Depending on the strength, ratio, or longevity of AFPs, FRET signals may be regulated. Synthetic peptide and protein biosensors are readily made by enzymatic labeling using synthetic fluorophores. They are appealing alternatives to genetically encoded AFPs because they are independent of AFPs and can improve signal-to-noise ratio and response sensitivity by adding chemical quenchers and photoactivatable groups.

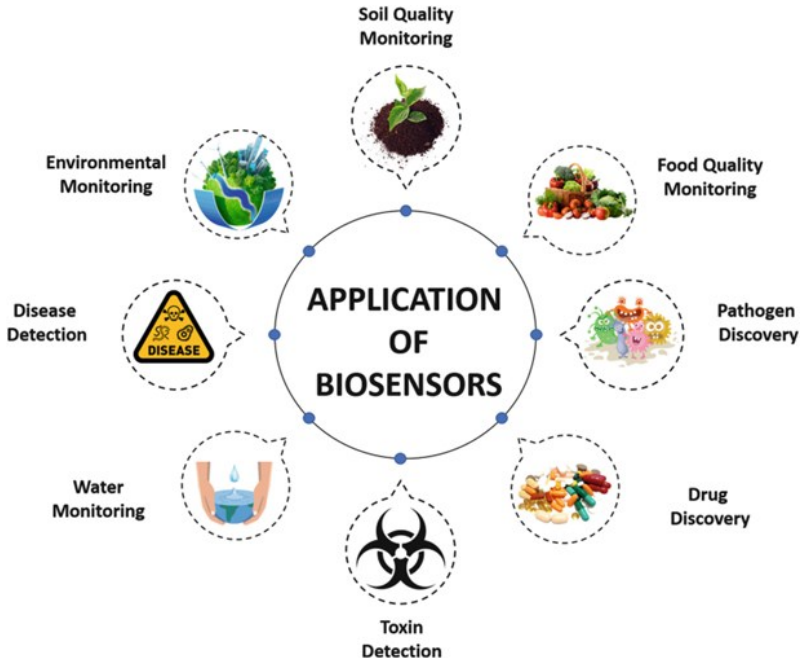

Fig. 2. Different applications of biosensors. [6]

2.2. *Applications of biosensors*

Biosensors have been applied in many fields namely food industry, medical field, marine sector etc., and they provide better stability and sensitivity as compared with the traditional methods.

2.2.1. In food processing, monitoring, food authenticity, quality, and safety

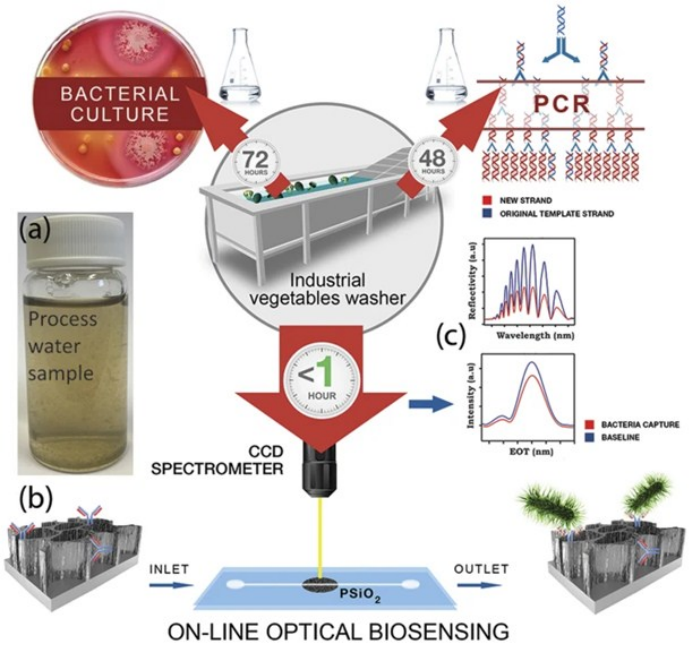

Fig. 3. (a) Water samples from a Dutch fresh-cut fruit firm were tested for E. coli using three methods: culturing, PCR, and label-free optical biosensors (bottom). (b) The biosensor is activated by specific capture probes (antibodies) mounted on the PSiO2 surface. (c) The observed optical signal comes from the porous nanostructure. [13]

The food processing sector has a difficult dilemma of quality, safety, and processing. Chemical experiments and spectroscopy are labor intensive, costly, and time consuming. The food sector seeks cost-effective alternatives for food verification and monitoring. Thus, the requirement for simple, real-time, selective, and economical procedures seems to favor biosensor development (Fig 3). [13] Ghasemi-Varnamkhasti [14] studied enzymatic biosensors based on cobalt phthalocyanine to monitor beer ageing. These biosensors might effectively monitor the aging of beer in storage. Biosensors detect infections in food. Escherichia coli in vegetables is a biomarker for feces contamination. [15] Ammonia (generated by urease–E. coli antibody conjugate) has been quantified using potentiometric alternative biosensing systems. washing veggies with peptone water gives us the liquid phase. It is then sonicated to dissociate bacterial cells from food. [16] Dairy uses enzymatic biosensors. A flow cell with a biosensor based on a screen-printed carbon electrode [17] Enzymes were engulfed in a photo cross linkable polymer to immobilize them. Automated flow-based biosensor might detect contaminants in milk. Sweeteners are one of the most widely used food additives today, and they are linked to problems including dental cavities, cardiovascular disease, obesity, and type 2 diabetes. Artificial sweeteners are thought to be addicting, allowing us to consume more high-calorie foods unwittingly, causing weight gain. So, their identification and measurement are crucial. Ion chromatographic techniques are used to differentiate the two kinds of sweet-enters. Multi-channel biosensors, which measure the electrophysiological activity of the taste epithelium, have been examined as a

more effective tool for rapid and sensitive screening of sweeteners. Spatial and temporal analysis of data using MATLAB, where glucose and sucrose are natural sugars and saccharin, and cyclamate are artificial sweeteners. Due to the heterodimeric G-protein coupled receptors in Type-II cells of the bud, they have several binding sites to recognize sweet stimuli of various structures. The cyclic adenosine monophosphate system uses natural sugars like sucrose, whereas the inositol triphosphate and diacylglycerol pathways use artificial sweeteners to transmit signals. The amino terminal domains of taste receptors act as ligand binding sites for artificial sweeteners. Taste receptor cells respond differently to natural and artificial sweeteners. When glucose was administered, the taste epithelium biosensor gave sparse positive waveforms, but sucrose maintained negative spikes. Artificial sweeteners elicited stronger responses from the taste epithelium than natural sugars, both in temporal and frequency domains.

2.2.2. In fermentation processes

Process safety and product quality are critical in fermentation. Developing, optimizing, and maintaining biological reactors requires good fermentation monitoring. Biosensors can detect process conditions by monitoring the presence of products, biomass, enzymes, antibodies, or by-products. Because of their cheap cost, high selectivity, and ease of automation, biosensors have revolutionized the fermentation business. Modern commercial biosensors can detect biochemical parameters (glucose, lactate, lysine, and alcohol) and are extensively utilized in China (approximately 90% of the market). The classic Fehiing technique was used to check saccharification. This method's results were erroneous due to decreased sugar titration. Since the commercialization of glucose biosensors in 1975, the fermentation industries have profited. To manage production in the saccharification and fermentation workshop, firms now employ glucose biosensors. In ion exchange retrieval, biosensors detect changes in biological composition. For example, glutamate biosensor was employed to study ion exchange retrieval of glutamate isoelectric liquor supernatant. Fermentation is a complex process with many variables, many of which are difficult to assess in real-time. Controlling biological processes requires continuous monitoring of key metabolites. Due to their simplicity and rapid reaction, biosensors have gained popularity in online fermentation monitoring. [18]

2.2.3. Biosensing technology for sustainable food safety

Food quality includes look, flavor, texture, and chemicals. (Fig 4). [19] In terms of food quality and safety, smart nutrient monitoring and rapid detection of pollutants are critical. Materials science, nanotechnology, electromechanical, and microfluidic systems are advancing sensing technologies. Control mechanisms for food quality and safety, and hence human health, are being developed. Glucose monitoring is required because food composition might change during storage. 28 German [20] investigated the electrochemistry of glucose oxidase immobilized on a graphite rod and enhanced with gold nanoparticles (AuNPs). Glutamine is essential for vital processes including (signaling, transport, and precursor in biosynthesis of nucleic acids, amino sugars, and proteins). The immune system, digestive function, and bacterial translocation are improved when

glutamine deficient patients are supplied. "Glutaminase-based microfluidic biosensor chip with flow-injection analysis for electrochemical detection" [21] Because biosensors can only react with the poisonous portions of metal ions, they are used to detect general and toxicity. Pesticides endanger the environment. Organophosphates and carbamic insecticides are widely used pesticides. Immunosensors have shown their value in agri-food and environmental monitoring. Many chemicals have AChE and butyrylcholinesterase biosensors. Arduino and coworkers created Oxon using screen-printed electrodes. 33 Pesticides in wine and orange juice are detected using a similar biosensor. [22] Bacterial bioassays can test arsenic. [23]

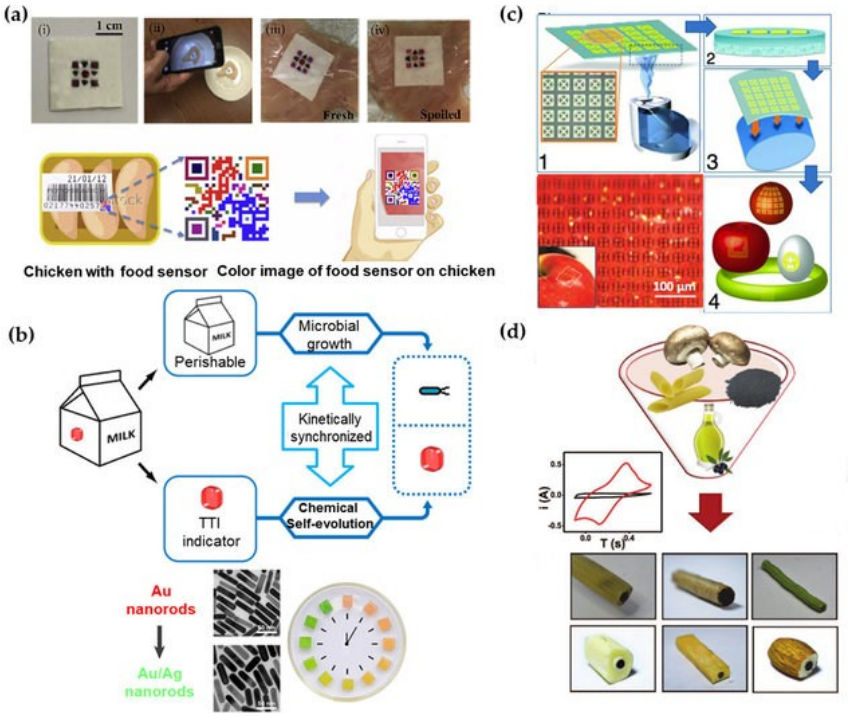

Figure 4. Various demonstrations of biosensors in the food industry. [19]

2.2.4. In medical field

The use of biosensors in medicine is rapidly expanding. Diabetes mellitus needs careful management of blood glucose levels; therefore, glucose biosensors are frequently utilized in clinical applications (Fig 5). [24] Home use of blood glucose biosensors accounts for 85% of the huge global market. Biosensors are widely utilized in medicine to diagnosis infectious illnesses. A potential biosensor method for UTI diagnosis, pathogen identification, and antibiotic susceptibility is being studied. Identifying end-stage heart failure patients at risk for complications following left ventricular aided device placement is critical. A new biosensor based on hafnium oxide (HfO2) has been utilized to detect IL-10 in early stages. [25] Early cytokine detection using recombinant human IL-10 and

a monoclonal antibody is explored. Fluorescence patterns and electromechanical impedance spectroscopy evaluate antibody–antigen interaction and bio-recognition of protein. Chen et al. used HfO2 as a bio-field-effect transistor. [26] The HfO2 biosensor detects a human antigen via electrochemical impedance spectroscopy. The main problem now is heart failure, which affects almost a million individuals. Cardiovascular disease detection methods include immunoaffinity column, fluorometric, and enzyme-linked immunosorbent test. [27] These are time intensive and need trained workers. For desired selectivity with a specific biomarker, electric biosensors use biological molecular recognition. In addition to these, other biosensor applications include quantitative measurement of cardiac markers in undiluted serum, microfluidic impedance assay for controlling endothelin-induced cardiac hypertrophy, immune sensor array for clinical immunophenotyping of acute leukemias, effect of oxazaborolidines on immobilized fructosyltransferase in dental diseases, histone deacetylase (HDAC) inhibitor assay from resonance energy transfer, biochip for fast and accurate.

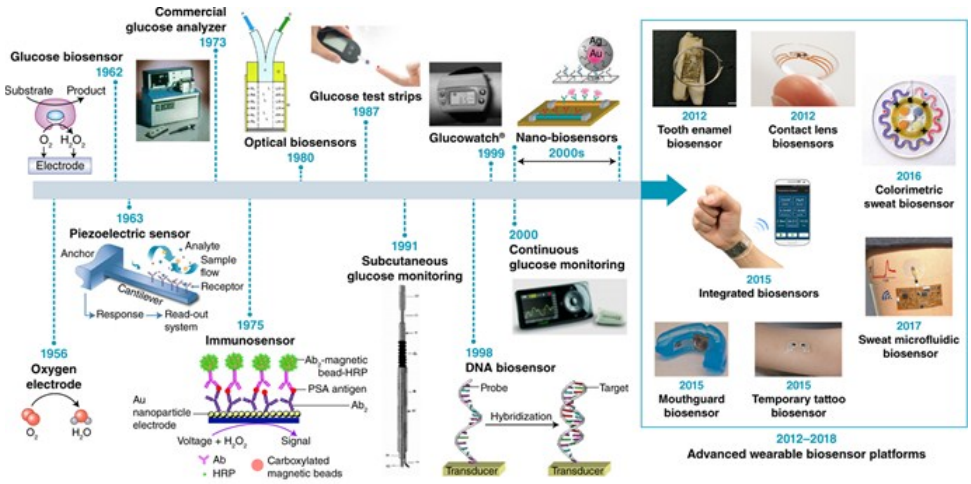

Figure 5. Some medical biosensors. [24]

2.2.5. *Fluorescent biosensors*

In cancer and drug discovery, fluorescent biosensors can image. They have shown the biological function and control of enzymes. FRET biosensors with GFP play an important function. An enzyme, chemical, or genetically modified fluorescent probe is attached to a fluorescent biosensor through a receptor. The receptor detects and measures a particular analyte or target by transducing a fluorescence signal. [28] Fluorescent biosensors can detect ions, metabolites, and protein biomarkers in complicated solutions and indicate their presence, activity, or status (serum, cell extracts). Signal transmission, transcription, cell cycle, and apoptosis all use them to probe gene expression, protein location, and conformation. Their use enables detection of illnesses including cancer and metastases as well as arthritic conditions. Fluorescent biosensors are employed in drug discovery programs for high throughput, high content screening, post screening analysis of hits,

and lead optimization. These are powerful techniques for assessing drug candidates' therapeutic potential, biodistribution, and pharmacokinetics. [29] Fluorescent biosensors are used for early biomarker detection in genetic and clinical diagnostics, disease progression monitoring, intravital imaging, and image guided surgery. [30] The use of a genetically encoded FRET biosensor to detect Bcr-Abl kinase activity on cancer patient cells helped demonstrate a link between Bcr-Abl kinase activity and disease status in chronic myeloid leukemia. This probe was also used to control treatment response and detect drug-resistant cells, allowing for alternate therapeutic prediction. [31]

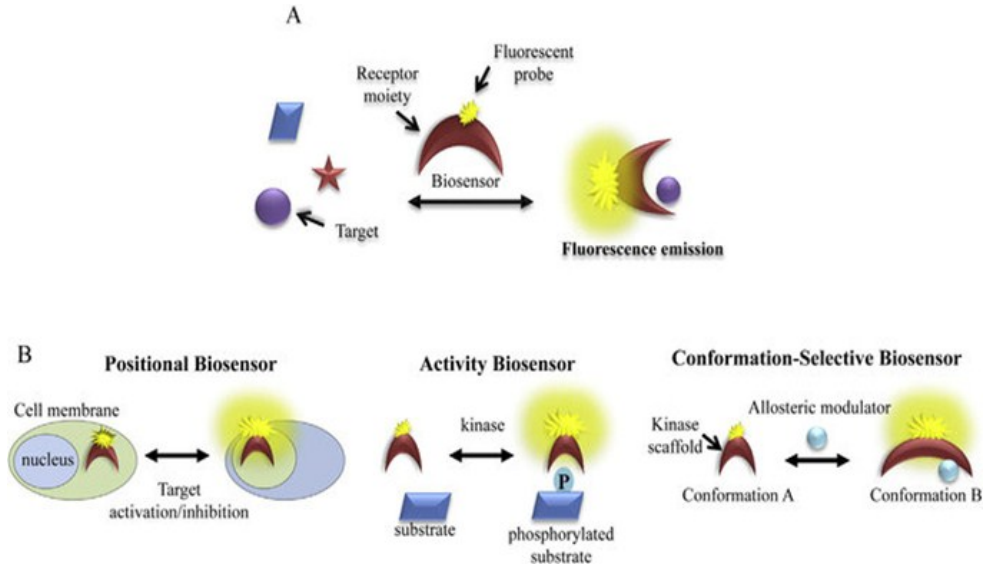

Fig. 6. Fluorescent Biosensors A. Schematic representation of a fluorescent biosensor B. Different examples of fluorescent biosensors. [28]

2.2.6. Biodefense biosensing applications

Biological assault biosensors may be employed for military objectives. These biosensors are designed to recognize biowarfare agents (BWAs), which include bacteria (vegetative and spores), poisons, and viruses. Several efforts have been made to design such biosensors utilizing molecular approaches that identify BWA chemical markers. Nucleic acid-based sensing systems are more sensitive than antibody-based detection approaches because they offer gene-based specificity without the need for amplification stages. The human papilloma virus (HPV) is divided into two types: HPV 16 and 18. A leaky surface acoustic wave peptide nucleic acid biosensor with twin two-port resonators can swiftly detect HPVs. This probe can bind to specific DNA sequences with high efficiency and accuracy.

2.2.7. In metabolic engineering

A growing demand for microbial cell factories for chemical synthesis is being driven by environmental concerns and petroleum-derived product insufficiency. Metabolic

engineering is seen as a key technique for a sustainable bioeconomy. [32] They also expect that rather of depending on petroleum refining or plant extraction, a large portion of fuels, commodity chemicals, and medications will be created from renewable feedstocks by microorganisms. The enormous variety creation capacity necessitates effective screening procedures to choose the target phenotype. Earlier enzymatic assay analytics approaches used spectroscopy but had low throughput. To overcome this barrier, researchers created genetically encoded biosensors that could be used for high-throughput screening and selection utilizing fluorescence-activated cell sorting (FACS) and cell survival. A ligand-binding peptide was sandwiched between two donor and acceptor fluorophores in FRET sensors. When a ligand of interest contacted the peptide, it changed conformation and therefore FRET. [33] Despite its high orthogonality, temporal resolution, and simplicity of assembly, FRET sensors could only report the abundance of metabolites and not regulate the signal downstream. [34] Transcription factors are naturally occurring proteins that control gene expression in response to environmental changes. [35] It is achieved by exploiting the host transcription system and driving a reporter gene with a synthetic condition specific promoter. These have weak orthogonality and noise. [36] The third family of biosensors is riboswitches, which are mRNA regulatory domains that may selectively bind ligands and modify their structure, hence controlling protein production. They are quicker than TF-based biosensors since the RNA is already transcribed, and they do not depend on protein–protein or protein–metabolite interactions. Ribosomes have recently been widely developed in bacterial systems. [37]

2.2.8. Biosensors in plant biology

Plant research has benefited from revolutionary new tools in DNA sequencing and molecular imaging. However, traditional mass spectroscopy approaches did not provide information on the position and dynamics of enzyme substrates, receptors, and transporters. Using biosensors, this data may be readily accessed. To quantify a dynamic process under physiological circumstances, we need to visualize it, such metabolite conversion or signaling events. Sensors that react dynamically may accomplish this depiction. To quantify caspase activity and manipulate calcium levels in live cells, Roger Tsien's lab was the first. [38] These sensors used FRET between two spectrum GFP versions. [39] Using chameleon sensors, researchers can monitor calcium oscillations in real time. Biosensors can discover missing components in analyte metabolism, regulation, or transport. The sucrose FRET sensor transports sucrose from the mesophyll to the phloem. Fluorimeter-based sugar transporter detection detects sugar transporters that work soon after glucose administration in deprived yeast cells. [40] Other studies have shown that biosensors may be used in genetic screening if high-throughput imaging tools are available. Using single molecule multifunctional nanocomposites, nanofilms, and nanoelectrodes [42] is still a difficulty. Processing, characterization, interface issues, availability of high-quality nanomaterials, nanomaterial tailoring, and processes influencing the behavior of these nanoscale composites on electrode surfaces are all major concerns. Improving signal-to-noise ratios, transduction, and signal amplification are other key obstacles. The next step should be to understand how nanomaterials and

biomolecules interact with electrodes or nanofilms, and to use innovative features to create a new generation of biosensors. Nonetheless, nanomaterial-based biosensors have a bright future in clinical diagnosis, food analysis, process control, and environmental monitoring.

3. Nano sensors for Detecting Plant Pathogens

Pathogen detection, identification, and evaluation are critical for scientific research, ecological monitoring, and food security. Investigators must ensure that the delicate ingredient of biological origin, or biomimetic component, interacts with the analyte in the examination. Many reliable and quick identification components, such as lectin, phage, aptamers, antibody, bacterial imprint, or cell receptor, have been discovered for bacterial exposure [43]. Bacterial receptors, antibodies, and lectins are the most often employed biosensing components. Because they may be combined into biosensors, these constituents are widely used to detect infections [44]. Aptamers, single-stranded nucleic acids, are cheaper and more stable than recognition elements based on antibodies for detecting bacteria [45]. However, they have drawbacks such as batch-to-batch variability, sturdiness in complicated materials, and preparation difficulty. The 'chemical nose' is a relatively new tool for identifying infections. It assigns diverse discriminating receptors to each aim, allowing ordering. It works like our brain when we smell anything [46]. To create a reference database, sensors are trained with competent bacterial samples. The reference catalog is used to identify bacterial pathogens [47].

4. Future scope

Ex vivo or in vivo injected genetically modified proteins into cells form cell-based biosensors. They use Biophotonics or other physical concepts to detect levels of hormones, medicines, or poisons continually and noninvasively. This might be useful in ageing studies. Marine biosensors detect eutrophication using nitrite and nitrate sensors. The Monterey Bay Aquarium Research Institute is developing an environmental sample processor that will automate the identification of harmful algae in situ from moorings using ribosomal RNA probes. Another purpose is to detect pollution, heavy metals, and pesticides using biosensors. Nanomaterials in biosensors may help develop a new generation of biosensors. Achieving single molecule biosensors with high throughput biosensor arrays requires nanomaterials with mechanical, electrochemical, optical, and magnetic capabilities. Using the structure and function of nanomaterials and biomolecules to manufacture single molecule multifunctional nanocomposites, nanofilms, and nanoelectrodes is still a problem. Processing, characterization, interface issues, availability of high-quality nanomaterials, nanomaterial tailoring, and processes influencing the behavior of these nanoscale composites on electrode surfaces are all major concerns. Improving signal-to-noise ratios, transduction, and signal amplification are other key obstacles. The next step should be to understand how nanomaterials and biomolecules interact with electrodes or nanofilms, and to use innovative features to create a new generation of biosensors. Nonetheless, nanomaterial-based biosensors have a bright future in clinical diagnosis, food analysis, process control, and environmental monitoring.

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