Review Paper:

Biosensors from the Perspective of Sensing Labelled and Unlabelled Targets

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Abstract

Biosensors are target-specific affinity based analytical tools. Their applications are vast in areas such as clinical diagnosis, food quality, environment monitoring and in other fields as well where timely and reliable analysis are required. Biosensing technology is gradually developing to produce nove.l biosensors for point-of-care diagnosis. The involvement of new advancements such as aptamer-based technologies and nano-bioelectronic technologies have great potentialto lead to the development of next generation biosensors with improved sensitivity, specificity, portability and cost effectiveness.

This review emphasizes several aspects of biosensors such as their classification, mechanism involved and their biomedical applications.

Keywords: Biosensors, aptamer-based technologies, nano-bioelectronic technologies.

Introduction

Health has been of prime importance due to the leaping life style changes. Numerous gadgets have emerged to track different health conditions. A crucial tool in the area of health research in this era of cutting-edge scientific technology is biosensors. It acts like a boon in the devil's world of diseases. It provides a suitable platform that comprises of a biological material and a sensing element. The importance of monitoring and controlling many various physiochemical parameters in fields including medical diagnosis, medication production, forensics, hygiene, food business and environmental safety is growing in modern times[111]. As a result, reliable analytical tools that deliver prompt and accurate analysis, are needed[39].

There is currently a great need for methods that are suitable for detecting and quantifying the quantities of specific elements in biological and environmental samples. It can be extremely user friendly and time-consuming to incorporate biosensors for detection, recognition and quantification. They are self-contained scientific explanatory investigative devices that metamorphose a biological response into an electrical wave. Quintessentially biosensors must be highly specific and independent of physical parameters.

In comparison to traditional photometric approaches, biosensor can operate as a sophisticated instrument that offers a number of operational benefits including speed, use, affordability, mobility and ease of mass production. It cannot be compared to other analytical equipments for the detection of a particular element. Multidisciplinary research is required for the instrumentation of biosensors, their materials, devices and immobilization techniques. It brings together specialists in chemistry, biology and engineering to create machinery that produces acceptable results.

As an analytical device, biosensors employ a biological element or bio mimic a recognition element integrated within a physicochemical transducing microsystem. The output of this is a digital electronic signal directly proportional to the concentration of a specific analyte or analytes. Miniaturization and decreased cost of biosensors further add to the enhanced analytical abilities of these devices. Research on biosensor is booming around as their applications span from medical to agriculture[115].

The biological entity of biosensors could be embodied with an enzyme, antibody, nucleic acid, lectine, hormone, cell structure or tissue. Its relevance is obvious through its specific interaction with targeted element. The impact of the biochemical interaction is consequently transformed through the transducer into a measurable response. The transducing systems can be electrochemical, optical, piezoelectric, thermometric, ion-sensitive, magnetic or acoustic one. The immobilization of a bio-component in the biosensor is of paramount significance. Performance of biosensors with immobilized molecules also depends on factors such as the chemical and physical conditions (pH, temperature and contaminants), thickness and stability of the materials[74]. Based on their applications, enzyme-based, tissue-based, immunosensors, DNA biosensors, thermal and piezoelectric biosensors have gained attention[100].

Bioreceptor Components

The newly-equipped class of sensors includes biosensors, a mix of physical and chemical sensing methods. Even IUPAC has bestowed recognition to these types of sensors[18]. A typical biosensor consists mostly of a sensing material and a transducer. Broadly biosensors can be classified into two main categories based on the sensing element used in it and depending on the transduction modes. Sensing elements include enzymes, antibodies (immunosensors), micro-organisms (whole cell biosensors), biological tissues and organelles.

The mode of transduction depends on the physiochemical change with credentials to the sensing element. Therefore, various transducers used in biosensors can be of electrochemical (amperometric, conductometric and potentiometric), optical (absorbance, fluorescence and chemiluminescence), piezoelectric (acoustic and ultrasonic) and calorimetric types[28].

Numerous substances including microorganisms, enzymes, nucleic acids, organelles, receptors, entire cells, biological tissues and biomimetic materials, can be found in bioreceptor components. There are several ways for classification of bioreceptor components but the reliable one is based on the type of biological signalling pathway they utilize or the type of signal transduction they employ.

Enzymes: Enzymes are proteins having some catalytic activity which depends on the integrity of the protein conformation from which it is generated. It always provides a special type of environment within which a reaction occurs. It confronts a pocket like configuration representing the active site, to which a target that is specific , or well suited in nature, gets attached. The attached molecule is called the substrate molecule. In the development of such target specific entities, enzymes are used as the bioreceptor components. These biosensors detect the formation of a desirable product which could be directly determined using one of the transducers. Assorted groups of enzymes are exploited to contrive the formulation of a biosensor such as oxidoreductase and malate[9].

Antibodies: When a foreign substance enters a person's body, it triggers a specific form of immune reaction against that substance by creating a particular kind of glycoprotein called an antibody; the substance in question is referred to as the antigen. All antibodies have distinct structural characteristics that enable them to bind with antigens and neutralize or eliminate those[141].

Because an antibody is always target-specific, it fits into its complementary specific targeted antigen in a very specific way. Because only the specific analytes of interest, the antigen can fit into the antibody binding site, these particular qualities of antibodies are essential to their effectiveness in immunosensors[10,180]. Such immunosensors can be developed to detect even the most severe disorders including cancer[41,92] or could be helpful to detect their markers[90,95]. They have also been of value in the bacterial and viral determination assays[21,76] and for toxin estimation[69].

Nucleic Acids: Nucleic acids are polypeptides, made up of phosphate esters of nucleosides. They have two different types of pentose sugar. The nucleic acids are of two types, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). The specific objectives of industrial and clinical chemistry are the detection of a specific nucleic acid segment connected to a specific microorganism that may be the source of an infection or the reason for food rotting[51]. This is accomplished by creating biosensors based on DNA and RNA that tie a single-stranded nucleic acid sequence to the electrode that binds to the target analytes[103]. Such biosensors based on DNA, RNA and peptides have high selectivity and sensitivity due to strong base pairing between the two complimentary nucleic acid strands[15].

Cells: The most crucial goal in the food and medical industries is the detection of bacterial cells. Diverse approaches, such as tissue-culture and microscopy, have progressed for the diagnosis of various disorders. However, there are significant drawbacks to those methods including the potential for time and financial commitment as well as the potential need for highly skilled staff. Additionally, conventional laboratory methods for detecting bacterial cells are not generally target-specific. Additionally, not all bacterial species require the same environment to survive which makes the identification process more difficult[2].

Biosensing may be an alternate resource to tackle these challenges because it offers quick, affordable detection methods without the requirement for skilled staff. This lab on a chip detection process is more trustworthy than conventional ones[151].

Methods of Signal Transduction

The several types of biosensors can also be categorized in accordance with how they transmit signals. There are various categories that the transducer component of biosensors might come inside such as electrochemical (amperometric and potentiometric), optical (absorbance, fluorescence, phosphorescence, Raman, SERS, SPR/SPRI, DHM and dispersion spectrometry), piezoelectric (acoustic and ultrasonic) and calorimetric[106].

Electrochemical Biosensors: The analytical tool known as an electrochemical biosensor combines sensitivity and selectivity. The biological components exhibit selectivity but the electro-analytical approach is sensitive. This leads to binding activity, which eventually produces an electrical signal that is proportional to the analytical concentration. For the recognition of biological components like enzymes, cells and antibodies, the chemical element present here acts as a transducer[23,40].

Existence of a matrix-bound bioactive substance paired with an electrochemical transducer is the compositional notion of an electrochemical biosensor. This will result in a charge transfer across the physio-chemical transducer's double layer which ultimately triggers detectable signals[133,154].

Classical invention of glucometer utilizing glucose oxidase-based biosensors is first in the line of introduction of electrochemical biosensors[178].

Electrochemical biosensor to determine the levels of antioxidants and reactive oxygen species in physiological systems[101] is another important contemporary achievement. Electrochemical biosensors also offer the potentiality of detecting damaged DNA as well as the carcinogens that cause the damage[183].

The electrochemical sensors have now become indispensable for clinical diagnosis of diseases[55]. Consequently, a variety of electrochemical biosensors are being created nowadays based on their merits. Due to their potential, a number of electrochemical biosensor types have arisen including the amperometric, impedimetric and potentiometric biosensors. The two most popular kinds of electrochemical biosensors among them are potentiometric and amperometric biosensors.

Amperometric Biosensor: Amperometric biosensors are among the diverse types of electrochemical biosensors that are more sensitive and suitable for mass production. Measurement of the current produced by the redox or oxidation process of the electroactive chemicals that interact with an electrode system constitutes the detection process in an amperometric biosensor. An adequate potential is established between the two electrodes in order to begin these stages and the precise potential is always dependent on the type of reaction occurring and the material employed in the electrode[19].

Here, a reference electrode receives a constant potential while the sensing electrode is subjected to a variable potential. The current between the sensing electrode and counter electrode is then seen and recorded[60,182]. The high sensitivity of an amperometric sensor contributes to the sensing ability and helps to detect the electroactive substances in biological samples. By applying a constant potential between the sensing and auxiliary electrode, the alteration of electroactive species takes place at the electrode.

This results in electron transfer, where the current is directly correlated to the bulk concentration of tested electroactive species[10,169]. Significant research efforts are put towards the detection of bacteria, virus and some other harmful molecules (Table 1). Amperometric biosensors find more use in it and are also used to determine the levels of vitamins and alpha amino acids analytically[5] and in identifying haemolytic bacteria from that of non-haemolytic in a mixed population[73].

Potentiometric Biosensor: It is well recognized that some ionic species can harm the food industry or behave as infectious agents in the medical or environmental fields. Therefore, it is essential to identify these ionic species in order to prevent food spoiling or illness. Only ionic concentration variation may be measured for this detection and the potentiometric biosensor is the most accurate tool for detecting these variations[125].

The first developed transducer for potentiometric biosensor was a pH glass and now a list of transducers are available like fluoride electrode for fabrication of the potentiometric biosensors.[126] It is also a promising tool for detection of cancer markers and cancer cells based on phage-modified Light Addressable Potentiometric Sensor (phage-LAPS).[67]

Since biosensor development has advanced significantly in recent years, their use in clinical diagnosis as opposed to other fields is quite important (Table 2). Most of the biosensors reported in the past decade are found to be based on the phenomena of molecular interactions which are essentially applied in various forms at various scales[110].

Impedimetric Biosensor: Although difficult, rapid microorganism detection is crucial for illness diagnosis and therapy. Electrochemical biosensors of the impedimetric kind, which produce accurate and unbiased data and take less time to use, would be the best option for it. The term impedimetric, derived from "impedance" implies combination of resistance or reactance. It appears to be an excellent investigation technique for both macromolecules and interfacial electrical characteristic of electrodes that is used to detect quantitative parameters .

They operate on the idea that when an analyte interacts with a bioreceptor molecule, this changes the capacitance and electron transfer resistance across the working electrode surface.When the analytes' concentration in the solution increases, the binding of analytes also increases and the impedance across the electrode surface is detected[32]. It acts as a powerful investigating device for detecting the interfacial properties associated with bio-recognition events that occur at the modified surface. The presence or absence of a redox couple can be measured by it and is referred to as faradic and non-faradic impedance measurement respectively[43].

Till date, this characteristic field of biosensors has almost got quite well in every area of life. Their recent advancements and improvements are exploited in the fields of agriculture, biomedicine, food and environmental studies (Table 3).

Optical Biosensor: Ultrasensitive biosensors were produced in huge quantities to meet the demand as a result of the rise in demand of sensors. The most diversified category of biosensors is optical biosensors which transmit signals in response to light illumination, light emission, or optical diffraction[107]. Optical biosensors use light to calculate changes in particular light wavelengths. These transducers come in a variety of configurations for luminescence, fluorescence, colorimetry and interferometry. Optical transducers transfigure the changes in wavelengths in response to analyte recognition into an electrical/digital readout[171]. Optical fibre sensors find immense potential in various fields (Table 4) such as biomedicine, environmental control, food quality test or navigation systems[29].

Sensors based on various physical or chemical principles can calculate multiple magnitudes, for example pressure, temperature or chemical compounds concentrations[30,31,42]. Use of fibre-optic chemical sensors has found use in varied fields such as drug discovery, biosensing and biomedicine. Recent studies have also indicated the use of hydrogels in DNA-based sensors[35].

Table 1
Chronological implication of Amperometric Biosensor

Analytes	Bioreceptor Elements	Application	Electrode Material	LOD
Organophosphorou[145]	Ascorbic acid oxidase	Agriculture	Clark oxygen	-
Polyphenols[52]	Laccase, *Coriolus versicolor*	Food Industry	Pt–Ag	1.0×10^{-6} M
Trypsin[66]	Glucose oxidase/ gelatin	Biomedical	Platinum	42 pM (low)
Phenolics[177]	Laccase	Environmental	Carbodiimide	-
Biogenic amines (histamine)[20]	Diamino oxidase	Food industry	Pt and Au	-
Glucose[75]	Glucose oxidase	Biomedical	ZnO nanotube	1 μM
H_2O_2 and cholesterol[33]	Cholesterol oxidase and cholesterol esterase	Biomedical	Platinum	0.5 nM (H_2O_2) 0.2 μM (cholesterol)
Lactate[150]	Lactate oxidase	Biomedical	Platinum	0.8 μM
Uric acid[24]	Uricase	Biomedical	Gold	0.01 mM
L-arginine[54]	Arginase I & urease	Biomedical	Platinum	0.038 mM
Penicillin G[124]	Penicillinase	Biomedical	Gold	4.5 nM (low)
Histamine[79]	Diamine oxidase and Horseradish Peroxidase	Food industry	Screen-printed polysulfone/carbon nanotubes/ferrocene membrane	(1.7×10^{-7} M) (low)
Glucose[58]	Polyphenilenediamine	Biomedical	Platinum disc	-
Protein p53[185]	Biofuel-Cell	Biomedical	Graphene/platinum	1 pM
Uric acid[56]	Alkanethiolate	Biomedical	Platinum black (Pt-B)	-
Lead & Mercury[78]	Urease	Environmental	Pt/CeO_2/urease	0.019 ± 0.001 μM
E. coli[34]	Antibody	Food industry	Nickel oxide	10^1 to 10^7 cells/mL
Triglycerides[96]	Lipase, glycerol-3-phosphate oxidase and glycerol kinase	Food industry	-	-
Tyramine[158]	Tyrosinase	Food industry	Glassy carbon	0.71 μM
Glyphosate[159]	Tyrosinase	Environmental	Screen printed chitosan	6.5 nM (1.1 μg L^{-1})
Glutamate[159]	Glutamate oxidase	Food industry	Platinum disc	-
Oxidized glutathione (GSSG)[4]	Glutathione reductase	Biomedical	GR-CoS_2/rGO	0.48 μM
L-phenylalanine[11]	L-phenylalanine dehydrogenase and Toluidine Blue O	Biomedical	Platinum	1.0×10^{-8} M
Brucella[25]	Graphene oxide/ polypyrrole nanohybrids	Biomedical	Gold	2.2×10^2 CFU/mL
Cholesterol[63]	Horseradish Peroxidase	Biomedical	Silver	2.5 to 60 mg dL^{-1}
Pyruvate[93]	Pyruvate oxidase	Biomedical	Pencil graphite	0.58 μM
Ascorbic acid (AA) & dopamine (DA)[161]	Graphene oxide	Biomedical	(GO/P(ANI-co-THI))	242 Mm/ 2 μM
Fucose[168]	L- fucose	Biomedical	Gold nanoparticle (AuNP)-modified	13.6 μM
D-serine[114]	D-amino acid oxidase	Biomedical	Platinum	1–5 μM

Table 2
Chronological implication of Potentiometric Biosensor

Analytes	Bioreceptor Elements	Application	Electrode Material	LOD
Mercury[77]	Urease	Environmental, Biomedical	Iridium oxide	0.2 -2 mM
Lysine[179]	Lysine oxidase	Food industry	$NH4^{+}$	-
Creatinine[160]	Creatinine deiminase	Biomedical	ISFETs	20 µM
Escherichia coli[44]	Antibody	Food industry	Silicon	10 cells/ml
Terbuthylazine[112]	Antibody	Environmental	LAPS urease conjugated	1.5–10 µg/l
Cyanide[71]	Cyanidase	Environmental	Ammonia	1×10^{-6} - 1×10^{-4}
Phosphate[1]	BSA and GLA	Environmental	-	20 -200 µM
Uric acid[87]	Uricase, Catalase	Biomedical	SnO/sub 2/ / ITO glass	2 mg/dl -7 mg/dl
Lactate[91]	Lactate dehydrogenase	Food industry/ Biomedical	Ag/AgCl	2×10^{-7} M
Creatinine[142]	Creatinine deaminase	Environmental	Enzymatic Membrane	0.3 µM
Triglycerides[155]	Lipase	Biomedical	Silicon	-
Urea[3]	Urease, Bovine Serum Albumin	Biomedical	Indiumtinoxide coated glass plate	6.6×10^{-6} to 7.5×10^{-4} M
Urea[173]	Urease	Food industry	NH_4^{+} ion/ Ag/AgCl	2.5×10^{-5} mol/L
Glucose[181]	Glucose oxidase	Biomedical	Platinum	-
Diclofenac[17]	Graphene and its derivative	Environmental	Carbon	9.79 µM
Urea[120]	Urease	Biomedical	Ammonium	0.77 µM
Staphylococcus aureus[61]	Graphene	Biomedical	Grapheme/ carbon	1 CFU/mL(graphene)8×10^{2} CFU /mL (high)
Formaldehyde[89]	Alcohol oxidase	Food industry	H^{+} ion/ Ag/AgCl	0.3–316.2 mM
Cholesterol[137]	Cholesterol oxidase	Biomedical	Copper	1×10^{-6} M to 1×10^{-3} M
Glucose[6]	Glucose oxidase	Biomedical	Ag/AgCl (quantum dots)	1×10^{-5} M to 1×10^{-2} M
Phosphate[84]	Purine nucleoside phosphorylase and Xanthine oxidase	Biomedical	Platinum	20.0 µM (low)
Creatinine[98]	Creatinine deiminase	Biomedical	-	0.02–2 mM
L-lysine[189]	Lysine oxidase	Biomedical	Ammoniumselective polyvinylchloride membrane	-
Urea[82]	Urease	Biomedical	Indium tin oxide glass	5 mM (high)
Cyanide[81]	Cyanide dihydratase	Environmental	Ammonium	1×10^{-9} M
Aflatoxin B1[164]	Acetylcholinesterase	Food industry	Enzyme	-
Salmonella typhimurium[157]	Antibody	Food industry	Paper-based strip	5 cells mL^{-1}
Serotonin[119]	Nano filter film/ aryldiazonium salt	Biomedical	Gold	-

Table 3
Chronological implication of Impedimetric Biosensor

Analytes	Bioreceptor element	Application	Electrode Material	LOD
Trypanosoma cruzi[37]	Antibody	Biomedical	Gold and platinum	-
Bacteria[140]	Antibody	Environmental	Gold	-
E. coli[139]	Antibodies	Food industry	Gold	10^4–10^7 CFU/mL
Salmonella[72]	antibody	Food industry	Gold	10^4 CFU/mL - 10^6 CFU/mL
Atrazine[148]	Antibody	Food industry	Gold/Cr	5.76 ppb
E. coli[53]	Antibody	Biomedical	Gold SPEs	104 CFU/ml
Aflatoxin M[36]	ss-HSDNA	Food industry	Cysteamine and gold	0.039 ng/mL
Trichloroethylene[62]	*Pseudomonas putida* F1 strain	Environmental	Gold	20 µg L^{-1}
Dengue[117]	Primer of ST1, ST2 and ST3	Biomedical	AuNpPANI	-
E. coli[27]	Antibody	Biomedical	Polyaniline	10^7 CFU mL^{-1}
DNA hybridization[57]	DNA probes	Biomedical/ Forensic	Glassy carbon electrode	1.10×10^{-14} M
Sulfate-reducing bacteria[138]	RGSs-CS hybrid film	Environmental	Indium tin oxide	0.7×10^4 cfu mL^{-1}
Diazinon[191]	Lipase	Environmental	Gold	10 nM
Dengue[22]	Anti-NS1	Biomedical	Gold	3 ng mL^{-1}
Progesterone[68]	ssDNA	Biomedical	Gold	0.90 ng/mL
Lindane[149]	*Streptomyces* strai n M7	Environmental	Stainless steel	10 µg L^{-1}
Influenza viruses H3N2[65]	Antibody	Biomedical	Glycans printed glass	13/1 µl
E. coli[188]	Lectin	Biomedical/ Food industry/ Environmental	Gold	75 cells/mL
Trinitrotoluene (TNT)[85]	Anti-TNT peptide	Environmental	Gold	0.15 pM
Bacteria[146]	Lectin *Concanava lin A*	Environmental	Carbon	1.9×10^3 CFU mL^{-1} (low)
E. coli[88]	Antibody	Biomedical/ Food industry	Gold	140 cfu mL^{-1} (low)
Hemagglutinin (HA)[143]	ss-cDNA	Biomedical	Gold	0.004 ng
Salmonella[94]	Nisin	Food industry	Gold	1.5 * 10^1 CFU/mL
Tetracycline (TET)[144]	Grapheme oxide	Food industry	Pencil graphite	3×10^{-17} M
Candida spp[152]	Concanavalin A	Biomedical	Gold	10^2 to 10^6 CFU mL^{-1}
ctDNA[174]	dCas9-sgRNA	Biomedical	GPHOXE	0.65 nM
ochratoxin[196]	thermolysin	Biomedical	Gold	0.2 nM

For these diverse applications, optical biosensors can use a variety of techniques including surface plasmon resonance (SPR), surface plasmon resonance imaging (SPRi), fluorescence, chemiluminescence, light absorbance, phosphorescence, light polarization and rotation, total internal reflectance and photothermal techniques[16].

Piezoelectric Biosensor: Piezoelectric sensors have gained popularity among biosensors and have begun to take the place of conventional immunoassay tools. Moreover, they can be fabricated without the need of high priced sophisticated or hazardous labels[99,135,162]. The ability of a material to generate voltage when mechanically strained is referred to as piezoelectricity or piezoelectric result[129]. The alternating voltage produced in it can cause mechanical oscillations of crystal, the frequency of oscillation is observed as the crystal is put into oscillation circuit[49]. Analyte or any other mass bound on the surface of crystal or on surface of electrodes located on the crystal results in change of oscillation frequency[132].

When designing such sensors, some special factors like fragility and the sensitivity in micrograms needed to make quantifiable changes in oscillations must be taken into account[128]. Piezoelectric biosensors act as DNA biosensors for diagnosis of genetically linked diseases like mutation in DC17 of beta-thalassemia gene that can be detected using a DNA probe[121]. Additionally it had an impact on industries like water, food, agriculture, pharmaceuticals, healthcare and cuisine (Table 5).

Calorimetric Biosensor: The calorimetric biosensor, which has many uses in the discipline of nanotechnology, is the most widely used biosensor in diagnostics. It is additionally utilized to measure exothermic processes. Since many enzymatic reactions produce heat, the analyte concentration is determined by changes in the heat produced. Enthalpy variations which provide information about substrate concentration indirectly, are measured and calculated to track the reaction[8].

Most biological activities in calorimetric transducers are accompanied by either heat production or absorption[8]. Exothermic reactions, which are those that are catalyzed by an enzyme, produce heat that can be utilized to estimate the rate of the reaction and the concentration of analytes (Table 6).

Limitations of Biosensors

The most crucial task of a biosensor is the selection and binding of a small molecule with the receptor element. However, tiny compounds have many constraints such as limited sensitivity and complicated sample processing, which make it exceedingly difficult to interact with the receptor element.

Discussion

SELEX (Systematic Evolution of Ligands by Exponential Enrichment) is also known as aptamer selection process. This technique is used to select aptamers for strong binding or fixing with the target molecule on the surface of the receptor. In comparison with the macromolecules, the binding of small molecules is difficult as the aptamers often do not recognise the target molecules and bind with the other derivatives[186]. The process of SELEX includes:

1) Incubation of target molecules with random sequence pool. 2) Separation of unbound molecules 3) Amplification of the bound molecules[187] which help to overcome the difficulties. Hence, the concept of SELEX could be employed as a tool to eliminate the limitation caused due to low sensitivity during the interaction of small molecules with the receptor.

Table 4
Chronological implication of Optical Biosensors

Analytes	Bioreceptor elements	Application	LOD
Carbaryl and dichlorvos[7]	Cholinesterase	Environmental	5.0–30 ppb and 108–5.2 ppb
Salmonella typhimurium[167]	Antibody	Food industry	8×104 CFU/mL
Chloramphenicol (CAP)[122]	Anti-CAP antibody	Food industry	10−8 M
Atrazine[45]	Polyclonal antibodies	Environmental	20 ppt
E. coli[38]	Antibody	Environmental	9×101 and 1.8× 105 CFU/mL
Mercury[136]	urease	Environmental	1.00 µMol
Ethanol determination[80]	Alcohol dehydrogenase	Biomedical	1.00–300 µMol
Propazine[123]	Microalgae	Environmental	7.6µg L^{-1}
Cadmium[175]	Bacillus badius and phenol	Food industry	0.1 µg/L
Toluene[194]	Toluene *ortho*-monooxygenase (TOM)	Environmental	3.00 µMol
E. coli[113]	Polyclonal antibody of anti-*E.coli*	Biomedical	15cells/ml
E. coli[172]	T4 bacteriophage	Food industry	10^3 CFU/ml
Salmonella typhimurium[46]	Polyclonal antibody of anti-Salmonella	Food industry	10 CFU/ml
Staphylococcus aureus[50]	Potato lectin	Biomedical	15000 CFU/ml
Mycobacterium tuberculosis[97]	Anti-TB antibodies	Biomedical	

Table 5
Chronological implication of Piezoelectric Biosensor

Analytes	Bioreceptor Elements	Application	Electrode Material	LOD
Aeromonas hydrophila[170]	DNA	Environmental	Gold	-
Helicobacter pylori[166]	Antibody	Biomedical	-	-
β-indole acetic acid (IAA)[85]	Antibody	Plant	-	-
Hepatitis B virus[195]	Nucleic acid	Biomedical	Gold	0.02–0.14 µg/ml
acetochlor[190]	Antibody	Agriculture	-	-
β-Thalassemia[105]	Oligonucleotide	Biomedical	Gold	-
DN[104]	Complimentary DNA strand	Biomedical	-	-
Mutation on *TP53*[12]	DNA	Biomedical	Gold	-
Francisellatularensis[127]	Antigen	Biomedical	-	-
E. coli[184]	DNA	Environment/ Food industry	Gold	-
Escherichia coli[26]	Thiol	Food industry	Gold	10^2 to 10^6 CFU/ml
M. tuberculosis[70]	Thiol-modified oligonucleotide	Biomedical	-	-
Prostate specific antigen and α-fetoprotein[165]	Antibody	Biomedical	Gold	0.25 ng/ml
Pesticide[156]	Acetylcholinesterases	Agriculture	Enzyme	-
Systemic Lupus Erythematosus[116]	TRIM21 and TROVE2 autoantigens	Biomedical	Gold	0.01 U/mL
Tumor Necrosis Factorα[130]	Antibody	Biomedical	-	1.62 pg/ml
C-reactive protein[131]	Antibody	Biomedical	Gold	0.080 mg/l
Tilletia indica[108]	Antibody	Agriculture	Microcantilever	-
Glomalin[134]	Antibody	Environment	Iron oxide	2.4 µg/g
Viral hemorrhagicsepticemia virus[109]	Thiol	Environment	PGE	10^{-4} to 10^{-10} M

Table 6
Chronological implication of Calorimetric Biosensor

Analytes	Bioreceptor Elements	Application	LOD
Glucose[59]	Glucose oxidase and catalase	Biomedical	-
Dichlorvos[192]	Chicken liver-esterase	Environmental	-
Ascorbic acid[176]	Ascorbate oxidase	Food industry	0.8 mM
Fructose[14]	Hexokinase	Food industry	0.12 mM
Organophosphorus[193]	Chicken liver esterase	Environmental	-
Creatinine[48]	Creatinine deiminase	Biomedical	-
Creatinine[47]	Creatinine Deiminase	Biomedical	-
TNF-α[13]	Antibody	Biomedical	14 pg mL^{-1}

With immense growth in science, nanotechnology also possesses a lot of potential to extend the range of detection. Nano sensors allow the flexibility of real-time sensing with reliability and speed. The efficiency of SPR and SERS based sensors has been increased by nano-patterning the substrates. Such nanofabrication strategies have led to research on the use of hyperbolic meta-materials[83]. The amalgamation of microfluidics and bio sensing has brought together several assays on a single platform, which has enabled handling volumes as low as Pico litres effortlessly[118].

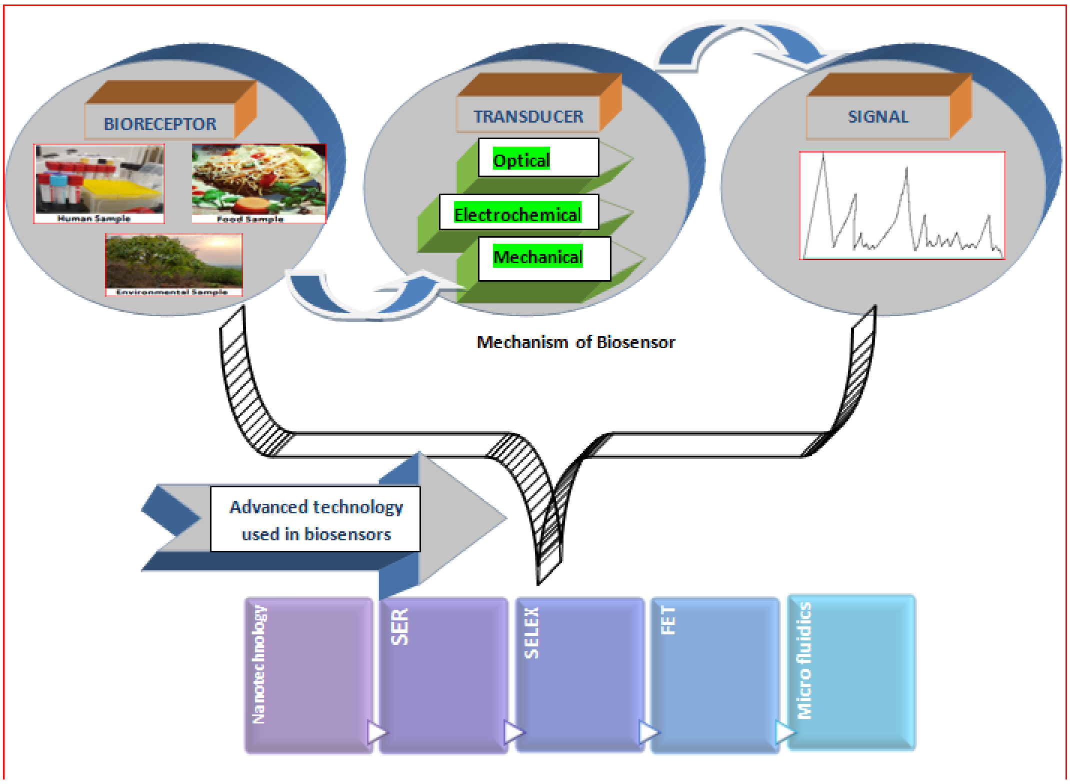

Figure 1: Methods to improve affinity of biosensors

Universal platforms for sensing have been designed using monolayer of graphene oxide as an inhibitor and specific DNA templates[64]. This has been reported to offer enhanced sensitivity, selectivity and detection. Such label-free technology has allowed increased analytical efficiency, reproducibility and cost-effective production methods. Since the output in these methods is dependent on the direct interaction of the target and the biomolecule, the probability of erroneous results is minimal.[147]

Among these, the recent advancements include the field effect transistor (FET) which are used as enzyme based and immune-based biosensors. Some other types of FET biosensors use carbon nanotubes, silicon nanowires and graphene. A magneto elastic biosensor uses a magnetic strip to detect any molecule of interest under an applied magnetic field[153].

Reflective phantom interface (RPI) has also enabled the detection of small molecules such as fluorinated materials based on the refractive index[163]. Numerous research studies have been carried out on the use of biosensors for application in diverse fields ranging from agriculture to medicine. Nevertheless, hardly few ideas are translated and reach the market. Often, several ethical, legal and technical issues limit the advancement of such research. However, with the rapidly increasing need, the scope and needs of such research will be met in the future (Figure 1).

Conclusion

Concept of sensing research and development has gained interdisciplinary acclamation in biological science as well as in engineering. The last decade has witnessed significant breakthroughs in the field of biosensors on a variety of fronts. It is explicated as "a device that detects physiological data and converts it to usable, distinguishable signals such as colour, fluorescence and electrical impulses by employing or emulating biological elements. This dynamic tool has been used in a variety of fields including life science research, health care, environment, food and military applications. In comparison with conventional assays, the dramatic advantages and numerous applications of biosensors in dynamic real-time application show the potential of biosensors in the practical arena. The development of biosensors is trending towards downsizing of devices and integration of technical breakthroughs such as surface chemistry and transduction systems. For such activity, biosensor technology has garnered considerable attention in the last decade since it is a good candidate for lower detection limits with rapid analysis time at relatively low cost. The sensitivity and selectivity of the various extant biosensor prototypes are extremely high and further advancements are anticipated.

However, at present, biosensor research is not only fuelling the never-ending race to build smaller, quicker, cheaper and more efficient gadgets, but it may also lead to the successful integration of electrical and biological systems. As a result, the future development of extremely sensitive, highly specific, multi-analysis, nanoscale biosensors and bioelectronics will necessitate the integration of a wide range of interdisciplinary expertise. Any innovation in this subject will have an impact on diagnostics and health treatment in the future.

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References
1. Adeloju S. and Lawal A., Polypyrrole-based bilayer biosensor for potentiometric determination of phosphate in natural waters, *International Journal of Environmental Analytical Chemistry*, **85**, 771-780 **(2005)**

2. Ahmed A., Rushworth J.V., Hirst N.A. and Millner P.A., Biosensors for Whole-Cell Bacterial Detection, *American Society of Microbiology*, **27(3)**, 631-646 **(2014)**

3. Ahujaa T., Mira I.A., Kumar D. and Rajesh, Potentiometric urea biosensor based on BSA embedded surface modified polypyrrole film, *Sensors and Actuators B*, **134**, 140-145 **(2008)**

4. Aksoy M. and Kiransan K.D., The Construction and Testing of an Amperometric Biosensor for Oxidized Glutathione with Glutathione Reductase Immobilized on Reduced Graphene Oxide Paper Modified with Cobalt Sulphur, *Chemistry Select*, **5(44),** 13925-13935 **(2020)**

5. Alaejos M.S. and Montelongo F.J.C., Application of Amperometric Biosensors to the Determination of Vitamins and α-Amino Acids, *Chemical Reviews*, **104**, 3239-3265 **(2004)**

6. Alvi N.H., Rodriguez P.E.D.S., Gomez V.J., Kumar P., Amin G., Nur O., Willander M. and Notzel R., Highly efficient potentiometric glucose biosensor based on functionalized InN quantum dots, *Applied Physics*, **101,** 153110 **(2012)**

7. Andreou V.G. and Clonis Y.D., A portable fiber-optic pesticide biosensor based on immobilized cholinesterase and sol-gel entrapped bromcresol purple for in-field use, *Biosensors and Bioelectronics*, **17**, 61-69 **(2002)**

8. Antonelli M.L., Spadaro C. and Tornelli R.F., A microcalorimetric sensor for food and cosmetic analyses: l-Malic acid determination, *Talanta*, **74**, 1450-1454 **(2008)**

9. Arif M., Setford S.J., Burton K.S. and Tothill I.E., L-Malic acid biosensor for field-based evaluation of apple, potato and tomato horticultural produce, *Analyst*, **127**, 104-108 **(2002)**

10. Arora N., Recent Advances in Biosensors Technology: A Review, *Octa Journal of Biosciences*, **1(2)**, 147-150 **(2013)**

11. Arslan H., Unal K., Koyuncu E.A., Yildirim E. and Arslan F., Development of a Novel Phenylalanine Biosensor for Diagnosis of Phenylketonuria, *IEEE Sensors Journal*, **20(20)**, 12127-12133 **(2020)**

12. Atti D.D. et al, Detection of clinically relevant point mutations by a novel piezoelectric biosensor, *Biosensors and Bioelectronics*, **21(10)**, 1876-1879 **(2006)**

13. Bari S.M.I., Reis L.G. and Nestorova G.G., Calorimetric sandwich-type immunosensor for quantification of TNF-α, *Biosensora and Bioelectronics*, **126**, 82-87 **(2019)**

14. Bhand S.G., Soundararajan S., Warnmark J.S., Milea J.S., Dey E.S., Yakovleva M. and Danielsson B., Fructose-selective calorimetric biosensor in flow injection analysis, *Analytica Chimica Acta*, **668(1)**, 13-18 **(2010)**

15. Borgmann S., Schulte A., Neugebauer S. and Schuhmann W., Amperometric Biosensors, Advances in Electrochemical Science and Engineering, 1-83 **(2011)**

16. Borisov S.M. and Wolfbeis O.S., Optical Biosensors, *Chemical Review*, **108(2)**, 423-61 **(2008)**

17. Boumya W., Taoufik N., Achak M., Bessbousse H., Elhalil A. and Bark N., Electrochemical sensors and biosensors for the determination of diclofenac in pharmaceutical, biological and water samples, *Talanta*, **3**, 100026 **(2021)**

18. Buenger D., Topuz F. and Groll J., Hydrogels in sensing applications, *Progress in Polymer Science*, **37(12)**, 1678-1719 **(2012)**

19. Cano-Quintero J.B., Buonasera K. and Pezzotti G., Transduction methods used on biosensors: amperometry and fluorescence, *Revista Facultad de Ingeniería*, **72**, 104-115 **(2014)**

20. Carelli D., Centonze D., Palermo C., Quinto M. and Rotunno T., An interference free amperometric biosensor for the detection of biogenic amines in food products, *Biosensors and Bioelectronics*, **23(5)**, 640-647 **(2007)**

21. Carnes E. and Wilkins E., The Development of A New, Rapid, Amperometric Immunosensor for the Detection of Low Concentrations of Bacteria Part I: Design of the Detection System and Applications, *American Journal of Applied Sciences*, **2(3)**, 597-606 **(2005)**

22. Cecchetto J., Carvalho F.C., Santo A., Fernandes F.C.B. and Bueno P.R., An impedimetric biosensor to test neat serum for dengue diagnosis, *Sensors and Actuator B: Chemical*, **213**, 150-154 **(2015)**

23. Chaubey A. and Malhotra B.D., Mediated biosensors, *Biosensors & Bioelectronics*, **17**, 441-456 **(2002)**

24. Chauhan N. and Pundir C.S., An amperometric uric acid biosensor based on multiwalled carbon nanotube-gold nanoparticle composite, *Analytical Biochemistry*, **413(2)**, 97-103 **(2011)**

25. Chen H., Cui C., Ma X., Yang W. and Zuo Y., Amperometric Biosensor for Brucella Testing through Molecular Orientation Technology in Combination with Signal Amplification Technology, *Chem Electro Chem*, **7(12),** 2672-2679 **(2020)**

26. Chen S.H., Wu V.C.H., Chuang Y.C. and Lin C.S., Using oligonucleotide-functionalized Au nanoparticles to rapidly detect foodborne pathogens on a piezoelectric biosensor, *Journal of Microbiological Methods*, **73(1)**, 7-17 **(2008)**

27. Chowdhury A.D., De A., Chaudhuri C.R., Bandyopadhyay K. and Sen P., Label free polyaniline based impedimetric biosensor for detection of E. coli O157:H7 Bacteria, *Sensors and Actuator B: Chemical*, **171**, 916-923 **(2012)**

28. Corcuera J.I. and Cavalieri P.R., Encyclopedia of Agricultural, Food and Biological Engineering, Biosensors **(2003)**

29. Culshaw B., Optical fiber sensor technologies: opportunities and - perhaps – pitfalls, *Journal of Lightwave Technology*, **22(1)**, 39-50 **(2004)**

30. Culshaw B. and Kersey A., Fiber-optic sensing: A historical perspective, *Journal of Lightwave Technology*, **26(9)**, 1064-78 **(2008)**

31. Cusano A., López-Higuera J.M., Matias I.R. and Culshaw B., Editorial optical fiber sensor technology and applications, *IEEE Sensors Journal*, **8(7)**, 1052-4 **(2008)**

32. Daniels J.S. and Pourmand N., Label-free impedance biosensors: opportunities and challenges, *Electroanalysis*, **19**, 1239-1257 **(2007)**

33. Dey R.S. and Raj C.R., Development of an Amperometric Cholesterol Biosensor Based on Graphene−Pt Nanoparticle Hybrid Material, *Journal of Physical Chemistry C*, **114(49)**, 21427-21433 **(2010)**

34. Dhull N., Kaur G., Jain P., Mishra P., Singh D., Ganju L., Gupta V. and Tomar M.O., Label-free amperometric biosensor for Escherichia coli O157:H7 detection, *Applied Surface Science*, **495,** 143548 **(2019)**

35. Dias A.D., Kingsley D.M. and Corr D.T., Recent advances in bioprinting and applications for biosensing, *Biosensors*, **4**, 111-136 **(2014)**

36. Dinckaya E., Kinik O., Sezginturk M.K., Altug C. and Akkoca A., Development of an impedimetric aflatoxin M1 biosensor based on a DNA probe and gold nanoparticles, *Biosensors and Bioelectronics*, **26(9)**, 3806-3811 **(2011)**

37. Diniz F.B., Ueta R.R., Pedrosa A.M.C., Areisa M.C., Pereira V.R.A., Silva E.D., Silva J.G., Ferreira A.G.P. and Gomes Y.M., Impedimetric evaluation for diagnosis of Chagas' disease: antigen-antibody interactions on metallic electrodes, *Biosensors and Bioelectronics*, **19(2)**, 79-84 **(2003)**

38. Dudak F.C. and Boyac I.H., Development of an immunosensor based on surface plasmon resonance for enumeration of Escherichia coli in water samples, *Food Research International*, **40(7)**, 803-807 **(2007)**

39. Dzyadevych S.V., Arkhypova V.N., Soldatkin A.P. and Elskaya, Amperometric enzyme biosensors: Past, present and future, *Elsevier*, **29**, 171-180 **(2008)**

40. Eggins B., Chemical sensors and biosensors. Analytical Techniques in the Sciences, John Wiley & Sons, West Sussex **(2002)**

41. Ehrhart J.C., Bennetau B., Renaud L., Madrange J.P., Thomas L., Morisot J., Brosseau A., Allano S., Tauc P. and Tran P.L., A new immunosensor for breast cancer cell detection using antibody-coated long alkylsilane self-assembled monolayers in a parallel plate flow chamber, *Biosensors and Bioelectronics*, **24**, 467-474 **(2008)**

42. Elosua C., Bariain C. and Matias I.R., Optical fiber sensing applications: detection and identification of gases and volatile organic compounds, Fiber Optic Sensors, 27-52 **(2012)**

43. Elshafey R., Tavares A.C., Siaj M. and Zouro M., Electrochemical impedance immunosensor based on gold nanoparticles-protein G for the detection of cancer marker epidermal growth factor receptor in human plasma and brain tissue, *Biosensors & Bioelectronics*, **50**, 143-149 **(2013)**

44. Ercole C., Gallo M.D., Mosiello L., Baccella S. and Lepidi A., *Escherichia coli* detection in vegetable food by a potentiometric biosensor, *Sensors and Actuators B: Chemical*, **91(1)**, 163-168 **(2003)**

45. Farre M., Martinez E., Ramon J., Navarro A., Radjenovic J., Mauriz E., Lechuga L., Marco M.P. and Barcelo D., Part per trillion determination of atrazine in natural water samples by a surface plasmon resonance immunosensor, *Analytical and Bioanalytical Chemistry*, **388**, 207-214 **(2007)**

46. Fronczek C.F., You D.J. and Yoon J.Y., Single-pipetting microfluidic assay device for rapid detection of Salmonella from poultry package, *Biosensors and Bioelectronics*, **40(1)**, 342-349 **(2013)**

47. Gaddes D., Reeves W.B. and Tadigadapa S., Calorimetric Biosensing System for Quantification of Urinary Creatinine, *ACS Sensors*, **2(6)**, 796-802 **(2017)**

48. Gaddes D.E. and Tadigadapa S., Microcalorimetric detection of creatinine in urine, Proceedings of the 2016 IEEE SENSORS; Orlando, FL, USA, 1-3 **(2016)**

49. Garcia-Martinez G, Bustabad E.A., Perrot H., Gabrielli C., Bucur B., Lazerges M., Rose D., Rodriguez-Pardo L., Farina J., Compere C. and Vives A.A., Development of a mass sensitive quartz crystal microbalance (QCM)-based DNA biosensor using a 50 mHz electronic oscillator circuit, *Sensors*, **11**, 7656-7664 **(2011)**

50. Gasparyan V.K. and Bazukyan I.L., Lectin sensitized anisotropic silver nanoparticles for detection of some bacteria, *Analytical Chimca Acta*, **766**, 83-87 **(2013)**

51. Ghindilis A.L., Atanasov P., Wilkins M. and Wilkins E., Immunosensors: electrochemical sensing and other engineering approaches, *Biosensors and Bioelectronics*, **13**, 113-131 **(1998)**

52. Gomes S.A.S.S., Nogueira J.M.F. and Rebelo M.J.F., An amperometric biosensor for polyphenolic compounds in red wine, *Biosensors and Bioelectronics*, **20(6)**, 1211-1216 **(2004)**

53. Gomez V.E., Campuzano S., Pedrero M. and Pingarron J.M., Gold screen-printed-based impedimetric immunobiosensors for direct and sensitive Escherichia coli quantisation, *Journal of Biosciences*, **24(11)**, 3365-3371 **(2009)**

54. Goncalves L.M., Callera W.F.A., Sotomavor M.D.P.T. and Buenno P.R., Penicillinase-based amperometric biosensor for penicillin G, *Electrochemistry Communications*, **38**, 131-133 **(2013)**

55. Gruhl F.J., Rapp B.E. and Lange K., Biosensors for diagnostic applica-tions, *Advanced Biotechnology and Biochemical Engineering*, **133**, 115-148 **(2013)**

56. Gumpu M.B., Krishnan U.M. and Rayappan J.B.B., Design and development of amperometric biosensor for the detection of lead

and mercury ions in water matrix-a permeability approach, *Analytical and Bioanalytical Chemistry*, **409**, 4257-4266 **(2017)**

57. Gupta V.K., Yola M.L., Qureshi M.S., Solak O., Atar N. and Ustundag Z., A novel impedimetric biosensor based on graphene oxide/gold nanoplatform for detection of DNA arrays, *Sensors and Actuator B: Chemical*, **188**, 1201-1211 **(2013)**

58. Han Y., Chabu J.M., Hu S., Deng L., Liu Y.N. and Guo S., Rational Tuning of the Electrocatalytic Nanobiointerface for a "Turn-Off" Biofuel-Cell-Based Self-Powered Biosensor for p53 Protein, *Journal of Chemistry*, **21(37)**, 13045-13051 **(2015)**

59. Harborn U., Raghavan B. and Danielsson V.B., Evaluation of a miniaturized thermal biosensor for the determination of glucose in whole blood, *Clinica Chimica Acta*, **267(2)**, 225-237 **(1997)**

60. Hayat A., Catanante G. and Marty J.L., Current trends in nanomaterial-based amperometric biosensors, *Sensors*, **14**, 23439−23461 **(2014)**

61. Hernandez R., Valles C., Maser W.K., Ruis X. and Riu J., Graphene-based potentiometric biosensor for the immediate detection of living bacteria, *Biosensor and Bioelectronics*, **54**, 553-557 **(2014)**

62. Hnaien M., Bourigua S., Bessueille F., Bausells J., Errachid A., Lagarde F. and Renault J.N., Impedimetric microbial biosensor based on single wall carbon nanotube modified microelectrodes for trichloroethylene detection, *Electrochemical Acta*, **56(28)**, 10353-10358 **(2011)**

63. Hooda V. and Gahlaut A., Amperometric Cholesterol Determination Using HRP Incorporated Carbon Paste Electrode, *Biosciences, Biotechnology Research Asia*, 10 **(2020)**

64. Huang Z., Luo Z., Chen J, et al. A Facile, Label-Free and Universal Biosensor Platform Based on Target-Induced Graphene Oxide Constrained DNA Dissociation Coupling with Improved Strand Displacement Amplification, *ACS Sensors*, **(2018)**

65. Hushegyi A., Pihikova D., Bertok T., Adam V., Kizek R. and Tkac J., Ultrasensitive detection of influenza viruses with a glycan-based impedimetric biosensor, *Biosensor and Bioelectronics*, **79**, 644-649 **(2016)**

66. Ionescu R., Cosnier S. and Marks, R.S., Protease Amperometric Sensor, *Analytical Chemistry*, **78(18)**, 6327-6331 **(2006)**

67. Jia Y., Qin M., Zhang H., Niu W., Li X., Wang L., Li X., Bai Y., Cao Y. and Feng X., Label-free biosensor: a novel phage-Modified Light Addressable Potentiometric Sensor system for cancer cell monitoring, *Biosensors & Bioelectronics*, **22(12)**, 3261-3266 **(2007)**

68. Jimenez G.C., Eissa S., Ng A., Alhadram H., Zourob M. and Siai M., Aptamer-Based Label-Free Impedimetric Biosensor for Detection of Progesterone, *Analytical Chemistry*, **87(2)**, 1075-1082 **(2015)**

69. Kadir M.K.A. and Tothill I.E., Development of an Electrochemical Immunosensor for Fumonisins Detection in Foods, *Toxins*. **2**, 382-398 **(2010)**

70. Kaewphinit T., Santiwatanakul S., Promptmas C. and Chansiri K., Detection of Non-Amplified Mycobacterium tuberculosis Genomic DNA Using Piezoelectric DNA-Based Biosensors, *Sensor*, **10(3),** 1846-1858 **(2010)**

71. Keusgen M., Kloock J.P., Knobbe D.T., Jungel M., Krest I., Goldbach M., Klein, W. and Schoning M.J., Direct determination of cyanides by potentiometric biosensors, *Sensors and Actuators B: Chemical*, **103**, 380-385 **(2004)**

72. Kim G., Mun, J.H. and Om A.S., Nano-particle enhanced impedimetric biosensor for detection of foodborne pathogens, *Journal of Physics*, **61**, 555-559 **(2007)**

73. Kim H.J., Bennetto H.P., Halablab M.A., Choi C.H. and Yoon S., Performance of an electrochemical sensor with different types of liposomal mediators for the detection of hemolytic bacteria, *Sensors & Actuators, B: Chemical*, **119**, 143-149 **(2006)**

74. Kissinger P.T., Biosensors-a perspective, *Elsevier*, **20(12)**, 2512-2516 **(2005)**

75. Kong T., Che,Y., Ye Y., Zhang K., Wang Z. and Wang X., An amperometric glucose biosensor based on the immobilization of glucose oxidase on the ZnO nanotubes, *Sensors and Actuators B: Chemical*, **138(1)**, 344-350 **(2008)**

76. Konig B. and Gratzel M., Detection of Viruses and Bacteria with Piezoelectric Immunosensors, *Analytical Letters*, **26**, 1567-1575 **(1993)**

77. Krawczyk T.K.S., Moszczynska M.G. and Trojanowicz M., Inhibitive determination of mercury and other metal ions by potentiometric urea biosensor, *Biosensors & Bioelectronics*, **15**, 681-691 **(2000)**

78. Kucherenko D.Y., Kucherenko I.S., Soldatkin O.O. and Soldatkin A.P., Application of glutamate-sensitive biosensor for analysis of foodstuff, *Biotechnology*, **11**, 4 **(2018)**

79. Kucherenko I.S., Didukh D.Y., Soldatkin O.O. and Soldatkin A.P., Amperometric Biosensor System for Simultaneous Determination of Adenosine-5′-Triphosphate and Glucose, *Analytical Chemistry*, **86(11)**, 5455-5462 **(2014)**

80. Kudo H., Sawai M., Wang X., Gessei T., Koshida T., Miyajima K., Saito H. and Mitsubayashi K., A NADH-dependent fiber-optic biosensor for ethanol determination with a UV-LED excitation system, *Sensors and Actuators B: Chemical*, **141(1)**, 20-25 **(2009)**

81. Kumar V., Kumar V., Singh A.K., Verma N. and Bhalla T.C., A Potentiometric Biosensor for Cyanide Detection using Immobilized Whole Cell Cyanide Dihydratase of Flavobacterium indicum MTCC 6936, *Journal of Analytical Chemistry*, **73**, 1014-1019 **(2018)**

82. Lai C.Y., Foot P.J.S., Brown J.W. and Spearman P., A Urea Potentiometric Biosensor Based on a Thiophene Copolymer, *Biosensor*, **7,** 13 **(2017)**

83. Lanfranco R. et al, Selective adsorption on fluorinated plastic enables the optical detection of molecular pollutants in water, *Physical Review Applied*, **5(5),** 054012 **(2016)**

84. Lawal A.T. and Adeloju S.B., Polypyrrole based amperometric and potentiometric phosphate biosensors: A comparative study B, *Biosensor and Bioelectronics*, **40**, 377-384 **(2013)**

85. Li J., Wu Z.Y., Xiao L.T., Zeng G.M., Huang G.H., Shen G.L. and Yu R,Q., A Novel Piezoelectric Biosensor for the Detection of Phytohormone β-Indole Acetic Acid, *Analytical Science*, **18(4)**, 403-407 **(2002)**

86. Li J., Xiao L.T., Zeng G.M., Huang G.H., Shen G.L. and Yu R.Q., A Novel Piezoelectric Biosensor for the Detection of Phytohormone β-Indole Acetic Acid, *Analytical Chimica Acta*, **494**, 177-185 **(2003)**

87. Liao C.W., Chou J.C., Sun T.P., Hsiung S.K. and Hsieh J.H., Preliminary investigations on a new disposable potentiometric biosensor for uric acid, *IEEE Transactions on Biomedical Engineering*, **53**, 7 **(2006)**

88. Lin D., Pillai R.G., Lee W.E. and Jemere A.B., An impedimetric biosensor for E. coli O157:H7 based on the use of self-assembled gold nanoparticles and protein G, *Microchimica Acta*, **186**, 1-9 **(2019)**

89. Ling Y.P. and Heng L.Y., A Potentiometric Formaldehyde Biosensor Based on Immobilization of Alcohol Oxidase on Acryloxysuccinimide-modified Acrylic Microspheres, *Sensors*, **10**, 11 (2010)

90. Liu Z., Yuan R., Chai Y., Zhuo Y., Hong C. and Yang X., Highly sensitive, reagentless amperometric immunosensor based on a novel redox-active organic-inorganic composite film, *Sensors & Actuators, B: Chemical*, **134**, 625-631 **(2008)**

91. Lupu A., Valsesial A., Bretagnol F., Colpo P. and Rossi F., Development of a potentiometric biosensor based on nanostructured surface for lactate determination, *Sensors and Actuators B: Chemical*, **17(2)**, 606-612 **(2007)**

92. Malhotra R., Patel V., Vaque J.P., Gutkind J.S. and Rusling J.F., Ultrasensitive Electrochemical Immunosensor for Oral Cancer Biomarker IL-6 Using Carbon Nanotube Forest Electrodes and Multilabel Amplification, *Analytical Chemistry*, **82**, 3118-3123 **(2010)**

93. Malik M., Chaudhary R. and Pundir C.S., An amperometric pyruvate biosensor based on pyruvate oxidase nanoparticles immobilized onto pencil graphite electrode, *Process Biochemistry*, **93**, 12-20 **(2020)**

94. Malvano F., Pilloton R. and Albanese D., A novel impedimetric biosensor based on the antimicrobial activity of the peptide nisin for the detection of Salmonella spp, *Food Chemistry*, **325**, 126868 **(2020)**

95. Mani V., Chikkaveeraiah B.V., Patel V., Gutkind J.S. and Rusling J.F., Ultrasensitive Immunosensor for Cancer Biomarker Proteins Using Gold Nanoparticle Film Electrodes and Multienzyme-Particle Amplification, *ACS Nano*, **3**, 585-594 **(2009)**

96. Manoj D., Auddy I., Nimbkar S., Chittibabu S. and Shanmugasundaram S.D., Development of co-immobilised enzymes amperometric biosensor for the determination of triglycerides in coconut milk, *International Food Research Journal*, **27(5)**, 875-882 **(2019)**

97. Maphanga C., Ombinda-Lemboumba S., Manoto S. and Mthunzi-Kufa P., Surface plasmon resonance (SPR) based biosensor for mycobacterium tuberculosis diagnosis, *Optical Diagnostic and Testing*, **1165**, 1165103 **(2021)**

98. Marchenko S.V., Kucherenko I.S., Soldatkin O.O. and Soldatkin A.P., Potentiometric Biosensor System Based on Recombinant Urease and Creatinine Deiminase for Urea and Creatinine Determination in Blood Dialysate and Serum, *Elan*, **27(7),** 1699-1706 **(2015)**

99. Marrazza G., Piezoelectric Biosensors for Organophosphate and Carbamate Pesticides: A Review, *Biosensors*, **4(3)**, 301-317 **(2014)**

100. Mehrotra P., Biosensors and their applications - A review, *Journal of Oral Biology and Craniofacial Research*, **6(2)**, 153-159 **(2016)**

101. Mello L.D., Kisner A., Goulart M.O. and Kubota L.T., Biosensors for antioxidant evaluation in biological systems, *Combinatorial Chemistry & High Throughput Screening*, **16(2)**, 109-120 **(2013)**

102. Mikkelsen S.R., Electrochemical biosensors for DNA sequence detection, *Electroanalysis*, **8(1)**, 15-19 **(1996)**

103. Millan K.M. and Mikkelsen S.R., Sequence-selective biosensor for DNA based on electroactive hybridization indicators, *Analytical Chemistry*, **65**, 2317-2323 **(1993)**

104. Minunni M., Tombelli S., Fonti J., Spiriti M., Mascini M., Bogani P. and Buiatti M., Detection of Fragmented Genomic DNA by PCR-Free Piezoelectric Sensing Using a Denaturation Approach, *American Chemical Society*, **127(22)**, 7966-7967 **(2005)**

105. Minunni M., Tombelli S., Scielzi R., Mannelli I., Mascini M. and Gaudiano C., Detection of β-thalassemia by a DNA piezoelectric biosensor coupled with polymerase chain reaction, *Analytical Chimica Acta*, **481(1)**, 55-64 **(2003)**

106. Mir T.A., Abrahim S., Nawaz A., Wani S.I. and Rehman M., Biosensors and their biomedical applications: Invited Review, Reyazuddin Research & Development Society, *JPPS*, **3(2)**, 104-112 **(2015)**

107. Mir T.A., Shinohara H. and Shimizu Y., Enzymeluminescence method: Tool for evaluation of neuronal differentiation based on realtime monitoring of dopamine release response from PC12 cells, *Analytical Methods*, **3(4),** 837-841 **(2011)**

108. Mishra M., Singh S.K., Shanker R. and Sundaram S., Design and simulation of diatom-based microcantilever immunobiosensor for the early detection of Karnal bunt, *3 Biotech*,**10,** 1-13 **(2020)**

109. Moattari G., Izadi Z. and Niaei M.S., Development of an electrochemical genosensor for detection of viral hemorrhagic septicemia virus (VHSV) using glycoprotein (G) gene probe, *Aquaculture*, **536,** 736451 **(2021)**

110. Mohanty S.P. and Kougianos E., Biosensors: a tutorial review, *IEEE Potentials*, **25**, 78 **(2006)**

111. Monosik R., Stredansky M. and Sturdik E., Biosensors - classification, characterization and new trends, *Acta Chemica Slovaca*, **5(1)**, 109-120 **(2012)**

112. Mosiello L., Laconi C., Gallo M.D., Ercole C. and Lepidi A., Development of a monoclonal antibody based potentiometric biosensor for terbuthylazine detection, *Sensors and Actuators B: Chemical*, **95**, 315-320 **(2003)**

113. Mouffouk F., Rosa da Costa A.M., Martins J., Zourob M., Abu-Salah K.M. and Alrokayan S.A., Development of a highly sensitive bacteria detection assay using fluorescent pH-responsive polymeric micelles, *Biosensors and Bioelectronics*, **26(8)**, 3517-3523 **(2011)**

114. Moussa S., Horn M.R.V., Shah A., Pollegioni L., Thibodeaux C.J., Ruthazer E.S. and Mauzero J., A Miniaturized Enzymatic Biosensor for Detection of Sensory-Evoked D-serine Release in the Brain, *Journal of The Electrochemical Society*, **168**, 025502 **(2021)**

115. Murugaboopathi G., Parthasarathy V., Chellaram C., Anand T.P. and Vinurajkumar S., Applications of Biosensors in Food Industry, *Biosciences Biotechnology Research Asia*, **10**, 2 **(2013)**

116. Nascimento N.M., Dolz A.J., Garcia E.G., Ivorr J.A.R., Puchades R., Maquieira A., Morais S. and Romero D.G., Label-free piezoelectric biosensor for prognosis and diagnosis of systemic Lupus Erythea, matosus, *Biosensors and Bioelectronics*, **90**, 166-173 **(2017)**

117. Nascimentoa H.P.O., Oliveirab M.D.L., Meloc C.P., Silva M.G.J.L., Cordeiroe M.T. and Andrade C.A.S., An impedimetric biosensor for detection of dengue serotype at picomolar concentration based on gold nanoparticles-polyaniline hybrid composites, *Colloids and Surface B: Biointerfaces*, **86(2)**, 414-419 **(2011)**

118. Nikoleli G.P. et al, Biosensors Based on Microfluidic Devices Lab-on-a-Chip and Microfluidic Technology, *Advanced Nanomaterials, Nanotechnology and Biosensors*, **1,** 375-394 **(2018)**

119. Nishitani S. and Sakata T., Enhancement of Signal-to-Noise Ratio for Serotonin Detection with Well-Designed Nanofilter-Coated Potentiometric Electrochemical Biosensor, *ACS Applied Materials*, **12(13)**, 14761-14769 **(2020)**

120. Ondes B., Akpinar F., Uygun M., Muti M. and Uygun D., High stability potentiometric urea biosensor based on enzyme attached nanoparticles, *Microchemical*, **160**, 105667 **(2020)**

121. Pang L. et al, DNA point mutation detection based on DNA ligase reaction and nano-au amplification: A piezoelectric approach, *Analytical Chemistry*, **358**, 99-103 **(2006)**

122. Park I.S. and Kim N., Development of a chemiluminescent immunosensor for chloramphenicol, *Analytica Chimica Acta*, **578(1)**, 19-24 **(2006)**

123. Pena-Vazquez E., Maneiro E., Perez-Conde C., Moreno-Bondi M.C. and Costas E., Microalgae fiber optic biosensors for herbicide monitoring using sol-gel technolog, *Biosensor and Bioelectronics*, **24(12)**, 3538-3543 **(2009)**

124. Perez S., Bartroli J. and Fabregas E., Amperometric biosensor for the determination of histamine in fish samples, *Food Chemistry*, **141**, 4 **(2013)**

125. Pisoschi A.M., Potentiometric Biosensors: Concept and Analytical Applications-An Editorial, *Biochemistry & Analytical Biochemistry*, **5**, 3 **(2016)**

126. Pisoschi A.M., Danet A.F. and Negulescu G.P., Glucose Determination by Cellophane-Based and Nylonbased Enzymic Electrodes; Application on Juices and Wine Analysis, *EJEAF Chem*, **5(1)**, 1185-1194 **(2006)**

127. Pohank M., Treml F., Hubalek M., Bandouchova H., Bekova M. and Pikula J., Piezoelectric Biosensor for a Simple Serological Diagnosis of Tularemia in Infected European Brown Hares (Lepus europaeus), *Sensor*, **7(11)**, 2825-2834 **(2007)**

128. Pohanka M., Overview of Piezoelectric Biosensors, Immunosensors and DNA Sensors and Their Applications, *Materials*, **11(3)**, 448 **(2018)**

129. Pohanka M., Biosensors containing acetylcholinesterase and butyrylcholinesterase as recognition tools for detection of various compounds, *Chemical Papers*, **69(1)**, 4-16 **2015**

130. Pohanka M., Piezoelectric biosensor for the determination of Tumor Necrosis Factor Alpha, *Talanta*, **178**, 970-973 **(2018)**

131. Pohanka M., Piezoelectric Immunosensor for the Determination of CReactive Protein, *International Journal of Electrochemical Science*, **14**, 8470-8478 **(2019)**

132. Pohanka M., The piezoelectric biosensors: Principles and applications, a review, *International Journal of Electrochemical Science*, **12**, 496-506 **(2017)**

133. Pohanka M. and Skladal P., Electrochemical biosensors-principles and applications, *Journal of Applied Biomedicine*, **6**, 57-64 **(2008)**

134. Pohanka M. and Vicek V., Immunoassay of Glomalin by Quartz Crystal Microbalance Biosensor Containing Iron Oxide Nanoparticles, *International Journal of Analytical Chemistry*, https://doi.org/10.1155/2020/8844151 **(2020)**

135. Pohanka M., Pavlis O. and Skladal P., Diagnosis of tularemia using piezoelectric biosensor technology, *Talanta*, **71**, 981-985 **(2007)**

136. Prakash O., Talat M., Hasan S.H. and Pandey R.K., Enzymatic detection of mercuric ions in ground-water from vegetable wastes by immobilizing pumpkin (Cucumis melo) urease in calcium alginate beads, *Bioresource Technology*, **99(10)**, 4524-4528 **(2008)**

137. Qadirul I.M., Kamran H., Rana S.J., Isak E., Omer N., Magnus W. and Danielsson B., Structural characterization and biocompatible applications of graphene nanosheets for miniaturization of potentiometric cholesterol biosensor, *Journal of Biosensors & Bioelectronics*, **2(3)**, 2155-6210 **(2011)**

138. Qi P., Wan Y. and Zhang D., Impedimetric biosensor based on cell- mediated bioimprinted films for bacterial detection, *Biosensors and Bioelectronics*, **39(1)**, 282-288 **(2013)**

139. Radke S. and Alocilja E.C., A high density microelectrode array biosensor for detection of *E. coli* O157:H7, *Biosensors and Bioelectronics*, **20(8)**, 1662-1667 **(2005)**

140. Radke S.M. and Alocilia E.C., Design and fabrication of a microimpedance biosensor for bacterial detection, *IEEE Sensors Journal*, **4**, 4 **(2004)**

141. Rasmussen C.D., Andersen J.E.T. and Christiansen B.Z., Improved Performance of the Potentiometric Biosensor for the Determination of Creatinine, *Chemical and Biosensor*, **40**, 39-52 **(2007)**

142. Rasmussen S. K., Rasmussen L.K., Weilguny D. and Tolstrup A.B., Manufacture of recombinant polyclonal antibodies, *Biotechnology Letters*, **9**, 845-852 **(2007)**

143. Ravina, Mohan H., Gill P.S. and Kumar A., Hemagglutinin gene based biosensor for early detection of swine flu (H1N1) infection in human, *International Journal of Biological Macromolecules*, **130**, 720-726 **(2019)**

144. Razdari A.M., Varnamkhasti M.G., Rostami S., Izadi Z., Ensafi A.A. and Siadat M., Development of an electrochemical biosensor for impedimetric detection of tetracycline in milk, *Journal of Food science & Technology*, **57(12)**, 4697-4706 **(2020)**

145. Rekha K., Gouda M.D., Thakur M.S. and Karanth N.G., Ascorbate oxidase based amperometric biosensor for organophosphorous pesticide monitoring, *Biosensors and Bioelectronics*, **15**, 499-502 **(2000)**

146. Rengaraj S., Izquierdo A.C., Scott J.L. and Lorenzo M.D., Impedimetric paper-based biosensor for the detection of bacterial contamination in water, *Sensors and Actuators B: Chemical*, **265**, 50-58 **(2018)**

147. Rhouati A. et al, Marty, Label-Free Aptasensors for the Detection of Mycotoxins, *Sensors*, **16(12)**, 2178 **(2016)**

148. Rodriguez A., Valera E., Ramon-Azcon J., Sanchez F.J., Marco M.P. and Castañer L.M., Single frequency impedimetric immunosensor for atrazine detection, *Sensor Actuators B*, **129**, 921-928 **(2008)**

149. Rodriguezab M.L., Benimelicd C., Madridef R.E. and Giacomelli C.E., A simple Streptomyces spore-based impedimetric biosensor to detect lindane pesticide, *Sensors and Actuator B: Chemical*, **207**, 447-454 **(2015)**

150. Romero D.G., Label-free piezoelectric biosensor for prognosis and diagnosis of systemic Lupus Erythea, matosus, *Biosensors and Bioelectronics*, **90**, 166-173 **(2017)**

151. Rushworth J.V. et al, A label-free electrical impedimetric biosensor for the specific detection of Alzheimer's amyloid-beta oligomers, *Biosensors and Bioelectronics*, **56**, 83-90 **(2014)**

152. Sa S.R., Junior A.G.S., Neto R.G.L., Andrade C.A.S. and Olivira M.D.L., Lectin-based impedimetric biosensor for differentiation of pathogenic candida species, *Talanta*, **220,** 121375 **(2020)**

153. Sasi Priya S.V.S., Basha Syed Hussain and Harish Kumar D.R., In-silico anticancer potential of active constituents from “Glycyrrhiza uralensis” targeting PPAR gamma protein, *Res. J. Chem. Environ.*, **26(5)**, 30-44 **(2022)**

154. Sethi R.S. and Lowe C.R., Electrochemical microbiosensors, Proceedings of IEE Colloquium on Microsensors **(1990)**

155. Setzu S., Salis S., Demontis V., Salis A., Monduzzi M. and Mula G., Porous silicon-based potentiometric biosensor for triglycerides, *Physica Status Solidi (a)*, **204(5)**, 1434-1438 **(2007)**

156. Shang Z.J., Xu Y.L., Gu Y.X., Wang Y., Wei D. and Zhan L., A Rapid Detection of Pesticide Residue Based on Piezoelectric Biosensor, *Procedia Engineering*, **15**, 4480-4485 **(2015)**

157. Silva N.F.D., Almeida C.M.R., Magalhaes J.M.C.S., Goncalves M.P., Freire C. and Matos C.D., Development of a disposable paper-based potentiometric immunosensor for real-time detection of a foodborne pathogen, *Biosensor and Bioelectronics*, **141,** 111317 **(2019)**

158. Silva W., Ghica M.E., Ajayi R.F., Iwuoha E.I. and Brett C.M.A., Tyrosinase based amperometric biosensor for determination of tyramine in fermented food and beverages with gold nanoparticle doped poly(8-anilino-1-naphthalene sulphonic acid) modified electrode, *Food Chemistry*, **282,** 18-26 **(2019)**

159. Sok V. and Fragoso A., Amperometric biosensor for glyphosate based on the inhibition of tyrosinase conjugated to carbon nano-onions in a chitosan matrix on a screen-printed electrode, *Microchimica Acta*, **186,** 1-8 **(2019)**

160. Soldatkin A.P., Montoriol J., Sant W., Martelet C. and Renault J.N., Development of potentiometric creatinine-sensitive biosensor based on ISFET and creatinine deiminase immobilised in PVA/SbQ photopolymeric membrane, *Materials Science and Engineering: C*, **21**, 75-79 **(2002)**

161. Song N.N., Wang Y.Z., Yang X.Y., Zong H.L., Chen Y.X., Ma Z. and Chen C.X., A novel electrochemical biosensor for the determination of dopamine and ascorbic acid based on graphene oxide /poly(aniline-co-thionine) nanocomposite, *Journal of Electroanalytical Chemistry*, **873,** 114352 **(2020)**

162. Splettstoesser W.D., Tomasu H., Al Dahouk S., Neubauer H. and Schuff-Werner P., Diagnostic procedures in tularaemia with special focus on molecular and immunological techniques, Journal of Veterinary Medicine, *Series B*, **52**, 249-261 **(2005)**

163. Sreekanth K.V. et al, Extreme sensitivity biosensing platform based on hyperbolic metamaterials, *Nat Mater*, **15(6),** 621-627 **(2016)**

164. Stepurska K., Dzyadevych S. and Gridin S., Potentiometric enzyme biosensor for aflatoxin B1 detection - Kinetic simulation, *Sensors and Actuators B: Chemical*, **259,** 580-586 **(2018)**

165. Su L., Zou L., Fong C.C., Wong W.L., Wei F., Wong K.Y., Wu R.S.S. and Yang M., Detection of cancer biomarkers by

piezoelectric biosensor using PZT ceramic resonator as the transducer, *Biosensors and Bioelectronics*, **46**, 155-161 **(2013)**

166. Su, X. and Li S.F.Y., Serological determination of Helicobacter pylori infection using sandwiched and enzymatically amplified piezoelectric biosensor, *Analytical Chimica Acta*, **429(1)**, 27-36 **(2001)**

167. Taitt C.R., Golden J.P., Shubin Y.S., Shriver- Lake L.C., Sapsford K.E., Rasooly A. and Ligler F.S., A portable array biosensor for detecting multiple analysis in complex samples, *Microbial Ecology*, **47**, 175-185 **(2004)**

168. Takeda K., Kusuoka R., Inukai M., Igarashi K., Ohno H. and Nakamura N., An amperometric biosensor of L-fucose in urine for the first screening test of cancer, *Biosensors and Bioelectronics*, **174,** 112831 **(2021)**

169. Thevenot D.R., Toth K., Durst R.A. and Wilson G.S., Electrochemical biosensors: Recommended definitions and classification, *Biosensors & Bioelectronics*, **16**, 121-131 **(2001)**

170. Tombelli S., Mascini M., Sacco C. and Tuner A.P.F., A DNA piezoelectric biosensor assay coupled with a polymerase chain reaction for bacterial toxicity determination in environmental samples, *Analytical Chimica Acta*, **418(1)**, 1-9 **(2000)**

171. Tothill I.E., Biosensors for cancer markers diagnosis, *Seminars in Cell and Developmental Biology*, **20(1)**, 55-62 **(2009)**

172. Tripathi S.M., Bock W.J., Mikulic P., Chinnappan R., Ng A., Tolba M. and Zourob M., Long period grating based biosensor for the detection of Escherichia coli bacteria, *Biosensors and Bioelectronics*, **35(1)**, 308-312 **(2012)**

173. Trivedi U.B., Lakshminarayana D., Kothari I.L., Patel N.G., Kapse H.N., Makhija, K.K., Patel P.B., and Panchal C.J. Potentiometric biosensor for urea determination in milk, *Sensors and Actuators B: Chemical*, **140(1),** 260-266 **(2009)**

174. Uyguni Z.O., Yeniay L. and Sagin F.G., CRISPR-dCas9 powered impedimetric biosensor for label-free detection of circulating tumor DNAs, *Analytical Chimica Acta*, **1121**, 35-41 **(2020)**

175. Verma N., Kumar S. and Kaur H., Fiber optic biosensor for the detection of Cd in milk, *Journl of Biosens ors and Bioelectronics*, **1**, 102 **(2010)**

176. Vermeir S., Nicolai B.M., Verboven P., Gerwen P.V., Baeten B., Hoflack L., Vulsteke V. and Lammertyn J., Microplate Differential Calorimetric Biosensor for Ascorbic Acid Analysis in Food and Pharmaceuticals, *Analytical Chemistry*, **79(16)**, 6119-6127 **(2007)**

177. Vianello F., Ragusa S., Cambria M.T. and Rigo A., A high sensitivity amperometric biosensor using laccase as biorecognition element, *Biosensors and Bioelectronics*, **21(11)**, 2155-2160 **(2006)**

178. Vigneswar S. et al, Recent Advances in Biosensor Technology for Potential Applications - An OverviewReview, *Front Bioengineering and Biotechnology*, **4,** 11 **(2016)**

179. Villar N.G., Saurina J. and Cassou S.H., Potentiometric sensor array for the determination of lysine in feed samples using multivariate calibration methods, *Fresenius' Journal of Analytical Chemistry*, **371**, 1001-1008 **(2001)**

180. Vo-Dinh T. and Cullum B., Biosensors and biochips: advances in biological and medical diagnostics. Fresenius, *Journal of Analytical Chemistry*, **366**, 540-551 **(2000)**

181. Walker N.L. and Dick J.E., Oxidase-loaded hydrogels for versatile potentiometric metabolite sensing, *Biosensr and Bioelectronics*, **178**, 112997 **(2021)**

182. Wang J., Amperometric biosensors for clinical and therapeutic drug monitoring: a review, *Journal of Pharmaceutical and Biomedical Analysis*, **19**, 47−53 **(1999)**

183. Wang J., Electrochemical biosensors: towards point-of-care cancer diagnostics, *Biosensors & Bioelectronics*, **21(10)**, 1887-1892 **(2006)**

184. Wang L., Wei O., Wu C., Hu Z., Ji J. and Wang P., The Escherichia coli O157:H7 DNA detection on a gold nanoparticle-enhanced piezoelectric biosensor, *Chinese Science Bulletin*, **53**, 1175-1184 **(2008)**

185. Wayu M.B., Pannell M.J. and Leopold M.C., Layered Xerogel Films Incorporating Monolayer-Protected Cluster Networks on Platinum-Black-Modified Electrodes for Enhanced Sensitivity in First-Generation Uric Acid Biosensing, *Chem Electro Chem*, **3(8),** 1245-1252 **(2016)**

186. Wu J., Zhu Y., Xue F., Mei Z., Yao L., Wang X., Zheng L., Liu J., Liu G., Peng C. and Chen W., Recent trends in SELEX technique and its application to food safety monitoring, *Microchimica Acta*, **181**, 479-491 **(2014)**

187. Wu Y.G., Zhan S.S., Wang L.M. and Zhou P., Selection of a DNA aptamer for cadmium detection based on cationic polymer mediated aggregation of gold nanoparticles, *Analyst*, **139**, 1550-1561 **(2014)**

188. Yang H., Zhou H., Hao H., Gong Q. and Nie K., Detection of Escherichia coli with a label-free impedimetric biosensor based on lectin functionalized mixed self-assembled monolayer, *Sensors and Actuator B: Chemical*, **229(297)**, 304 **(2016)**

189. Yarar S. and Karakus E., A novel potentiometric biosensor for determination of L-lysine in commercial pharmaceutical L-lysine tablet and capsule, *Artificial Cells Nanomedicine and Biotechnology*, **44**, 2 **(2016)**

190. Yu M., Eremin S.A. and Skladal P., Development of the Piezoelectric Biosensor for Acetochlor Detection, *Sensors and Biosensors*, **36(11),** 2443-2457 **(2003)**

191. Zehani N., Dzyadevyc S.V., Kherrat R. and Renault N.J.J., Sensitive impedimetric biosensor for direct detection of diazinon based on lipases, *Frontiers in Chemistry*, **2,** 44 **(2014)**

192. Zheng Y.H., Hua T.C., Sun D.W., Xiao J.J., Xu F. and Wang F.F., Detection of dichlorvos residue by flow injection calorimetric biosensor based on immobilized chicken liver esterase, *Journal of Food Engineering*, **74(1)**, 24-29 **(2006)**

193. Zheng Y.H., Liu J., Ma Y.Z., Xu Y., Xu F. and Hua T.C., Temperature Effects on Enzyme Activity of Chicken Liver

Esterase Used in Calorimetric Biosensor, *Artifical Cells Blood Substitutes and Biotechnology*, **40**, 125-131 **(2012)**

194. Zhong Z., Fritzsche M., Pieper S.B., Wood T.K., Lear K.L., Dandy D.S. and Reardon K.F., Fiber optic monooxygenase biosensor for toluene concentration measurement in aqueous samples, *Biosensors and Bioelectronics*, **26(5)**, 2407-2412 **(2011)**

195. Zhou X., Liu L., Hu M., Wang L. and Hu J., Detection of hepatitis B virus by piezoelectric biosensor, *Journal of Pharmaceutical and Biomedical Analysis*, **27**, 1-2 **(2002)**

196. Zinoubi K., Chrouda A., Soltane R., Ghamdi Y.A., Almalki S.G., Osman G., Barhoumi H. and Renault N.J., Highly Sensitive Impedimetric Biosensor Based on Thermolysin Immobilized on a GCE Modified with AuNP-decorated Graphene for the Detection of Ochratoxin A, *Electroanalysis*, **33(1),** 136-145 **(2021)**.

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