

A Review on Studies and Research on Biosensors : An Interdisciplinary Pursuit

Sunil Jayant Kulkarni

Chemical Engineering Department, Datta Meghe College of Engineering, Airoli, Navi Mumbai, Maharashtra, India

ABSTRACT

The detection and transfer of signals enable quick response in the diagnosis. Generally, for detection of components in samples, chromatographic methods are used. Other methods such as energy dispersed X-ray analysis, atomic absorption methods are used for detection of various compounds and impurities in water samples. Also, the compounds in gasses are detected by using various chromatographic, calorimetric and chemical analyses. It is always desired to measure the real time concentration and convey the signals to other display systems. A biosensor is an analytical device which converts a biological response into an electrical signal. These are analytical devices in which specific recognition of the chemical substances is performed by biological material, usually an enzyme. The current review summarizes research and studies on biosensors.

Keywords: Signals, Enzymes, Sensitivity, Selectivity, Cost, Promoter.

I. INTRODUCTION

Biosensor development is widely studied area of research due to its potential. In biosensors, biological material, usually, an enzyme is used for recognition of analyte. The biosensor is capable of identifying response due to change in environment. Easy operation and fast measurements are driving forces in the development of biosensors. A bio-recognition component, bio transducer component, and electronic system form a biosensor. The electronic system contains a signal amplifier, processor, and display. Pharmaceutical, food, environmental and medical applications of biosensors include detection of concentrations of components like glucose, clinical diagnosis, food control and environmental screening. The present review is an attempt to summarize research and studies on biosensors.

II. RESEARCH AND STUDIES ON BIOSENSORS

Baronas et.al. carried out research on optimization of bi-layer biosensors[1]. They experimentally investigated the influence of the parameters of the biosensor on the objectives of the problem. They formulated the multi-objective optimization problem for the determination of optimal maximal enzymatic

rate and thicknesses of the layers of the bi-layer mono-enzyme biosensor. For this purpose, they utilized Michaelis-Menten kinetics. According to these studies, it is always beneficial to use the thickest dialysis membrane. If sensitivity is the priority, then according to this investigation, thinner enzyme layer is a better choice. Gokhale et.al. carried out an investigation on the development of biosensors for environmental pollutants using marine isolates[2]. They isolated *Vibrio* spp. from the surface of fresh liquids. They studied bioluminescence exhibited by the bacteria during its growth. They observed that it was a maximum of 30 hours. They also observed that in the presence of water pollutants like heavy metal ions, complex aromatic hydrocarbons, and pesticides, bioluminescence decreased. According to Sagadevan and Periasamy, nanotechnology plays an important role in the development of biosensors[3]. Biosensing demands low concentration detection and high specificity. Also according to them, biomolecule-functionalized surfaces can drastically boost the specificity of the detection system. They observed that materials such as nanomaterials like gold nanoparticles, carbon nanotubes, magnetic nanoparticles and quantum dots are being actively investigated for their application in

biosensors. Kim et.al. developed an amperometric glucose biosensor [4]. For encapsulation of glucose oxidase, they used the nanoporous composite film of sol-gel-derived zirconia and perfluorosulfonate monomer, Nafion. They carried out an encapsulation on a platinumized glassy carbon electrode. For the preparation of zirconia/Nafion composite film, they used Zirconium isopropoxide (ZrOPr). They observed that faster response time and higher sensitivity was obtained due to the presence of Nafion polymer in the sol-gel-derived zirconia in the biosensor. At the pure zirconia- and pure Nafion-based biosensors, comparatively low sensitivity was observed. Ahmad et.al. investigated amperometric biosensor based on Pt-incorporated fullerene-like ZnO hybrid nanospheres[5]. In their work, they synthesized Pt-ZnO nanospheres (PtZONS) by electrodeposition on a glassy carbon electrode (GCE). They used high-resolution transmission electron microscopy (HRTEM) and energy dispersive X-ray spectroscopy (EDS) for identification of the Pt nanoparticles in ZnO nanospheres. They observed that the sensitivity of the PtZONS/GCE to hydrogen peroxide was much higher than that of a conventional electrode. According to these studies, the biosensor exhibited a good anti-interference ability and favorable stability over relatively long-term storage.

Prodromidis and Karayannis reviewed enzyme-based amperometric biosensors for food analysis[6]. They explained the principles of amperometric detection. They presented categorization and description of the materials commonly used for the construction of electrodes. A review on electrochemical nanobiosensors was done by Pumera et.al.[7]. They discussed main techniques and methods which use nanoscale materials for construction of electrochemical biosensors. According to them, electrochemical nanobiosensors offered an important step toward development of selective, down to few target molecules sensitive bio recognition device for medical and security applications. They concluded that electrochemical nanobiosensors consisting from single carbon nanotube are another future path of biosensor development. An overview of fiber-optic biosensors was presented by Marazuela and Moreno-Bondi[8]. They reviewed research work carried out between 1997 to 2002. According to them, there is a growing need for real-time, low-cost technology. Their review provided information about the analytical characteristics and

applications of fiber-optic biosensors. They found that biosensor research is directed toward the development of simple applications that can solve specific problems, otherwise difficult to tackle. They concluded that there is need for more research for the development of more robust biomolecules or biomimetic receptors, which can be used as receptors for sensor design. Raba et.al. carried out an investigation on analytical biosensors, which are used for the determination of pathogenic microorganisms(9). Their studies were focused on applications of analytical biosensors to microbiological diagnostics in areas such as diagnosis of diseases and food quality control. Their studies revealed that analytical biosensors can detect pathogens in a much shorter time with high sensitivity, selectivity. Also, they offer the possibility to perform multiple analyses. For on-site monitoring, they can be used extensively. A review of biomedical application of surface plasmon resonance (SPR) biosensors was carried out by Ramanavičius et.al.[10]. They discussed the general principles of SPR sensor action. They also briefly described immobilization methods used in the design of SPR biosensors. According to them, major tasks in developing new SPR sensors includes improvement of detection limits, multichannel performance, development of advanced recognition elements. Frederickx et.al. discussed biosensors used in forensic sciences[11]. According to them, most commonly used detector is dog. Law enforcement and private agencies use sniffing dogs. The purposes served by using dogs include detection of drugs, ignitable liquid residues, explosives, human remains, and human scent. The research nowadays is being carried out to use rats and rodents for some applications. Insects can also be used in some application for detection of odours and explosives. They are highly sensitive, flexible, portable and cheap to reproduce.

Gil et.al reviewed electrochemical biosensors used in pharmaceutical analysis [12]. According to them, the biosensor remains a focus of research in spite of the difficulties concerning the reproducibility of the electrochemical methods. Also, stability of enzymes and other biological recognizing agents is a limiting factor. The advantages of biosensors are low cost, the simplicity of analysis, selectivity and good sensitivity. Patel and Ranade discussed the development of glucose biosensors over the last 50 years[13]. They also discussed principles of various glucose biosensors. According to them, there are still many challenges

awaiting researcher's attention. Still, there is scope for the investigation to obtain stable, accurate, reproducible and less painting glucose biosensors. For non-enzymatic glucose biosensors, it is important to know the mechanism of the metal electrodes. Sekella et.al. investigated theophylline based on fluorescence detection by using biosensor[14]. They coupled a donor-acceptor fluorophore pair to the termini of the substrate RNA. Also, they measured the theophylline dependence profile of this biosensor. To destabilize the inactive conformation of the ribozyme, they mutated a single nucleotide in the communication domain between the catalytic and ligand-binding domains. Monosik et.al. discussed classification, characterization and new trends in biosensors [15]. They also discussed commonly used immobilization methods such as adsorption, covalent bonding, matrix entrapment, cross linking and encapsulation. Also, they discussed the application of biosensors in clinical diagnosis, food industry, environment monitoring. According to them, interferences with unwanted molecules are often a problem in biosensor functioning. They concluded that there is a need to measure a group of analytes which makes the process of biosensor development complicated.

Leatherbarrow and Edwards carried out the review on molecular recognition using optical biosensors [16]. In their review, they recovered developments in the field of optical biosensors since mid-1998. The ever increasing demand for higher sensitivity is driving force for investigations on biosensors. It is predicted that there will be considerable development in the factors such as sensitivity, throughput and the user interface of the biosensor. Biran et.al. carried out an investigation on electrochemical biosensing of cadmium[17]. They studied out in situ and online monitoring of cadmium. In their paper, they described a novel use of promoter based electrochemical biosensing for online and in situ monitoring of gene expression. Biosensors applications in agricultural diagnosis sector were discussed by Tothill[18]. Medical analysis, food, and the environment are major fields of the usefulness of biosensors. Need for high sensitivity, speed, and accuracy of analytical measurements have stimulated investigation on biosensors. The combination of the computer (molecular) modeling and combinatorial synthesis or molecularly imprinted polymers is a new approach to producing synthetic receptors in sensor development. Huang et.al. designed

a low-cost and standalone potentiostat for the signal processing of electrochemical biosensors[19]. They used a personal digital assistant (PDA) to set the experimental parameters to the potentiostat through Bluetooth instead of using a personal computer (PC). According to this research, potentiostat proposed by them has the merits of good accuracy, low cost, low power consumption, and high portability.

Hahn et.al. studied the nucleic acid biosensors[20]. They discussed the current state of the art concerning the high-throughput analysis of nucleic acids. According to them, DNA sensor technologies are promising. However, it is necessary to bridge the gap between experimental status and the harder reality of clinical/diagnostic applications. These new technologies have huge potential and may lead to the development of new tools, which are simple and cheap enough to be used at point-of-care sites. Jia et.al. studied real-time noninvasive lactate monitoring in human perspiration by using electrochemical tattoo biosensors[21]. They observed that production of sweat lactate resulted in a change in the resulting temporal lactate profiles reflect due to variation in the exercise intensity. They used biosensors to human subjects for real-time continuous monitoring of sweat lactate dynamics. The lactate profiles obtained provided useful insights into physical performance and overall physiological status. Liu et.al. demonstrated that a novel, highly efficient enzyme electrode can be directly obtained by using covalent attachment between carboxyl acid groups of graphene oxide sheets and amines of glucose oxidase [22]. They observed that the glucose oxidase-immobilized graphene oxide electrode exhibited good a reproducibility and a good storage stability. Amaro et.al. carried out an investigation on whole-cell biosensors for detection of heavy metal ions in environmental samples[23]. They used two gene constructs using the *Tetrahymena thermophile* MTT1 and MTT5 metallothionein promoters. They employed the eukaryotic luciferase gene as a reporter. They validated whole cell biosensors by both artificial and natural samples. They concluded that the most sensitive eukaryotic metal biosensors were *Tetrahymena* metallothionein promoter-based biosensors. Bora et.al. carried out an investigation on the use of biosensors based on nucleic acid[24]. Their investigation was focused on clinical applications. High sensitivity and selectivity make these biosensors very attractive

alternative. They studied different transducer platform (optical, electrochemical, piezoelectrical) based NABs.

In their review, Garcia-Gonzalez and Aparicio the described current state-of-the-art of this sensor technology[25]. They analyzed design, technology and sensing mechanism of each type of sensor. Also, they described the applications of some statistical procedures. Park et.al. carried out the review on microbial biosensors[26]. According to them, whole-cell biosensors are a good alternative to enzyme-based biosensors. Low cost and improved stability are advantages of these biosensors. They studied the use of microorganisms that are genetically modified with the desirable outputs. The purpose of these modifications is to improve the biosensor performance. They also discussed different aspects such as signal outputs, sensitivity, and selectivity. Rapid, point-of-care applications, developing better materials to interface with the biological elements can be some applications of these whole-cell biosensors. Raja and Selvam studied construction of green fluorescent protein-based bacterial biosensor[27]. In their work, they focused on heavy metal remediation. The high cost is the limiting factor in conventional methods for heavy metal remediation. They used bacteria, which when comes in contact with metal ions produces a signal. Quantification and detection of the specific cell population, gene expression and constructing whole cell biosensors as specific and sensitive devices can be carried out with reporter genes as genetic tools. They constructed a reporter gene enhanced green fluorescent protein. Rawal et.al. carried out studies on wearable biosensor applications[28]. A dramatic growth of interest in wearable technology gives rise to the concept of wearable biosensors. Small physiological sensors, transmission modules, and processing capabilities are features of these biosensors. These are, according to the authors, are low-cost wearable unobtrusive solutions for continuous all-day and anyplace health, mental and activity status monitoring. They are not as reliable as conventional sensors. According to them, there is a need for a new technology for eliminating motion artifact and recovering corrupted signals. Arya et.al. described fundamental applications of biosensors[29]. In their paper, they highlighted the recent advances in the area of biosensors. According to them, the collaboration and cooperation between many areas of academia and industry can effect into improvement in technology of

biosensors. It can also help in making their application more feasible and easy.

III. CONCLUSION

Biosensor research is aimed at the development of simple applications that can solve specific problems. The collaboration and cooperation between many areas of academia and industry are required for meaningful research on biosensors. Biosensors provide sensitive, fast, inexpensive and less laborious alternative for detection and analysis. Price of instrumentation, accuracy, speed and portability are major controlling influences in application of biosensors

IV. REFERENCES

- [1] Romas Baronas, Algirdas Lanciskas, Antanas Zilinskas, "Optimization of Bi-Layer Biosensors: Trade-Off Between Sensitivity and Enzyme Volume", *Baltic J. Modern Computing*, Vol. 2, No.4, pp.285-296, 2014.
- [2] Trupti Gokhale, Almas Wali, Shailee Parikh, Neeru Sood, "Research of Marine Isolates in Development of Biosensors for Environmental Pollutants", *Engineering Review*, Vol. 32, No. 1, pp.17-22, 2012.
- [3] Suresh Sagadevan And Nathan Periasamy, "Recent Trends in Nanobiosensors and their Applications - A Review", *Rev. Adv. Matter Sci.*, Vol. 36, pp.62-69, 2014.
- [4] Hyung Jung Kim, Soon Hyun Yoon, Han Nim Chai, "Amperometric Glucose Biosensor Based On Sol Gel Derived Zirconia Nafian Composite Film As Encapsulation Matrix", *Bul Korian Chemical Society*, Vol.27, No.1, pp.65-70, 2006.
- [5] Mashkoo Ahmad, Caofeng Pan, Lin Gan, Zeeshan Nawaz, Jing Zhu, "Highly Sensitive Amperometric Cholesterol Biosensor Based on Pt-Incorporated Fullerene-Like ZnO Nanospheres", *J. Phys. Chem. C*, Vol. 114, No. 1, pp. 243-250, 2010.
- [6] Mamas I. Prodromidis And Miltiades I. Karayannis, "Enzyme Based Amperometric Biosensors for Food Analysis", *Electroanalysis*, Vol.14, No.4, pp.241-261, 2002.
- [7] Martin Pumera, Samuel Sanchez, Izumi Ichinose, Jie Tang, *Electrochemical Nanobiosensors, Sensors And Actuators*, B 123, 2007, 1195-1205.
- [8] María Dolores Marazuela, María Cruz Moreno-Bondi, "Fiber-Optic Biosensors – An Overview", *Anal Bioanal Chem*, Vol.372, pp.664-682, 2002.
- [9] Julio Raba, Martín A. Fernández-Baldo, Sirley V. Pereira, Germán A. Messina, Franco A. Bertolino, Santiago Tosetti, María I. Sanz Ferramola, "Analytical

- Biosensors For The Pathogenic Microorganisms Determination”, *Formatex*, Vol.1, pp.227-230, 2013.
- [10] Arūnas Ramanavičius, Friedrich W. Herberg, Silke Hutschenreiter, Bastian Zimmermann, Ingrida Lapėnaitė, Asta Kaušaitė, Arnonas Finkelšteinas, Almira Ramanavičienė, “Biomedical Application Of Surface Plasmon Resonance Biosensors (Review)”, *Acta Medica Lituanica*, Vol.12, No. 3, pp. 1-9,2005.
- [11] Christine Frederickx, François J.Verheggen, Eric Haubruge, “Biosensors in Forensic Sciences”, *Biotechnol. Agron. Soc. Environ.*, Vol.15, No.4, pp.449-458, 2011.
- [12] Eric De Souza Gil, Giselle Rodrigues De Melo, “Electrochemical Biosensors In Pharmaceutical Analysis”, *Brazilian Journal Of Pharmaceutical Sciences*, Vol. 46, No. 3, pp.375-390, Jul./Set., 2010.
- [13] Riddhi Patel, Ashwini Ranade, “Biosensors: A Sensitive Strategy To Detect Glucose In Body Fluids”, *International Journal Of Applied Biology And Pharmaceutical Technology*, Vol.6, No.1, pp.25-30, Jan-Mar-2015.
- [14] Phillip T. Sekella, David Rueda, And Nils G. Walter, “A Biosensor For Theophylline Based on Fluorescence Detection of Ligand-Induced Hammerhead Ribozyme Cleavage”, *RNA*, Vol.8, pp.1242-1252, 2002, Cambridge University Press, Printed In The USA Copyright © 2002 Rna Society
- [15] Rastislav Monošíka, Miroslav Stred’anskýb, Ernest Šturdíka, “Biosensors — Classification, Characterization and New Trends”, *Acta Chimica Slovaca*, Vol. 5, No. 1, pp. 109-120, 2012.
- [16] Robin J Leatherbarrow and Paul R Edwards, “Analysis of Molecular Recognition using Optical Biosensors”, *Current Opinion In Chemical Biology*, Vol.3, pp.544-547, 1999.
- [17] Israel Biran, Reuven Babai, Klimentiy Levcov, Judith Rishpon And Eliora Z. Ron, “Online and In Situ Monitoring of Environmental Pollutants: Electrochemical Biosensing of Cadmium”, *Environmental Microbiology*, Vol.2, No.3, pp.285-290, 2000.
- [18] Ibtisam E.Tothill, “Biosensor Development and Potential Application in Agricultural Diagnosis Sector”, *Computers And Electronics In Agriculture*, Vol. 30, pp.205-218, 2001.
- [19] Chun-Yueh Huang, Wen-Chih Li And Hung-Yin Lin, “Design and Implementation of a Standalone Potentiostat for Electrochemical Biosensors”, *International Journal Of Science And Engineering*, Vol.3, No.2, pp.5-9, 2013.
- [20] Sanuhe Han, Sussane Mergenthaler, Bernhard Zimmermann, Wolfgang Holzgreve, “Nucleic Acid Based Biosensors: The Desire Of The User”, *Bioelectrochemistry*, Vol.67, pp.151-154, 2005.
- [21] Wenzhao Jia, Amay J. Bandodkar, Gabriela Valdés-Ramírez, Joshua R. Windmiller, Zhanjun Yang, Julian Ramírez, Garrett Chan, And Joseph Wang, “Electrochemical Tattoo Biosensors For Real-Time Noninvasive Lactate Monitoring In Human Perspiration”, *Analytical Chemistry*, Vol.1, pp.6553-6560,2013.
- [22] Yong Liu, Dingshan Yu, Chao Zeng, Zongcheng Miao, Liming Dai, “Biocompatible Graphene Oxide-Based Glucose Biosensors”, *Langmuir*, Vol.26, No.9, pp.6158-6160, 2010.
- [23] Francisco Amaro, Aaron P. Turkewitz, Ana Martín-González and Juan-Carlos Gutiérrez, “Whole-Cell Biosensors for Detection of Heavy Metal Ions in Environmental Samples Based on Metallothionein Promoters From *Tetrahymena Thermophile*”, *Microbial Biotechnology*, Vol.1, pp.1-10, 2011.
- [24] Utpal Bora, Arghya Sett And Deepika Singh, “Nucleic Acid Based Biosensors For Clinical Applications”, *Biosens J.*, Vol.2, No.1, pp.1-8, 2013.
- [25] Diego L. Garcia-Gonzalez and Ramon Aparicio, “Sensors: From Biosensors to the Electronic Nose”, *Grasas Y Aceites*, Vol. 53. No. 1, pp.96-114, 2002.
- [26] Miso Park, Shen-Long Tsai and Wilfred Chen, “Microbial Biosensors: Engineered Microorganisms as the Sensing Machinery”, *Sensors*, Vol.13, pp. 5777-5795, 2013.
- [27] C. Edward Raja, G. S. Selvam, “Construction Of Green Fluorescent Protein Based Bacterial Biosensor For Heavy Metal Remediation”, *Int. J. Environ. Sci. Tech.*, Vol.8, No.4, pp. 793-798, Autumn 2011.
- [28] Vidhu Rawal, Ashutosh Dhamija, Sonam Gupta, “Recent Advancements in Wearable Bio-Sensor Applications”, *International Journal Of Scientific Research Engineering and Technology*, Vol. 1, No. 5, pp. 154-159, August 2012.
- [29] Sunil K Arya, Asha Chaubey And B D Malhotra, “Fundamentals and Applications Of Biosensors”, *Proc Indian Natn Sci. Acad.*, Vol.72, No.4, pp.249-266, 2006.