International Journal of Basic and Applied Biology
p-ISSN: 2394-5820, e-ISSN: 2349-2539, Volume 3, Issue 1; January-March, 2016, pp. 46-49

http://www.krishisanskriti.org/Publication.html

Biosensor and Molecular Diagnostics: An Overview

Akanksha Suman[1]*, Nidhee Chaudhary[2] and Neetu Jabalia[3]

[1,2,3]Amity Institute of Biotechnology, Amity University, Uttar Pradesh, Noida
E-mail: [1]akankshas206@gmail.com, [2]nchaudhary@amity.edu, [3]njabalia@amity.edu

Abstract—*Biosensor is a term used to cover sensor devices. It is broadly used to determine the concentration of substances and other parameters of biological interest. Biosensor is an analytical device which converts biological response into electrical signal. It has proven to be most beneficial in health care area. Molecular diagnostic technique is used to analyse biological markers in the individual's genetic code and how their cells express their genes as proteins. It is used to diagnose and monitor disease, detect risk and decide which therapies will work best for individual patients. It is even useful for infectious disease, oncology, human leukocyte antigen, coagulation and pharmacogenomics. They work in co-ordination with clinical chemistry i.e. medical tests on body fluids. It even uses techniques such as mass spectrometry and gene chips to capture expression patterns of genes and proteins. In 2012, Molecular Diagnostic techniques for thalassemia use genetic hybridization tests to identify the specific single nucleotide polymorphism causing an individual's disease. In this review we describe the biosensors and molecular diagnostics techniques and their applications.*

Keywords*: Biosensor, Molecular diagnostic, biological markers*

1. INTRODUCTION

Biosensor is an analytical device that utilises biological components with a physicochemical detector. It is used for the detection of an analyte. For eg: Enzymes to indicate the amount of a biomaterial[1][2].The biocatalyst converts the substrate to product. Biocatalyst is followed by a transducer or the detector element. It transforms the signal produced due to the interaction of the analyte with the biological element into the another signal. This signal can be more easily measured and quantified[3]. Now, the electrical signal generated from the transducer is amplified, processed and displayed(Fig. 1). At the present time, biosensors represent a rapidly expanding field with an estimated 60% annual growth rate. Research and development in this field is wide and multidisciplinary.

Molecular diagnostics is a technique which is used to analyse biological markers in the genome and proteome i.e., the individual's genetic code. It even analyses how their cells express their genes as proteins by applying molecular biology to medical testing. The technique is used to diagnose and monitor disease, detect risk and decide which therapies will work best for individual patients[4][5]. Molecular diagnostics even offers the prospect of personalised medicine by analysing the condition of the patient and their disease[6]. These tests are useful in variety of medical specialisms which includes, infectious disease, oncology, human leukocyte antigen typing, coagulation and pharmacogenomics i.e, the genetic prediction of the action of the drug[7].

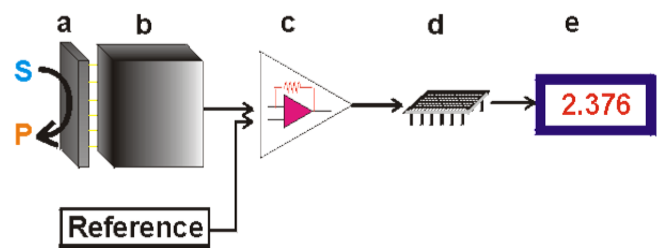

Fig. 1: Schematic diagram showing the main components of a biosensor. (a) Biocatalyst (b) Transducer (c)Amplifier (d)Signal Processor (e)Display

2. FEATURES OF BIOSENSOR

(i)The biocatalyst must be highly specific for the analyses purpose, should be stable under normal storage conditions and show good stability over a large number of assays.

(ii)The reaction should be independent of physical parameters such as stirring, pH and temperature. This would help us in the analysis of samples with minimal pre-treatment. If the reaction involves cofactors or coenzymes then these should also be co-immobilised with the enzyme.

(iii)The response should be accurate, precise, reproducible and linear. It should also be free from electrical noise.

(iv)If the biosensor is to be used for invasive monitoring in clinical situations, the probe must be tiny and biocompatible. It should have no toxic or antigenic effects. If it has to be used in fermenters then it should be sterilisable. This can be done by autoclaving but presently no biosensor enzymes can withstand wet-heat treatment. In either case, the biosensor should not be prone to fouling or proteolysis.

(v)The complete biosensor should be cheap, small and portable. It should be capable of used by semi-skilled operators.

(vi)There should be market for the biosensor. There is clearly very little purpose developing a biosensor if the other factors like, government subsidies, poor customer perception etc encourage the use of traditional methods and discourage the decentralisation of laboratory testing.

(vii)The biological response of the biosensor is determined by the biocatalytic membrane which helps in the conversion of reactant into product. Immobilised enzymes possess a number of advantageous features which makes them suitable for the use in such systems.

3. GENERATIONS OF BIOSENSORS

In First generation biosensors the normal product of the reaction diffuses to the transducer and causes the electrical response. Second generation biosensors, involves specific mediators between the reaction and the transducer in order to generate improved response. In third generation biosensors, the reaction itself causes response and no product or mediator diffusion is directly involved[8].

4. TECHNIQUES OF MOLECULAR DIAGNOSTICS

Due to the industrialisation of molecular biology assay tools has made it practical to use them in clinics[5]. Molecular diagnostics uses biological assays such as PCR-ELISA or Fluorescence in situ hybridization[9][10]. The assay detects a molecule often in low concentrations which proves to be a marker of disease or risk in a sample taken from a patient. Sample preservation before analysis is critical. Manual handling should be minimised[11]. As molecular diagnostics can detect sight markers, it is less presumptuous than biopsy. For eg: Cell free nucleic acids exist in human plasma, a simple blood sample can be enough to sample genetic information from tumours, transplants or an unborn foetus. Molecular diagnostics based on nucleic acids use Polymerase Chain Reaction(PCR) to increase the number of nucleic acid molecules on large scale and thus, finally amplify the target. For the detection of the marker real time PCR, direct sequencing or microarrays i.e., prefabricated chips that test many markers at once[5]. The same principle is applied to the proteome and genome. High throughput protein arrays can use complementary DNA or antibodies to bind and hence can detect many different proteins in parallel[12].

5. RELATION BETWEEN BIOSENSOR AND MOLECULAR DIAGNOSTICS

Analysis in medical diagnostics can be made effective, sensitive, and fast by developing biosensors. The next generation of biosensors have the ability to make use of various biological elements such as antibodies, nucleic acid etc. Clark was the person who initiated his research in this field of biosensors. A large number of biosensors since then have made their presence felt in the literature and has shown its application in molecular diagnostics. YSI(Yellow Spring Instruments) incorporated the apparatus for the determination of glucose that lies within the 80% of the commercial devices that is based on biosensors. The existence of some pathogenic organisms can also be detected using these biosensors that have their application in clinical diagnostics. Identification of genetic polymorphisms and detection of point mutations are among others. The DNA/RNA fragments, biological or chemical species can also be detected using the nucleic acid based biosensors specially designed for the purpose.[13]

6. APPLICATIONS

Biosensors are devices comprising a biological element and a physiochemical detector that are used to detect analytes. These instruments have wide range of applications which ranges from clinical through to environmental and agricultural. The devices are also useful in the food industry. Some examples of the fields that use biosensor technology includes:

Clinical and Diagnostic Applications- Glucose monitor is an example of one of the well knowned clinically applied biosensor. It is used on a routine basis by diabetic individuals to check the blood sugar level. These devices detect the amount of blood glucose in undiluted blood samples. Thus, allows easy self-testing and monitoring. Hence, it has revolutionized diabetes management(Fig. 2).

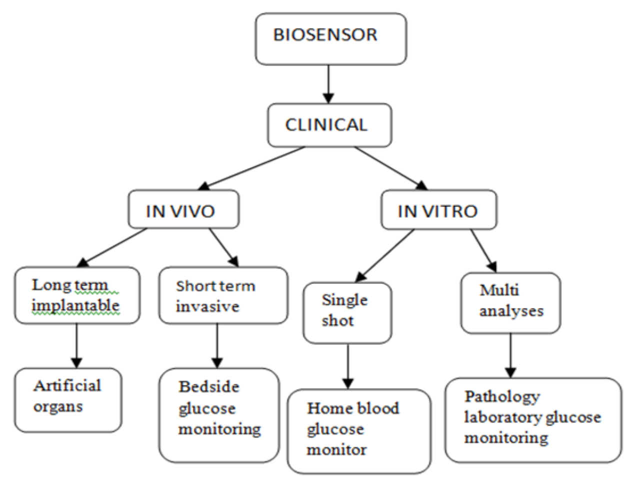

Fig. 2: Clinical applications of biosensor

Applications in Industry- Biosensors are used in food industry to measure carbohydrates, alcohols and acids. These devices may also be used to check the fermentation during the production of bee, yoghurt and soft drinks. It is even useful in detecting pathogens in fresh meat, poultry or fish.

Environmental Applications- Biosensors are used to check the quality of air and water. They are used to pick up the traces of organophosphates from pesticides or to check the toxicity levels of wastewater.

General healthcare monitoring

Screening for disease

Veterinary and agricultural applications[14].

(Fig. 3).

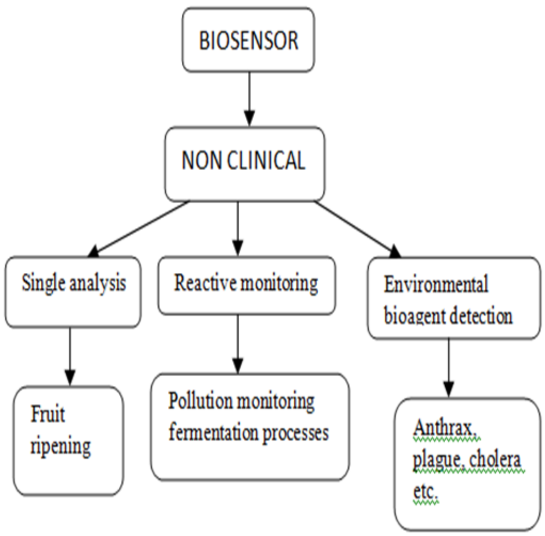

Fig. 3: Non clinical applications of biosensor

Following are the applications of molecular diagnostics:

Prenatal- Conventional prenatal tests for chromosomal abnormalities such as down syndrome is based on the analysis of number and appearance of the chromosomes. Molecular diagnostics tests such as microarray comparative genomic hybridisation test a sample of DNA[15].

Treatment- Some of patient's single nucleotide polymorphisms slight differences in their DNA can help us in predicting how quickly they will metabolise particular drug. This is called pharmacogenomics[16]. For eg: The enzyme CYP2C19 metabolises several drugs such as the anti-clotting agent Clopidogrel into their active forms. Some of the patients possess polymorphisms in specific places on the 2C19 gene. Physicians can test for these polymorphisms and find out whether the drugs will be fully effective for that patient[17]. Due to the advancement in molecular biology it is evident that some syndromes that were preciously classed as a single disease are infact multiple subtypes with entirely different causes and treatments. Molecular diagnostics can thus help to diagnose the subtype of infections and cancers or the genetic analysis of a disease with an inherited component such as Silver-Russell Syndrome[4][18].

Infectious disease- Molecular diagnostics are used to diagnose infectious disease like, influenza virus[19], tuberculosis[20] or specific strains such as H1N1 virus[21]. This technique is even helpful to understand the specific strain of the pathogen by detecting which drug resistance genes it possesses and hence gives an account of the therapies to be avoided[22].

Disease risk management- The genome of a patient may include an inherited or random mutation. It may affect the probability of developing a disease in future[16]. For eg: Cardiovascular risk is indicated by biological markers and screening helps in measuring the risk of child being born with Cystic fibrosis[23]. On the other hand, genetic testing is ethically complex because the patients may not want the stress of knowing their risk[24]. In countries which do not have universal healthcare a known risk may raise insurance premiums[25].

Cancer- The cellular process that causes a change i.e., a tumour to grow out of control is cancer. By analysing the molecular signature of cancerous cells, the DNA and its levels of expression via messenger RNA enables physicians to characterise the cancer and hence, to choose the best therapy for their patients[16]. From the data of 2010, assays that includes an array of antibodies against specific protein marker molecules are an emerging technology. It is thought that these multiplex assays could measure many markers at once[26]. Other potential future biomarkers consist of micro RNA molecules which are expressed more by cancerous cells than that of healthy ones[27].

7. CONCLUSION

Over the last decade, tremendous amount of activity has been witnessed in the field of biosensors. Biosensors for monitoring blood glucose at home has proven to be of great importance in the world diagnosis market. They are even followed by variety of array of biosensors for detecting other analytes of clinical importance[13].

Personalised medicine, including the molecular diagnostic tests that provide information to our healthcare providers may ultimately revolutionize cancer prevention, diagnosis, treatment and other follow-ups. It provides us with higher probability of desired outcomes and reduces the probability of negative side effects. Thus, due to these techniques focus is more on prevention and prediction of disease rather than primarily reaction[28].

8. ACKNOWLEDGEMENT

We are grateful to our Director of Amity Institute of Biotechnology, Amity University Uttar Pradesh, Noida for his constent support and encouragement during this study.

REFERENCES

[1] Turner, Anthony, Wilson, George, Kaube and Isao, "Biosensors: Fundamentals and Applications", Oxford University Press, UK,1987,pp.770.

[2] Banica, Florinel and Gabriel, “Chemical Sensor and Biosensors: Fundamentals and Applications”, UK, pp.576.

[3] Cavalcanti, Shirinzadeh, ZhaNG and Kretly, “Nanorobot Hardware Architecture for Medical Defence”, *Sensors*,8,5,2008, pp.2932-2958.

[4] Poste,G.;”Molecular diagnostics: A powerful new component of the healthcare value chain”; *Expert Review of Molecular Diagnostics* 1,1,2012,pp.1-5.

[5] Carl, A. Burtis, Edward,R. Ashwood, David, E. Bruns and *Tietz, Textbook of Clinical Chemistry and Molecular Diagnostics,2012.*

[6] Hamburg, M.A., Collins and F.S., “The Path to Personalised Medicine”, *New England Journal of Medicine, 364,4,2010,pp.301-304.*

[7] Grody, Wayne, Nakamura, Robert, Strom, Charles, Kiechle and Frederick, “Molecular Diagnostics: Techniques and Applications for the Clinical Laboratory”, Academic Press Inc., Boston, 2010.

[8] www1.Isbu.ac.uk

[9] “Molecular Diagnostics: Current Technology and Applications”, *July 7 2006*,pp.97.

[10] Van Ommen, G.J.B., Breuning, M.H., Raap and A.K., “FISH in genome research and molecular diagnostics”, *Current Opinion in Genetics & Development*,5,3,1995, pp.304-308.

[11] Hammerling and J.A., “A Review of Medical Errors in Laboratory Diagnostics and Where We Are Today”, *Laboratory Medicine*,43,2,2012, pp. 41-44.

[12] Walter, Gerald, Bussow, Konard, Leuking, Angelika, Glokler and Jorn, “High-throughput protein arrays prospects for molecular diagnostics”, *Trends in Molecular Medicine*,8,6,2002, pp.250-253.

[13] M. Mascini and S.Tombelli, “Biosensors for biomarkers in medical diagnostics”, *Biomarkers*,13,7-8,2008,pp.637-657.

[14] www.news-medical.net

[15] “Advances in Prenatal Molecular Diadnostics Conference”, HealthTech,2013.

[16] “Molecular Diagnostics: National Cancer Institute”, Cancer govt, January 28 2005.

[17] Desta Z.,, Zhao, X., Shin, J.G., Flockhart and D.A., “Clinical Significance of the Cytochrome P4502C19 Genetic Polymorphism”, *Clinical Pharmacokinetics*,41,12,2002, pp. 913-958.

[18] Eggermann, T., Spengler, S., Gogiel, M., Begemann and Elbracht, “Epigenetic and genetic diagnosis of Silver-Russell Syndrome”, *Expert Review of Molecular Diagnostics*,12,5,2012,pp.459-471.

[19] Deyde, V.M., Sampath, R., L.V. and Gubareva, “RT-PCR/ electrospray ionization mass spectrometry approach in detection and characterization of influenza viruses”, *Expert Review of Molecular Diagnostics*, 11,1,2011,pp. 41-52.

[20] Pai, M., Kalantri, S., Dheda and K., “New tools and emerging technologies for the diagnosis of tuberculosis: Part I. Latent tuberculosis”, *Expert Review of Molecular Diagnostics*,6,3,2006,413-422.

[21] Bukardt and H.J., “Pandemic H1N1 2009(‘swine flu’): Diagnostic and other challenges”, *Expert Review of Molecular Diagnostics*,11,1,2011,pp. 35-40.

[22] Tang, Yi-Wei, Procop, Gary W., Persinga and David H., “Molecular diadnostics of infectious diseases”, *Clinical Chemistry*, 43,11,November 1 1997, pp. 2021-2038.

[23] Shrimpton and A.E., “Molecular diagnosis of cystic fibrosis”, *Expert Review of Molecular Diagnostics*, 2,3,2002,pp. 240-256.

[24] Andorno and R., “The right not to know: An autonomy based approach”, *Journal of Medicine Ethics*,30,5,2004,pp.435-439.

[25] Harmon and Amy, “Insurance Fears Lead Many to Shun DNA Tests”, *New York Times*, February 24 2008.

[26] Brennan, D.J., O’Connor, D.P., Rexhepaj, E., Ponten, F., Gallagher and W.M., “Antibody-based proteomics: Fast-tracking molecular diagnostics in oncology”, *Nature Reviews Cancer*,10,9,2010, pp.605-617.

[27] Ferracin, M., Veronese, A., Negrini and M., “Micromarkers: MiRNAs in cancer diagnosis and prognosis”, *Expert Review of Molecular Diagnostics*,10,3,2010,pp.297-308.

[28] “Impact Report: Analysis and Insight into Critical Drug Development Issues”, *Tufts Center for the Study of Drug Development*,12,6,2010.