REVIEW ARTICLE

DNA Based Biosensors

Mohammed Fadhil Haddad[1,2]

[1]Department of Chemistry, Faculty of Arts and Sciences, Yıldız Technical University, 34220, Istanbul, Turkey
[2]Mosul Technical Institute, Northern Technical University, 41002, Mosul, Iraq
Mobile: 00905350337392- 009647706159000,
Email: Mf_mf_mf8@yahoo.com / mohammed.8.haddad@gmail.com
ORCID: https://orcid.org/0000-0002-9319-6502
Received: 11/7/2019 Accepted:24/8/2019 Published:1st, January 2020

Abstract

Biosensors especially DNA biosensors find use in diverse fields like clinical, food adulteration prevention, and in the monitoring of the environment. The DNA based biosensors have gained prominence in detection and monitoring and are the ultimate choice due to their high sensitivity and selectivity. Novel synthetic probes have been exploited for their use in various clinical settings. Here in this review, the major DNA biosensor technologies available in the market is discussed with the addition of two crucial technological breakthrough in detecting mercury poisoning as well as DNA damage due to ultraviolet light is also discussed. DNA biosensors technology is evolving at a faster pace and is coming up with the rational solution in the detection of various clinical conditions as well as coverage area like environmental pollution, which we can now detect at a faster rate with the help of state of the art DNA biosensors in no time. Thus DNA biosensors are becoming part and parcel of the mainstream science, and through this review, a try has been made to address the various issues relating to DNA biosensors in today’s world.

Keywords: DNA biosensor technologies; ultraviolet light; phosphorus; clinical; food adulteration; monitoring of the environment.

Introduction

A biosensor is a device which comprises of a biological sensing element along with a transducer to produce a signal which is in turn proportional to the material to be analysed or in other words the concentration of the analyst. The signal produced is primarily due to a release of a gas or a due to a difference in the number of protons, some light is being emitted, or there is some change in the mass. The transducer then takes up the signal and just converts it into a form that is measurable through piezoelectric electrochemical, production of heat or light, which can be measured by appropriate equipment. The basic characteristics of a biosensor are linearity, sensitivity, selectivity and response time [1].

DNA biosensors work on the principle of hybridization of single-stranded DNA molecules to its complementary molecules which are present in the sample. Generally, DNA biosensors are used for medical diagnostics, forensic science, agriculture, or during environmental clean-up. There is hardly any need of any external monitoring for DNA-based sensing devises, which is indeed a significant advantage in itself.

The various types of DNA biosensors are broadly divided into three, and they are optical, electrochemical, and piezoelectric. The category of optical biosensor involves the biosensors based on fiber optics, surface plasmon resonance, biomolecular interaction analysis, and Raman spectroscopy. The electrochemical biosensors have DNA as the biological element, and they use carbon paste electrodes as a transducer. The DNA biosensors using piezoelectric effect as their working principle use DNA as their biological element and the transducer used in this case is mainly made up of crystals.

1.1.Optical DNA biosensors:

Optical DNA biosensors mainly rely on the property of fibre optic to carry light from one place to another. Hence whenever there is any fluorescence produced the fibre optic cable will relay the fluorescent signal to appropriate place through the means of a series of internal reflections [2]. The operation of fibre-optic DNA biosensors involves placement of an ssDNA probe at the end of the fibre and monitoring the fluorescent changes resulting from the association of a fluorescent indicator with the double-stranded (ds) DNA hybrid [3] .The different types of optical biosensors are

1.1.1. Molecular Beacons (MBs)

Molecular Beacons are a sort of stem loop structure with two main parts, one is the fluorophore at one end and the other is quencher at the other. Molecular Beacon probes are popular for their sensitivity and specificity [3].

1.1.2. Surface Plasmon Resonance (SPR)

These biosensors work on the principle that there is change in surface optical properties which obviously results from surface binding reaction and are continuously monitored by the biosensor to give adequate signal outputs which can be read. The change in surface properties is due to change in resonance angle due to change in the interfacial refractive index [3].

1.1.3. Quantum–Dot

The working principle behind the quantum-dot biosensor is mainly Fluorescence resonance energy transfer an ultrasensitive nanosensor based on fluorescence resonance energy transfer (FRET) can detect very low concentration of DNA and do not require separation of un-hybridized DNA. Such type of technique is based on quantum-dots (QDs) which are linked to specific DNA probes to capture target DNA [3].

1.2. Piezoelectric DNA Biosensor

The working principle of this biosensor is mainly based on the oscillation of quartz crystals, at a particular frequency when a certain amount of oscillating voltage is applied. These types of biosensor are simple and cost effective. Piezoelectric DNA biosensor allows for label free detection [4].

1.3. Strip Type DNA Sensor

Here in this type of biosensor, changes in optical properties of the gold nanoparticle due to the occurrence of hybridization is closely monitored. It allows direct detection of DNA hybridization without any interference. These types of biosensors do not require any complicated instrument and washing and incubation steps as in other biosensors are avoided completely [3].

1.4. Electrochemical DNA Biosensors

These kinds of biosensor are mainly sequence specific and a great deal of miniaturization in them can be brought about, which make them excellent means for diagnostics. The main idea behind such a biosensor is to monitor or observe the current at a particular fixed [4].

1.5. Literature review

DNA based biosensors have been used in the identification of pathogenic bacteria and fungus. Bora et al in their published review [5] in 2013 in Biosensors Journal indicates that DNA biosensors can be used for various clinical applications. Electrochemical biosensors were primarily used for the identification of AIDS virus in humans as well as the deadly Hepatitis B virus. The human papilloma virus which is a deadly virus causing cancer in humans has been detected using biosensors which are having piezoelectric transducers. About sixteen strains of the deadly virus were detected. This particular biosensor worked by using degenerate probes and specific probes and these probes were immobilized for the detection to work well [6].The detection of cancer has been a great challenge in recent times. There is an answer to this problem and that is nothing but nucleic acid based biosensors, which are able to detect early certain types of cancers by means of quantifying the levels of expression of various cancer Here they use DNA and RNA probes as a diagnostic tool [7].

Vasopressin, a biomarker for traumatic injuries have been detected in recent times using aptamer based electrochemical biosensors. These aptamers were immobilized on carbon nanotubes and measurement was done based on the formation of aptamer-vasopressin conjugation [8]. The tuberculosis biomarker was detected based on QCM based biosensor [9]. This biosensor mainly works on the principle of hybridization between gold nanoparticles and magnetic particles (MPs) each functionalized with DNA probes and tuberculosis specific DNA fragment [10].

An aptamer-based biosensor was developed for the rapid detection of level of The Retinol binding protein in serum samples were detected based on a particular kind of aptamer based biosensor. SPR based detection method was used after the specific aptamers were immobilized on gold chips [11].

Hepatitis B virus DNA detection was also carried out recently using the gold nanoparticle based DNA biosensors with extreme sensitivity in detection being observed [12]. Food-borne diseases are mainly due to pathogens like bacteria, streptococcus, clostridium, cholera causing organism. Aptamer based biosensor was reported for the detection of food borne pathogens which includes mainly coliforms, cholera causing bacteria, Streptococcus etc. These types of biosensors use unmodified gold nanoparticles by colorimetric assay [13]. A DNA biosensor was developed for the detection of PCR amplicons of cholera causing *Vibrio cholera* [10]. A particular kind of electrochemical-DNA biosensor which works on the principle of nanoporous membrane technology has been developed, which can detect the cDNA sequence in Dengue virus [14].Using electrochemical DNA sensing technology a 31-mer oligonucleotide sequence of Dengue virus has been detected. It involves the measurement of impedance changes that occur due to cross linking of DNA probes on the surface of nanoporous alumina membrane, during probe-target DNA hybridization [15].

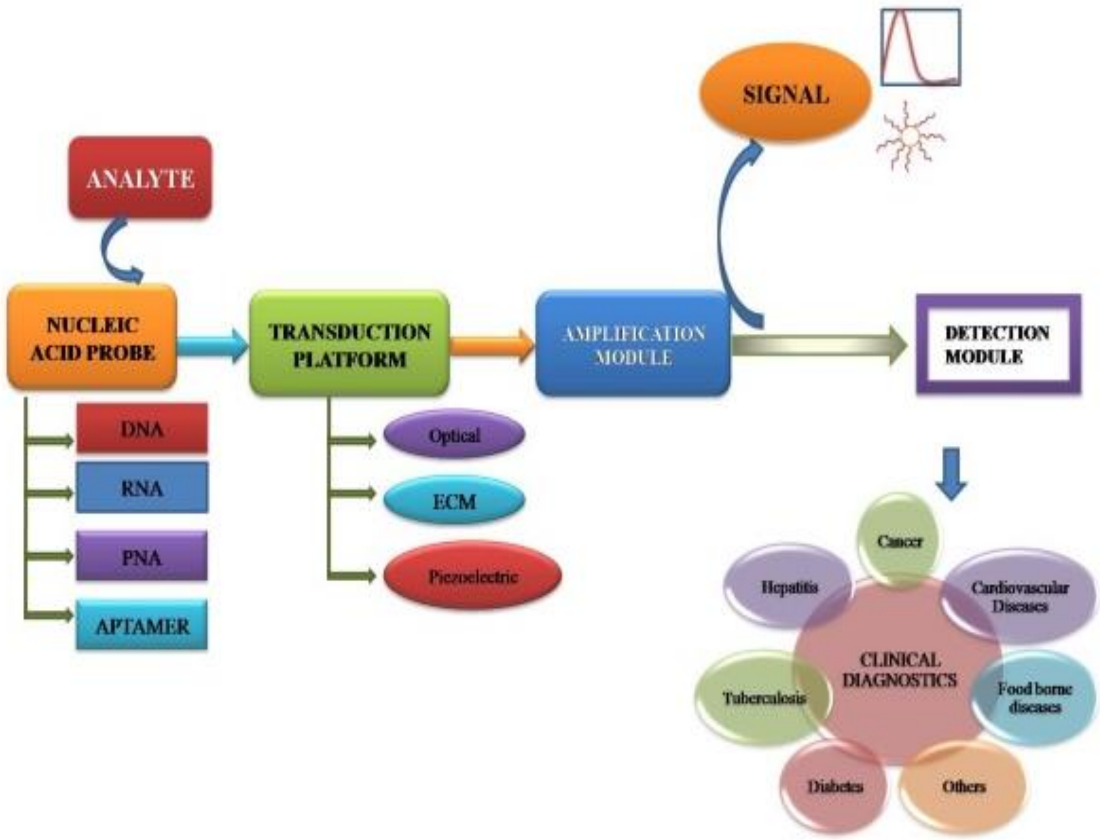

Fig.1. Schematic representation of various DNA based biosensors

Adapted from Bora et al. [5]

Discussion

In a particular work published in the journal Biosensors and Bioelectronics [16] have developed a new electrochemical DNA-based biosensor for the selective determination of the mercury ions. Here the working principle is the use of electrodes modified by polythymine, which bears methylene blue as a probe. Here the formation of Thymine–Mercury ion–Thymine complex is basic working principle of this biosensor. The coupling of mercury ion to thymine is more pronounced than adenine thymine coupling which serves as a means of accurately detecting the mercury ions in the sample. This is a new electrochemical DNA biosensor based on "signal on" assay mode for the selective determination of the Hg2+ ion by the use of a gold electrode where polythymine, modified in 3′ position with methylene blue as redox probe, was immobilized as self assembled monolayer (SAM). Methylene blue is already known as electrochemical probe for DNA-based biosensors, in this case is covalently bound to polythymine strand. In the presence of the mercury ions in solution, the formation of Thymine-mercury-Thymine is favoured more and this complex causes hairpin like folding of the oligonucleotide and which causes the methylene blue approach the electrodic surface. Once the methylene blue approaches the electrodic surface an electronic exchange takes place between the methylene blue and the gold electrode thereby resulting in the production of faradic current, detected by square wave voltammetry. This difference in current is directly proportional to the amount of mercury ions present in the. The results pave the way for miniaturization of such biosensors which can be deployed to trace the environmental pollutants like mercury [17]

DNA based biosensor was developed that can detect damage to DNA caused by UV-C radiation. The sensor is composed of a glassy carbon electrode whose surface was modified with a layer of dsDNA and another layer of Cadmium telluride (CdTe) Quantum Dots. The working principle of this biosensor is based on the intrinsic anodic signal of the guanine moiety in the DNA that is measured by square-wave voltammetry and the cyclic voltammetric response of the redox indicator system hexacyanoferrate (III/II). This type of biosensor is simple and effective in evaluating the damage caused to DNA by various physical agents and various types of nanoparticles [8].

Conclusion

In the past decade or so enormous progress has been made in the field of DNA based biosensors especially in the clinical domain which affects the health care sector in a great way. The high stability and specificity of nucleic acid based biosensors are a boon to the clinical field for their routine diagnostics of various kinds of illness. But the bottleneck involved in the investment for commercialization of biosensor technologies are to be addressed thoroughly. Recent developments in the area of DNA based biosensors involve more and more use of nano materials in the manufacture of DNA biosensors. These nanomaterials should be specialized in their specificity and sensitivity. The other major breakthrough is to use other nano materials apart from the DNA. Polymers, enzymes and doped oxides can be used for better detection. In the coming years DNA based nano biosensors will push the existing frontiers in the Biosensor technologies and strive to achieve perfection in not only clinical diagnostics but also other fields like food science and environmental aspects, and will be dominated by the next generation DNA biosensors.

In distant future, the rapidly growing medical diagnostic field will be essentially dependent on the state-of-the-art biosensors. Day by day new technologies are emerging from the various labs around the world which caters to the growing demands of not only the medical field but other areas as well.

References

1. Kuswandi B, Mascini M. Enzyme inhibition based biosensors for environmental monitoring. Current Enzyme Inhibition, 2005; 1(3):207-22.
2. Byoungho L. Review of the present status of optical fiber sensors, Optical Fiber Technology, 2003; 9:57-79.
3. Kumar A, Dash SK, Suman DPS. DNA based biosensors for detection of pathogens. In Plant Fungal Disease Management, 1st ed.; Westville: New York, NY, USA, 2015; pp. 31–35.

4. Bunde RL, Jarvi EJ, Rosentreter JJ. Piezoelectric quartz crystal biosensors, Talanta, 1998; 46:1223-1236.
5. Bora, U, Arghya S, Deepika S. Nucleic acid based biosensors for clinical applications. Biosens J 2013; 2(1):1-8.
6. Dell'Atti D, Zavaglia M, Tombelli S, Bertacca G, Cavazzana AO, et al. Development of combined DNA-based piezoelectric biosensors for the simultaneous detection and genotyping of high risk Human Papilloma Virus strains. Clinica Chimica Acta 2007; 383: 140–146.
7. Bohunicky B, Mousa SA. Biosensors: the new wave in cancer diagnosis. Nanotechnology Sci Applica 2011; 4:1-10.
8. He P, Oncescu V, Lee S, Choi I, Erickson D. Label-free electrochemical monitoring of vasopressin in aptamer-based microfluidic biosensors. Analytica Chimica Acta, 2013; 759:74-80.
9. Kaewphinit T, Santiwatanakul S, Chansiri CPK. Detection of Non- Amplified Mycobacterium tuberculosis Genomic DNA Using Piezoelectric DNA-Based Biosensors. Sensors 2010;10: 1846-1858
10. Chua A, Yean CY, Ravichandran M, Lim B, Lalitha P. A rapid DNA biosensor for the molecular diagnosis of infectious disease. Biosens Bioelectronics 2011; 26: 3825–3831.
11. Lee SJ, Youn BS, Park JW, Niazi JH, Kim YS, Gu MB. ssDNA aptamer-based surface plasmon resonance biosensor for the detection of retinol binding protein 4 for the early diagnosis of type 2 diabetes. Analytical Chemistry, 2008; 80(8): 2867-2873.
12. Lu X, Dong X, Zhang K, Han X, Fang X, Zhang Y. A gold nanorods-based fluorescent biosensor for the detection of hepatitis B virus DNA based on fluorescence resonance energy transfer. Analyst, 2013; 138(2):642-650.
13. Wu WH, Li M, Wang Y, Ouyang HX, Wang L, Li CX, Lu JX. Aptasensors for rapid detection of Escherichia coli O157: H7 and Salmonella typhimurium. Nano Scale Res Letters, 2012; 7(1):658.
14. Rai V, Hapuarachchi HC, Ng LC, Soh SH, Leo YS, et al. Ultrasensitive cDNA Detection of Dengue Virus RNA Using Electrochemical Nanoporous Membrane-Based Biosensor. PLoS ONE 2012; 7: e42346.
15. Deng J, Toh CS. Impedimetric DNA Biosensor Based on a Nanoporous Alumina Membrane for the Detection of the Specific Oligonucleotide Sequence of Dengue Virus. Sensors 2013; 13: 7774-7785.
16. Torres-Chavolla E, Alocilja EC. Nanoparticle based DNA biosensor for tuberculosis detection using thermophilic helicase-dependent isothermal amplification. Biosensors Bioelectronics, 2011; 26(11):4614-4618.
17. Rai, Varun, Hapuarachchi HC, Ng LC, Soh SH, Leo YS, Toh CS. Ultrasensitive cDNA detection of dengue virus RNA using electrochemical nanoporous membrane-based biosensor. PloSone 7.8 (2012): e42346.