ISSN: 2278-5213

REVIEW ARTICLE

Commercial Biosensors: An outlook

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Abstract

Significant development has been occurred in the improvement of biosensor technology in terms of use of transduction and bio-receptor techniques. Reported literature reflects that electrochemical biosensors are most suited for field purposes (e.g. hand-held). On the other hand amperometric based technology biosensors are most suited for implantable biosensors. Optical biosensors still maintain its position in processing of large number of sample simultaneously. This review is focused to give an outlook of some of the commercial biosensors available in market.

Keywords: Biosensor technology, hand-held biosensors, implantable biosensors, commercial biosensors.

Introduction

Biosensors are detecting devices that rely on the specificity of cells and molecules to identify and measure substances at extremely low concentrations (Mongra and Kaur, 2012). Recent advancements in the field of bio electronics and biotechnology particularly, the tailoring of new biomaterials by bio-genetic engineering allows to create new enzymes and protein receptors, and to engineer monoclonal antibodies, aptamers or nucleic acids for non-biological substrates has helped their integration in electronic devices and use of carbon Nanotubes, Nanowires, Graphene sheets, Field Effect Transistors, piezoelectric crystals, scanning tunneling microscopy tips and others are recent development steps in biosensor technology. The field is not limited by a lack of information regarding the fundamental technology However, biosensors market is characterized by slower pace of commercialization, which is primarily attributed to high cost, availability of effective alternative technologies, and issues related to stability, sensitivity, and quality assurance.

The continual research and development efforts being undertaken would go a long way in making sure that biosensor technology would continue to evolve as the years come, with faster, more specific and high specialty applications. Biosensors in medical applications remains a hugely untapped market, attracting several new players, who in hopes of leveraging dormant market opportunities, are foraying into the marketplace. The biosensors industry comprises of 2 types of participants including companies developing biosensor-based devices and developers of biosensor technology. Key players engaged in developing biosensor technology include AgaMatrix Inc., Cranfield Biotechnology Center, LifeSensors Inc., M-Biotech, and Nova Biomedical.

Leading manufacturers of biosensor-based devices include-Abbott Point Of Care Inc., Affinity Sensors, Neosensors Limited, Siemens Healthcare Diagnostics Inc, Animas Corporation, LifeScan Inc., Medtronic Diabetes, and Roche Diagnostics Ltd. The growth for biosensors market is robust in emerging markets in Asia-Pacific with 11% CAGR (2008-2018) closely followed by 10.7% in highly developed market of the United States. Europe is the second largest in terms of value, after the US with an estimated $2.6 billion in 2012 (Griffiths and Hall, 1993; Luong *et al.,* 2008). Practically, biosensors can take 4 forms: hand-held devices, laboratory instruments, flow type sensors (for large volumes) and implanted sensors (for whole body monitoring). In this review, the survey of various types of biosensors has been covered to see which is more suitably used in field and lab or in implantable way in term of commercial perspective.

Some commercial biosensors

There are well over 500 companies worldwide presently working in the area of biosensors and bioelectronics (Weetall, 1999). Some of these companies are directly involved in biosensor fabrication/marketing, whereas others play an important role in providing the necessary raw-materials/reagents/instruments for the production of biosensors (e.g., Applied Enzyme Technologies, Biozyme Laboratories, Dupont Ltd., Eco Chemie, Ercon Incorporated, Gwent Electronic Materials Ltd., Palm Instruments, Uniscan Instruments Ltd., etc). Most of these companies are working on existing biosensor technologies that were developed over a decade ago (Weetall, 1999). Few of them are developing new technologies, although they appear to be improving existing technologies in order to move them into the commercial arena.

Some of the companies make the parts of biosensors while, others assembled the parts and launch in the markets and still some are manufactures of parts and complete sets of biosensors. Hence, it is difficult to follow the criteria to give credit of development of commercial biosensors for all of them. Commercial biosensors can be divided into 2 categories on the basis of whether they are laboratory or portable/field devices. The most successful handheld biosensor to date is the blood glucose monitor for people with diabetes, which is based on electrochemical transduction technology (D'Orazio, 2003). Commercial blood-glucose meters are produced by many companies. However, in terms of laboratory-based instrumentation an optical detection system appears to be more commercially viable.

Companies such as Affymetrix and Agilent have developed various commercial micro-array optical detectors and scanners for genomic and proteomic analysis. Optical sensors that employ Surface Plasmon resonance (SPR) detection have also been successfully used in many laboratories and universities (Rich and Myszka, 2002). In terms of implantable biosensors, several companies are investigating such systems, but are only looking at monitoring the level of glucose in the blood. The device developed by Medtronic Minimed, the diabetes management business of Medtronic, is a tiny enzyme-based sensor that is implanted under the skin for up to 3 d. By contrast, VeriChip are presently developing an implantable microprocessor. Although a step in the right direction, these devices still suffer from the limitations.

It is important to note that several multinational companies dominate the biosensor industry. Reports suggest that MediSense, Bayer and Roche Diagnostics are the major players in terms of market hand-held "meter" style devices with disposable one-shot electrodes (Newmann *et al.,* 2004). However, the recent merger of Therasense and i-STAT with Abbott has significantly reinforced its position in the top biosensor companies worldwide (Newmann *et al.,* 2004). By contrast commercially available optical bench-size immune-sensor systems such as BIAcore™ (Biacore AB, Uppsala, Sweden) and IAsys (Affinity Sensors, Cambridge, UK) have found their market in research laboratories for the detection and evaluation of bio-molecular interactions, noting that these technologies are based on the principles of surface plasmon resonance. Pharmacia Biosensor AB, now BIAcore AB, was the pioneer of the commercial based SPR and currently holds approximately 90% of the market in this technology (Rich and Myszka, 2002). It is important to note that BIAcore offer a range of biosensors with various specifications and a recent review suggests that BIAcore instruments are the most sensitive (Leonard *et al.,* 2003). Unfortunately, most of the SPR instruments are relatively expensive and are not designed for studies in the field.

However, Texas Instruments have recently developed a low cost, rapid, and portable SPR-based biosensor (Spreeta™) which can be deployed in the field. Some reports suggest that this technology is not as sensitive compared to the standard enzyme-linked immunosorbent assay (ELISA) (Spangler *et al.,* 2001). Nevertheless, there appears to be a general push for developing hand-held devices. The development of disposable sensors in conjunction with handheld devices for point of care measurements has featured prominently. Micro-fabrication technology has played an important part in achieving miniaturised biosensors. Such technology has provided cheap mass-producible and easy-to-use/disposable sensor strips. Electrochemical methods have played a pivotal role in detecting the changes that occur during a bio-recognition event and the merging of micro-fabrication with electrochemical detection has enabled various handheld biosensor devices to be developed. In fact, i-STAT have developed the world's first hand-held device for point-of-care clinical assay of blood noting that this biosensor array employs several electrochemical-based transduction methods (i.e., potentiometric, amperometric, conductometric). i-STAT Corporation is an international company that manufactures and markets diagnostic products for blood analysis. The i-STAT Portable Clinical Analyser™ is a hand-held silicon-based multiple-analyte sensor array which is used to monitor various blood electrolytes (i.e., sodium, potassium, chloride, calcium, pH) gases (i.e., carbon dioxide, oxygen) and molecules (i.e., urea, glucose, hematocrit).Oxford Biosensors have also developed a portable hand-held device (Multisense™) for cholesterol detection. The biosensor consists of disposable test strips (microelectrodes) and uses the electrochemical detection strategy. Likewise, SenDx Medical Inc. (acquired by Radiometer) has fabricated a compact and portable potentiometric sensor array for determining various ions in the blood.

Various organisations have directed their efforts towards developing DNA chips and lab-on-chip devices. DiagnoSwiss is a company specialising in protein analysis on miniaturised platforms. They have recently fabricated a lab-on-a-chip (or biochip) device for high-performance and high-throughput immunological testing. The unique feature of this device is that it incorporates both a micro-analytical system for separating various components along with a detection platform (electrochemical-based). GeneOhm Sciences have developed a DNA chip that employs the electrochemical detection platform. Established in San Diego, California in 2001, GeneOhm Sciences is a company that focuses on molecular diagnostics for a wide range of diseases. Likewise, Motorola Life Sciences Inc is another organization that has produced an electrochemical-based DNA chip. A number of small companies appear to be making some progress in the development of various handheld devices.

Chemel (Lund, Sweden) have developed a portable biosensor (SIRE biosensor) that is based on enzymatic/amperometric measuring principles. This technology has only been used to measure various sugars and alcohols. Sensor Tech. Ltd. (Cambridge, UK) has recently developed an immunosensor (Universal Transducer System) for *in vitro* diagnostic and biosensor applications. The Universal Transducer System (UTS™) employs a potentiometric detection platform and it is reported that this biosensor is rapid (<15 min), stable (i.e., 4 months), reproducible (CV <5% at 0.1 ng/mL), and sensitive (~50 fM). Sensor Tech. Ltd. has taken a patent which covers this platform technology. The biosensor is fabricated using screen-printing technology and this allows a multi-array sensor to be developed. The production of screen-printed electrodes was based on glassy carbon powder containing tyrosinase and transduction chemistry (Hedenmo *et al.,* 1997). The University of Ulster has developed a biosensor for the determination of flavanols using either plant tissue material (polyphenoloxidases or commercial tyrosinase) (Eggins, 1996; Cummings *et al.,* 2001) immobilized in either a carbon paste electrode or screen-printed in with modified polypyrrole.

Conclusion

A search of the scientific literature on biosensors has revealed that biosensors play a significant role in medicine, agriculture/food, environmental and industrial monitoring. It describes some of the technologies behind the various types of biosensors in terms of transduction and bio-receptor techniques. This document is not a comprehensive review, but rather a critical review, presenting a selection of the most significant technologies and advances in this field. It is noticed that biosensors have recently undergone significant improvements in terms of their achievable selectivity and detection limits. Although there is a host of biosensor technologies available, either commercially or in the scientific literature, but electrochemical-based sensors appear more suited for field monitoring applications (e.g. hand-held). Likewise, the amperometric-based technology is the most appropriate platform for the development of implantable biosensors. However, in terms of screening a large number of samples simultaneously, optical biosensors are more suited for this type of applications. This review is expected to serve the community for selection of the biosensors for different applications.

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