Biosensors and its applications

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Introduction

"Biosensor" term refers to analytical devices which are innovative as well as powerful by involving biological sensing element with wide range of applications, such as biomedicine, environmental monitoring, defence, diagnosis, drug discovery, security and food safety and processing. Since then, incredible progress has been made (Turner, 2013) both in technology and applications of biosensors with innovative approaches involving electrochemistry, nanotechnology to bioelectronics. Biosensors provide a basis to understand technological improvement in the instrumentation involving sophisticated high-throughput machines for quantitative biologists and portable qualitative or semi-quantitative devices for non-specialists.

Technical strategy

On the basis of label free and label based detection are the technical strategies which are used in biosensors (Turner, 2013). The target molecules which are not tagged or labelled are detected by the label free method (Sang et al. 2015). It has its wide applications in the field of environmental and medicine science. While the method of label-based detection is dependent on the specific properties of label compounds to target detection. It requires a target protein (immobilized) which is fabricated with specific sensing element.

Types of Biosensors

1. Electrochemical Biosensors

First discovery of electrochemical biosensors is glucose oxidase based biosensors (Clark and Lyons, 1962). Because of monitoring blood glucose level in diabetic patients, these biosensors are widely used and popular in diagnostic clinic and in hospital. Due to inhomogeneity and instable activity of enzyme, these glucose biosensors have some drawbacks and some calibration is needed. By using biomaterials such as antibody, DNA and enzyme, surface (carbon and metal electrode) of electrochemical biosensors are prepared. These biosensors have asees to physiological system levels such as reactive oxygen species and antioxidant. Uric acid detection is the major application of this biosensors, which provide diagnostic tool for many diseases and clinical abnormalities and it is important to develop a method which is sensitive as well as cost-effective. In the measurement of hormones, it has been used successfully, but detail study should be needed (Bahadir and Sezginturk, 2015). On the targeted nucleic acid, biosensors occur an important potential area of technology

2. **Optical or visual biosensors**

In many sectors such as biosensing, biomedicine and drug discovery, fiber-optic chemical sensors have lot of relevance. By using fiber-optic biochemistry, DNA-based sensor, are emerging materials for immobilization, which are used by hydrogels (Dias et al., 2014). While compared with other materials, in hydrogels immobilization in occurs in 3D which allows loading capacity (high) for sensing molecules. Hydrogels (polyacrylamide) are hydrophilic cross-linked polymers (Khimji et al., 2013) and can be made into different forms for immobilization ranging from thin films to nanoparticles. Detailed methods for immobilizing DNA biosensors (Khimji et al., 2013) in monolithic polyacrylamide gels and gel micro particles are often considered as technical advancement in the field of biosensor technology. Single molecule detection has also been developed using electrochemical oxidation of hydrazine for DNA detection.

3. **Silica, glass and crystal/ quartz biosensors**

Due to their unique properties, use of silica, glass, crystal/quartz results in the biosensors development. Silicon based nanomaterials have potential and have numerous application (cancer therapy, bioimaging and biosensing) (Peng et al., 2014) because of its abundance, biocompatibility, mechanical, optical and electronic properties. These nanomaterials have less toxicity which is an important aspect for its application. In bioimaging, fluorescent silicon nanomaterials have long term applications. Considering the unique features of silica or quartz or glass materials, several new biosensors were developed with high-end technology for improving bioinstrumentation to biomedicine technology yet cost-effectiveness and biosafety requires attention (Peng et al., 2014).

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4. **Nanomaterial based biosensors**

For developing biosensor immobilization, nanomaterials ranging from copper, silver, silicon and gold nanoparticles, which are based on carbon materials like grapheme, carbon and graphite are used (Sang et al., 2015). For development of biosensors, nanoparticle-based materials provide specificity and sensitivity. Gold nanoparticle is used potentially among all due to its stability against oxidation and no toxicity, while if silver nanoparticles used in drug delivery it causes toxic manifestation. For understanding nano-medicine delivery and microenvironment for tumor, quantum dots technology has been applied.

5. **Genetically encoded or synthetic fluorescent biosensors**

Tagged biosensor are developed for genetically encoded or synthetic fluorescence pathway which are used for understanding biological process which include various molecular pathway inside the cell (Randriamampita and Lellouch, 2014). Fluorescent-tagged antibodies are discovered first for developing image fixed cells. Unill the last decade, for understanding of mitochondrial physiology better, these pathways are related to reactive oxygen species, cAMP and energy production. For visualizing cAMP, Ca^{2+}, cGMP in cells, forster resonance energy transfer (FRET) based biosensors have been developed. In modern physiology, the best biosensors are fluorescence resonance energy transfer-probes for kinase sensing and small-angle X-ray scattering for developing calcium sensors. In terms of sensitivity and applications, optical- based biosensors in combination with small nanomaterials/molecules and fluorescence have gained much success.

Table.1 Types of biosensors and their application

S.No	Type	Principle	Applications
1.	Glucose oxidase based biosensor	Electrochemistry by using oxidation of glucose	Glucose analysis in biological sample
2.	Uric acid biosensor	Electrochemistry	clinical abnormalities detection

3.	Micro fabricated biosensors	Visual/optical biosensor by using enzyme (cytochrome P450)	Drug development
4.	Hydrogel based biosensor	Visual/ optical biosensor	Immobilization f biomolecules
5.	Silicon biosensor	Visual/ optical fluorescence	Cancer therapy, bioimaging and biosensing
6.	Crystal- quartz biosensor	Electromagnetic	Development of ultrahigh-sensitive detection of proteins
7.	Nanomaterial based biosensor	Visual/ optical fluorescence or Electromagnetic	Biomedicine (eg- diagnostic tool)
8.	Fluorescence tagged or genetically encoded biosensor	Fluorescence	Biological process understanding which includes molecular system
9.	Microbial fuel cell based biosensors	Optical	For monitoring toxicity in pesticides, environment and biochemical oxygen demand

Application of Biosensors

1. **Food Processing**

For detecting pathogens from food biosensors are used. If *Escherichia coli* is present in vegetables, then it indicates contamination (faecal) in food. In dairy industry enzymatic biosensors are employed. Updike and Hicks in 1967 first reported enzyme-based sensor. On the method of immobilization enzyme biosensors have been divided (i.e. ionic bonding, covalent bonding and enzymes adsorption by van der Waals forces).

2. Fermentation Process

For monitoring the presence of antibody, biomass, enzymes, products or byproducts, for measuring(indirectly) the process conditions biosensors are utilized. Because of its easy automation, low prices, simple instrumentation and formidable selectivity biosensors control the fermentation industry and produce reproducible results. In the process of ion exchange retrieval biosensors are also applied, where detection of change of biochemical composition is carried out. In online monitoring of fermentation process biosensors have attracted a lot of attention in the past years, due to its quick response and simplicity.

3. In medical field

Biosensors are growing rapidly the field of medical science. In clinical applications, for diagnosis of diabetes mellitus glucose biosensors are widely used. Diagnosis of urinary tract infection (UTI) with anti-microbial susceptibility and pathogen identification which is promising biosensor technology is under study. For early stage detection of human interleukin (IL), biosensor based on hafnium oxide (HfO_2) has been used. Other application of biosensors is: immunosensor array for clinical immunophenotyping of acute leukemia, effect of oxazabor- olidines on immobilized fructosyltransferase in dental diseases, effect of oxazabor- olidines on immobilized fructosyltransferase in dental diseases.

4. Fluorescent biosensors

They are imaging agents which are used for discovery of drugs and cancer. These biosensors can probe metabolites, protein biomarkers and ions with great sensitivity and can also detect the activity, status or presence of the target (cell extracts, serum) in complex solution. In programs of drug discovery, they are used for the identification of drugs by high throughput, for post-screening analysis of optimization and hits of leads high content screening approaches. For early detection of biomarkers in clinical and molecular diagnostics, fluorescent biosensors are used which monitors disease progression and response to treatment/therapeutics for image guided surgery and intravital imaging.

Table 2. Biosensor used in disease diagnosis

S.No	Biosensors	Medical applications
1.	Glucose oxidase based biosensors and HbA1c biosensor	Diabetes
2.	Uric acid biosensor	General disease and cardiovascular diagnosis
3.	Micro fabricated biosensor	Optical corrections
4.	Hydrogel based biosensor	Regenerative medicine

5.	Silicon biosensor	Development of cancer biomarkers and its applications
6.	Nanomaterials based biosensor	Therapeutic applications

Current trend in research, future challenges and limitation of biosensor technology

As the demand and need for using biosensor for rapid analysis with cost-effectiveness require bio-fabrication that will pave way to identify cellular to whole animal activity with a detection limit of high accuracy for single molecules. To work under multiplex condition, biosensor should be targeted. Detection of 2D and 3D are required with sophisticated transducers which quantifies and targets small analytes of interest. In recent years any discoveries are made with contact or non-contact-based patterning at different levels. Next level of development should aim for discovering more robust regenerative biosensors for long-term use. If this process success, then for therapeutic used new diagnostic biosensors can be developed which will help patients and clinicians in long run. Invention on this line leads to discovery of electrochemical biosensors as reliable analytical devices for pathogen detection of avian influenza virus in the complex matrices. Development in biosensors for the detection of biological warfare agents ranging from virus, bacteria and toxins is often attempted using various devices of biosensors ranging from nucleic acid, piezoelectric, optical and electrochemical which will have immense applications in health and military and as well in security and defense.

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