

Review Article

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## The Commercial Application of Biosensors as an Analytical Device

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### ABSTRACT

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Here various types of biosensors such as physicochemical, bioluminescent, electrochemical, opto-electric, piezoelectric, thermometric and magnetic has been deliberated to show their usefulness and applications in multiple field. Food industry requires suitable analytical methods for the safety and quality checking of foods. Chemical and biological hazards detection in foods is important to the human health. By on line measurement of different food components such as glucose, fructose, sucrose, lactose, lactic, malic, acetic, ascorbic, citric and amino acids, ethanol, glycerol, and triglyceride, polyphenols, oxygen, hydrogen peroxide, mycotoxin, vitamins, heavy metals, the food safety and microbiological quality aspects could be beneficial. Fluorescent biosensors have a large application in drug discovery and in cancer cell determination. Current and future researches may include a miniature array of biosensors, with rapid performance, high specificity, reproducibility and sensitivity.

### Introduction

A biosensor is a measuring instrument that consists of biologically active molecules such as enzymes, antibiotics, phages, aptamers, or single-stranded DNA with a suitable physicochemical transducer. Bioluminescent, electrochemical, opto-electric, piezoelectric, thermometric and magnetic transducers are common types. There is an also immuno-chromatographic device, which does not use any of the transducers mentioned above. They

have lateral flow strips which used in ultrasensitive tests for on-site visual detection of analytes. Mostly used commercial lateral flow strips are the home pregnancy strip and glucose testing strip.

Biosensors consist of a receptor, a transducer, an amplifier and a display monitor. A bioreceptor identifies the target analytic and a transducer converts the recognition event into a measurable electrical signal. A wide range of subjects from small protein to large

pathogens can be detected by biosensors. An electrochemical biosensor is more appropriate for onsite analysis and they can easily be miniaturized for handheld devices.

Biosensors have a potential market for commercial application in the area of medical science, food science, agriculture, veterinary services, microbial contamination and environmental biothreat.

### **Component of biosensors**

#### **Receptors**

#### **Enzymes**

Enzymes are often used as biomaterials for the development of biosensors. These biosensors utilize enzymes (Table. 1) which are specific for the desired molecules and catalyze generation of the product, which is then directly determined using transducer.

Some factors are influence on the performance of enzyme-based biosensors, i.e. enzyme loading, suitable pH, temperature and cofactors in some cases.

#### **Antibodies**

An antibody is a complex biomolecule. It consists of hundreds of individual amino acids arranged in an ordered sequence. An antigen-specific antibody fits its specific antigen in a unique way. This property of antibodies is most important to their usefulness in immunological biosensors or immunosensors (J.M.Song and Vo-Dinh T2004). For non-fluorescent analyte systems, sensitivity increases with decreasing amounts of immobilized reagent (Tromberg *et al.*, 1987). In microplates, tubes, capillaries or on glass strips are acoupled with some kind of electrochemical sensor and by this the common enzyme-linked solid phase immune

assay (ELISA) is performed to measure the label generated signal (Skládal 1997). Cancer cells can be monitored by immunosensors (Ehrhart *et al.*, 2008, Malhotra *et al.*, 2010).

#### **Nucleic acids**

Biosensors gain their high sensitivity and selectivity on DNA, RNA and peptide nucleic acid from the very strong base pair affinity between nucleotide strands (Borgmann *et al.*, 2011). Nowadays, as probe material mainly synthetic oligodeoxyribonucleotides (ODNs) are used in the DNA hybridization sensors. End-labels, such as thiols, disulfides, amines, or biotin, are incorporated to immobilize ODNs to transducer surfaces (Labuda *et al.*, 2010). The complementarity of adenine-thymine and cytosine-guanosine pairing in DNA forms the basis for the specificity of biorecognition in DNA biosensors (Vo-Dinh and Cullum 2000).

DNA biosensors were deeper reviewed for example by Drummond *et al.*, (2003) or Sassolas *et al.*, (2008). Different uses of DNA based biosensor are mentioned in Table 3.

#### **Cells**

These kinds of bioreceptors are either based on biorecognition by an entire cell (Figure.1.) or a specific cellular component that can make a specific binding to certain species. The major advantage of this class of bioreceptors is that the detection limits can be very low because of signal amplification. Based on bioreceptors catalytic or pseudo catalytic properties many biosensors are developed (Vo-Dinh and Cullum 2000). For example, viable or non-viable microbial cells are utilized in case of microbial biosensors. Non-viable cells obtained after permeabilization and viable cells utilize the respiratory and metabolic functions of the cell; thus, the analyte may be monitored as a substrate or an

inhibitor of these processes (D'Souza 2001). Cell-based biosensors (CBBs) may be applied to analyze the effect of pharmaceutical compound on a given physiological system (Xu *et al.*, 2002).

Living cells can be treated as the primary biosensor, but there are some difficulties in the selection, the culture and the maintenance of living cells. The coupling of living cells and the secondary sensor are difficult (Wang *et al.*, 2005).

### **Transducers**

It is an analytical tool which provides an output quantity having a relationship to the input quantity (McNaught and Wilkinson 1997). Biosensors can be classified according the physiological properties and methods they utilize. Transducers can be differentiated in six main types: electrochemical, electrical, optical, piezoelectric (mass detection methods), thermal and bioluminescent.

### **Electrochemical**

Electrochemical biosensors are based on monitoring electroactive species that are attached with the biological components (e.g., enzymes and cells). This kind of transduction can be performed under two broad methods: potentiometry and amperometry.

### **Amperometric**

In Amperometric biosensors constant potential (D.C.) is applied. By using a potentiostat the constant potential is applied. This current is produced by the biological element and related to an electrochemical species. The electrochemical set-up frequently consists of a reference electrode Such as Ag/AgCl and a working electrode such as gold, platinum, glassy carbon, graphite or carbon paste. The Table-4 shows various

types of amperometric biosensors and their inventors.

Mostly used enzyme-based biosensors are the detection of glucose with glucose oxidase. These biosensors are better than the potentiometric ones; these are very sensitive and more suitable for mass production (Ghindilis *et al.*, 1998).

### **Potentiometric**

Under conditions of zero current flow, potentiometric biosensors are based on monitoring the potential of a system at a working electrode, with respect to an accurate reference electrode. A small change in the charge of the proteins is observed due to Antibody-antigen binding, that charge difference can be detected by this biosensor.

Ion selective electrodes (ISEs) are example of this type of biosensors. The change in pH due to enzyme activity, can easily be monitored with a pH sensitive ISE. Table.5. shows types of potentiometric biosensors.

Estimating monophenolase activity in apple juice, determining the concentration of sucrose in soft drinks, measuring isocitrate concentrations in fruit juices, and determining urea levels in milk this type of biosensor used.

### **Electrical**

#### **Conductometric (Impedimetric)**

The inverse value of resistance is called conductance and thus the name conductometric has been used. When ions or electrons are produced, the overall conductivity or resistivity of the solution is changing. Conductance measurements have relatively low sensitivity. The table-6 shows various inventors along with their works on conductometric biosensors.

### **Ion-sensitive**

In earlier days, biosensors, which are based on Ion-Selective field-Effect Transistors (ISFETs) considered as a category of potentiometric sensor, but now, separated into the fourth class of electrochemical sensors (Thévenot *et al.*, 1999), according to the last IUPAC technical report on electrochemical biosensors. These semiconductor FETs consists an ion sensitive surface. Electrical potential of that surface changes due to the interaction between ions and the semiconductor. Its developed version is called ENFET (Enzyme Field Effect Transistor) (Mohanty and Kougianos 2006). Enzyme biosensors based on ISFETs (Dzyadevych *et al.*, 2006).

### **Optical**

These sensors are based on measuring the illumination or to light emission. Optical biosensors can employ a number of techniques to detect a target analyte and are based on well-founded methods including chemiluminescence, light absorbance, fluorescence, phosphorescence, photothermal techniques, light polarization and rotation, surface plasmon resonance (SPR), and total internal reflectance. By measuring the intensity or decay time, these types of sensors are worked.

### **Surface plasmon resonance (SPR)**

SPR occurs when light is reflected at the interface of a material with high refractive index and a material with low refractive index. Between these two layers, a thin layer of a good conductor such as gold or silver is required (Glaser, 2000) an evanescent wave developed at this interface can interact with electron packages in the conductive layer. A very specific energy is required to raise those surface plasmons.

The plasmon excitation energy can be measured with monochromatic light which is reflected at different angles. Deoxyribonucleic acid (DNA) binding or Antibody antigen interactions can be observed by SPR.

Commercially, one of the most popular optical-based biosensor systems supplied by BIAcore (Uppsala, Sweden). This instrument can be used to study a wide range of biological interactions, automatically and in real-time. The instrument is based on SPR. SPR sensors have been used extensively to investigate the presence of contaminating microorganisms in food and to determine food quality. For example, an optically based biosensor was recently used to screen poultry liver and eggs for the presence of the drug nicarbazin, a feed additive used to prevent outbreaks of coccidiosis in boiler chickens (B.D. Meshram *et al.*, 2018).

Mohammed *et al.*, have also demonstrated the use of this technique to detect the presence of allergens, in particular peanuts, during food production. Another study shows that *E. coli* and *Salmonella* could be detected in skim milk (limits of detection of 25 and 23 CFU/mL, respectively).

### **Piezoelectric**

The piezoelectricity phenomenon is used in mass sensitive transducers (Luong and Guilbult, 1999).

If an oscillating current field is applied in a quartz disc with two deposited electrodes, an acoustic wave is generated and that propagates through the crystal of the disc. The frequency dependent on the crystal properties (such as chemical structure, density and the orientation the crystal is cut). The frequency is also influenced by mass deposited onto the crystal surface (or in many cases onto the electrode

surface which is deposited on the crystal). This allows very sensitive detection of small mass changes on the crystal surface.

Principle wise mainly two waveforms are used. One of them is surface acoustic wave (SAW) device. High frequencies of 30-200 MHz give the crystal a very good theoretical sensitivity, but due to practical difficulties biosensors are mainly based on bulk acoustic wave (BAW) devices (Leonard *et al.*, 2003).

### **Thermometric**

Thermometric biosensors measure the change in temperature which occurs due to heat fluctuation that occurs during biochemical reactions. Highly sensitive thermistors are used to monitor the change in temperature. Most biological reactions are exothermic, some of them are endothermic. In enzymatic reactions the change in enthalpy is 20100kJ/mol.

Measurements can be developed by co-immobilizing enzymes for signal amplification or by using high-protonation enthalpy buffers such as TRIS (Giese, 2002).

### **Immobilization**

The immobilization of the biological element on the transducer is very important for the biosensor performance. The biomolecule immobilized on the surface of a transducer, and retained with its full activity and long-term stability regarding its function and immobilization. By the immobilization step, the transducer should be unaffected. Many immobilization methods also have some disadvantages. Therefore, the immobilization method must be chosen and adapted for the particular bio element, transducer, matrix and other assay requirements (Kuhnert *et al.*, 2000).

The most common immobilization methods used for biosensors can be divided into physical and chemical methods. Physical methods include adsorption, entrapment, encapsulation and confining. Chemical methods are cross-linking and covalent immobilization. However, cross-linking of biomolecule is carried out to improve the stability of physical methods (Leonard *et al.*, 2003).

### **Applications of biosensors in food industries**

Food industry requires suitable analytical methods for the safety and quality checking of foods. Chemical and biological hazards detection in foods is important to the human health. Also, sugars, alcohols, amino acids, flavours, sweeteners analysis can be done by using biosensors. In food sector the uses of biosensors mainly focus on analysis of food composition and detection of allergens, toxins, pathogens, additives etc. In food and fermentation process, quick, cheap, and safe analytical processes are generally required to measure sugar (glucose, sucrose, lactose and fructose) content.

There are many scientific publications on biosensor but very few biosensors are commercially available in market. There are few commercial biosensors used in food industry are shown in Table 7.

### **Biosensors in food quality**

Now a days many batch operations in the food industry are being replaced by automated continuous processing. Accordingly, there is an increasing demand for instruments suitable for automatic in line quality control and at the end of the line so that the real time state of the process can be described.

This will increase the food safety and also provide less effective control, less employment, time and energy saving (Velasco-Garcia and Mottram, 2003).

These also can be used as analytical tools in some food industries, especially applied to the determination of the composition, degree of contamination of raw materials and processed foods, and for the on-line control of the fermentation process.

Enzymatic biosensor based on cobalt phthalocyanine has a good capability to monitor the ageing of beer during storage (Ghasemi-Varnamkhasti *et al.*, 2012).

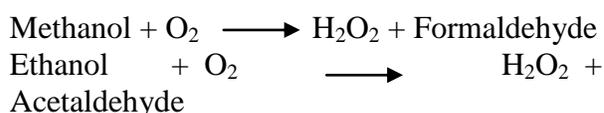
### Ethanol Biosensor

To monitor ethanol production, the combination of alcohol dehydrogenase (ADH) and alcohol oxidase (AO) is used with an oxygen electrode. A second dehydrogenase enzyme linked to the ADH and AO system allows the determination of many other dehydrogenases and their substrates. Provesta Corporation (Bartlesville, OK) has innovated the Multipurpose Bioanalyzer, by using this concept. Depending on the enzyme systems the Bioanalyzer can detect more than 100 biochemical and chemical substances. ISFET is also used for ethanol determination.

To determine ethanol concentration in alcoholic beverages microbial biosensors were can be used. Generally, dilutions between 40 and 500 times were performed. Results were compared with the enzymatic spectrometric method. The correlation coefficient of those experimental values is 0.9983 shows a good correlation between biosensor and spectrometric method (B.D. Meshram. *et al.*, 2018)

The biosensor consists of immobilized cells (yeast or bacteria), a gas permeable

membrane (Teflon) and an oxygen electrode. Porous membranes retaining the microbial cells, but those cells are fixed on the surface of the electrode's outer teflon membrane. Thus, the cells are trapped between the two membranes. A gas permeable membrane is placed on the surface of electrode and covered with nylon net. These membranes are attached by rubber-O-rings. The steady state current obtained depend on the concentration of ethanol/methanol. The response time is 10 min at 30°C (Rajasekhar *et al.*, 2005).



### Monitoring of wine quality

Wine is a complex mixture of various compounds, at different concentrations, present simultaneously. The compounds are water, ethanol, glycerol, sugars, organic acids and various ions. Ethanol and glycerol have a higher concentration, other aliphatic and aromatic alcohols, amino acids and phenolic compounds are in fewer concentrations.

Newly three different PQQ-dehydrogenases [glucose dehydrogenase (GDH), alcohol dehydrogenase (ADH), and glycerol dehydrogenase (GIDH)] are isolated and purified from *Gluconobactersppor Erwiniaspp.* have been used for determination of main compounds of wine.

The main enzyme substrate (glucose for GDH, glycerol for GIDH and ethanol for ADH) is firstly oxidized while the enzymes cofactor is simultaneously reduced. The active form of the enzyme is regenerated via the interaction with the electrochemical mediator (modified redox polymer), which is maintained in its oxidized form by the positive potential applied at the electrode.

### **Antioxidants and free radicals**

Antioxidants are one of the main ingredients that protect food attributes by preventing oxidation that occurs during processing, distribution and end preparation of food. Amperometric biosensors are generally used for the determination of antioxidants in various food (Mello and Kubota, 2007).

### **Tea biosensor**

In case of determining quality of black and green tea polyphenols play a crucial role. The polyphenol contents affect the Major quality attributes such as colour and astringency. Therefore, it is necessary to know quantity of polyphenols in tea. Also, tea polyphenols also have a strong antioxidant property which improves the nutrition and health of human bodies. In this context CFTRI, Mysore developed an enzyme based amperometric biosensor (Fig. 2) for the quantification of total polyphenol content in tea infusions. Both lab and industry trials were successfully observed for tea polyphenols detection and tea biosensor technology (Sujith Kumar *et al.*, 2011).

### **Fermented food seasoning sensor**

For food and fermentation industry applications, glutamate oxidase can be immobilized and used in conjunction with an electrochemical device to determine L-glutamic acid, which is fermented for use as a food seasoning. Glutamate oxidase catalyses the oxidation of glutamate with the consumption of oxygen. This allows for the use of an oxygen probe as the transducer for the glutamate sensor.

### **Determination of ascorbic acid in fruit juices**

Flow injection Potentiometric system is

improved for continuous determination of ascorbic acid and other parameters. The oxygen consumption is detected by the electrode. Oxygen consumption rate is proportional to the ascorbic acid amount of the sample (Ashkenazi *et al.*, 2000).

### **Plant tissue biosensors**

To form a biocatalytic sensor, the use of plant tissue in conjunction with electrochemical elements is inexpensive, simply constructed and requires few co-factors and also an alternative to enzyme and microbial electrodes. Plant tissue biosensors can be particularly selective if the substrate to be determined is either a major nutrient or a functional metabolite of the enzyme-containing tissue (biocatalyst). An example of such a biosensor is the banana electrode shown in Figure 3.

Ascorbic acid is measured by using a probe, depend on the catalytic reaction of ascorbic acid oxidase (mainly present in cucumber peel, cabbage, zucchini, and yellow squash). Using sugar beet tissue fixed to an electrode measure the amount of Tyrosine within 5 to 10 min. Cysteine carbon-sulphur lyases catalyse (present in garlic, onion, cabbage, broccoli, cauliflower, and mushrooms) rapid enzymatic reactions which initiate flavour and colour producing chemical processes and can be used for sulfoxide sensors.

Dialysis membranes can fix chopped cabbage to an ammonia gas-sensing electrode, which is creating a selective, though not overly sensitive, detector for S-methyl-L-cysteine sulfoxide. Commercially available gas-sensing electrochemical probes have been combined with tissues; squash sensors determine glutamic acid; cucumber leaves are used to detect L-cysteine and corn-based sensors detect pyruvate.

### **Fish freshness analysis**

Fish freshness has been examined chemically and expressed as K-value which is useful index of raw fish freshness. The K-value consists the sample preparation and the complex sensor system with various kinds of biochemical substances because the K-value is calculated from the concentrations of hypoxanthine (Hx), inosine (HxR), inosine 5-monophosphate (IMP) and in the fish-extract solution. Also, various biochemical process reagents are used. Then, a new method is required at restaurants, kitchens and fish markets, i.e., non-destructive methods with simple biochemical reaction, such as smell evaluation of bad fish-odour with human smell sense (Mitsubayashi *et al.*, 2004).

Trimethylamine (TMA) is common substance in sea-food, and it is produced due to decomposition of trimethylamine N-oxide (TMAO) in sea animals. The fresh marine products contain little TMA. Mitsubayashi *et al.*, (2004) constructed a TMA biosensor by immobilizing flavin containing mono oxygenase type 3 (FMO3) and contain a dissolved oxygen electrode. With flow injection analysis (FIA) this sensor is calibrated against TMA solutions. It was obvious that the TMA sensor with FMO3 would be most useful for evaluating fish-freshness (Coefficient of variation 4.39%, n=5) (B.D. Meshram. *et al.*, 2018).

### **Quality control of meat**

For quality control of meat, meat check and bio check sensors are used commercially. A four-electrode array attached to a knife in the meat check, which can be inserted into meat to analyse the glucose gradient immediately below the surface. The gradient informs the microbial activity on the surface, which is an indicator of meat quality. The device shows results in seconds where laboratory-based

microbiological test takes days. The bio checks method transformed the glucose sensor into a device, which helps in detecting and analysing microorganisms present in aqueous solutions. From the respiratory pathways of microorganisms, the system transfers electrons and it takes less than two minutes.

The lactic acid concentration indicates the pre-mortem metabolic activity, physical stress and deficiency in the meat quality. Enzymatic biosensor based on immobilized lactate oxidase as bioreceptor and an amperometric transducer (Bergann *et al.*, 1999). This biosensor estimates lactic acid very quickly and at low cost and does not need sample preparation.

### **Biosensors for the detection of microorganisms**

Microorganisms produce current when they to the contact of an electrode, so an electrochemical method can be used to detect microbial loads. In 1979, a two electrodes system (a determination electrode and a reference electrode) is used to measure microbial populations and this having a 15 min response time. Each electrode consists a silver peroxide cathode and a platinum anode. The anode of the reference electrode was covered with a cellulose dialysis membrane, which prevent penetration of microorganisms.

On the surface of the anode the microorganisms were oxidized and a current was produced. Current differences were proportional to the number of cells of *Saccharomyces cerevisiae* and *Lactobacillus fermentum*. By using an electrochemical system *Bacillus subtilis* populations can be continuously monitored in a fermenter. Nishikawa *et al.*, constructed a fuel cell-type electrode system to detect load of microorganism in polluted water, but it can

probably be used to rapidly (10-20 min) assay wash water in food processing plants. The current generated varies between different microorganisms but, at equivalent cell concentrations  $> 10^4$  cells/ml, a linear relationship is obtained between the current at the electrode and plate count data.

The Cranfield Institute of Technology has developed a biosensor for the rapid detection of cells in a variety of water-based fluids. This device, Biocheck, is portable, hand-held, battery-operated, robust, and easily operated. The lowest contamination level detected in Biocheck is approximately  $2 \times 10^6$  organisms/ml.

### **Biosensors in dairy industry**

#### **Online monitoring of milk**

The increasing demand for on-line monitoring of milk quality directs the industry to look for practical solutions, and biosensors could help in this.

However, biological research is needed to determine how sensor derived information can be used to improve the product quality (table.8) other than by separating the milk into sources of high and low quality (B.D. Meshram. *et al.*, 2018).

#### **Biosensor for quality control in milk**

The food industry requires suitable analytical method for quality control, methods must be reliable, specific, rapid and cost effective. The study was carried out to measure the recent problem, the analysis of the presence of urea in milk, called "synthetic milk". This urea biosensor is immobilized urease enzyme with the ammonium ion selectively electrode of a potentiometric transducer. However, it is worth the mentioned that since milk is a complex system it contains much

interference, which makes conventional methods less reliable (Verma and Singh, 2003).

#### **On- line determination of lactose concentration in milk**

Online determination of lactose content of milk is generally measured by the cascade enzyme biosensor. The enzyme galactosidase (GAL) makes a cleavage in the disaccharide lactose and produces glucose and galactose. The glucose reacts with glucose oxidase (GOD) to produce  $H_2O_2$ . Horseradish peroxidase (POD) oxidizes  $H_2O_2$  in presence of 5-ASA (amino-salicylic acid) as a mediator. The oxidized form of the mediator is reduced at the electrode resulting in an amperometric signal proportional to the lactose concentration (Ferreira *et al.*, 2003).

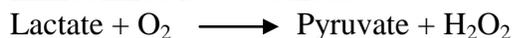
#### **Milk urea biosensor**

Animal feed protein supplements are highly expensive. The conversion of feed protein into milk protein is observed here. Excessive levels of nitrogen derived from feed may increase the urea concentration of milk, without increase in milk production. This high concentration of urea may impair reproductive functions and also causes excess nitrogen in dairy waste which is harmful for environment. The normal range of milk urea nitrogen (MUN) data is 5-20 mg/dl.

#### **Biosensor for lactic acid**

Among the organic acids present in food, glutamic acid, lactic acid and ascorbic acid are important. On the acidity of the curd the quality of mozzarella cheese strongly depends. Biosensor has been used to measure the lactic acid, to control the acid development. The system consists of an electrochemical (flow-through flow-jet) cell assembled + connected to an amperemeter

with platinum sensor covered with the immobilized lactate oxidase.



H<sub>2</sub>O<sub>2</sub> probe is used to detect the amount of lactate in the curd. The real time analysis of lactate helps to control of the curd ripening at different pasteurization temperature. This method is more sensitive than pH probe

(Rajasekhar *et al.*, 2005). A biosensor, based on screen printed carbon electrode, was integrated into flow cell. And enzymes were immobilized on electrode by engulfment in a photo cross linkable polymer. The automated flow-based biosensor could quantify the tree organophosphate pesticides in milk. (Mishra *et al.*, 2014).

**Table.1** List of different analytes with corresponding receptor enzymes along with references

| <b>Enzymes</b>                                | <b>Analytes</b>       | <b>References</b>   |
|---|-----------------------|---|
| <b>Glucose Oxidase, Glucose Dehydrogenase</b> | Glucose               | Monošik <i>et al.</i> , 2012  |
| <b>Oxidoreductase</b>                         | Lactate               | Huang <i>et al.</i> , 2008, Katrlík <i>et al.</i> , 1999, Pereira <i>et al.</i> , 2007                          |
| <b>Oxidoreductase</b>                         | Malate                | Arif <i>et al.</i> , 2002, Monošiket al., 2012, Prodromidis <i>et al.</i> , 1996, Wang <i>et al.</i> , 2008     |
| <b>Oxidoreductase</b>                         | Ascorbate             | Vermeir <i>et al.</i> , 2007, Wang <i>et al.</i> , 2008),   |
| <b>Oxidoreductase</b>                         | Amino Acids           | Pollegioni <i>et al.</i> , 2007, Sacchi <i>et al.</i> , 1998  |
| <b>Oxidoreductase</b>                         | Alcohol               | Katrlík <i>et al.</i> , 1998, Pena <i>et al.</i> , 2002, Smutok <i>et al.</i> , 2006, Tkáč <i>et al.</i> , 2003 |
| <b>Oxidoreductase</b>                         | Cholesterol           | Lia and Gub 2006, Umar <i>et al.</i> , 2009, Vidal <i>et al.</i> , 2004   |
| <b>Oxidoreductase</b>                         | Glycerol              | Alvarez-Gonzalez <i>et al.</i> , 2000, Monošik <i>et al.</i> , 2012, Niculescu <i>et al.</i> , 2003             |
| <b>Oxidoreductase</b>                         | Fructose              | Tkáč <i>et al.</i> , 2001, Tkáč <i>et al.</i> , 2002),  |
| <b>Transferase</b>                            | Acetic Acid           | Mieliauskiene <i>et al.</i> , 2006, Mizutani <i>et al.</i> , 2003   |
| <b>Hydrolase</b>                              | sucrose               | Soldatkin <i>et al.</i> , 2008, Surareungchai <i>et al.</i> , 1999  |
| <b>Lyase</b>                                  | citric acid           | Maines <i>et al.</i> , 2000, Prodromidis <i>et al.</i> , 1997   |
| <b>Ligase</b>                                 | DNA point mutation    | Pang <i>et al.</i> , 2006   |
| <b>Isomerase</b>                              | 19-norandrostenedione | Sheu <i>et al.</i> , 2008   |

Source: Rastislav Monošika, Miroslav Stred'anskýb, Ernest Šturdíka. Biosensors - classification, characterization and new trends, 2012

**Table.2** List compound discovered for using in DNA immobilization with references

| Occurrence         | Compounds   | Reference   |
|--------------------|---|---|
| DNA immobilization | carbon paste<br>pyrolytic graphite<br>glassy carbon<br>carbon fiber<br>carbon nanotubes | Girousi <i>et al.</i> , 2004<br>Chen <i>et al.</i> , 2000<br>Pedano <i>et al.</i> , 2003<br>Tian <i>et al.</i> , 2005<br>Mani <i>et al.</i> , 2009,<br>Niu <i>et al.</i> , 2008 |

Sources: Monošík R. *et al.*, Biosensors — classification, characterization and new trends, 2012

**Table.3** Applications of DNA based biosensors with references

| Application   | Reference and Source   |
|---|--|
| Determination of drug in blood serum matrix                                 | Vaničková <i>et al.</i> , 2005   |
| Detection of the DNA damage and antioxidants protecting DNA from its damage | Bučková <i>et al.</i> , 2002; Galandová <i>et al.</i> , 2009; Labuda <i>et al.</i> , 2009; Vyskočil <i>et al.</i> , 2010 |
| Voltammetric determination of 1-aminopyrene and 1-hydroxypyrene             | Ferancová <i>et al.</i> , 2005   |
| For detection of the effect of berberine on DNA from cancer cells           | Ovádeková <i>et al.</i> , 2006   |

Source: Fojta, Electrochemistry of Nucleic Acids and Proteins - Towards Electrochemical Sensors for Genomics and Proteomics, 2005

**Table.4** The working principle of various types of amperometric biosensor and their inventors

| Working principle   | Inventor     |
|---|--------------|
| Enzyme-catalysed electro-oxidation or electro-reduction, or their enzyme-catalysed hydrolysis   | Heller 1996  |
| Electron transfer or enzymes with a direct electron transfer from the active Centre to the electrode (consumption of O <sub>2</sub> and production of H <sub>2</sub> O <sub>2</sub> ) | Glaser, 2000 |

Source: Subramanian Viswanathan, Hanna Radecka, Jerzy Radecki. Electrochemical biosensors for food analysis. 2009.

**Table.5** Types of potentiometric biosensor

| Types                          | Inventors                    |
|--------------------------------|------------------------------|
| Ion Selective Electrodes (Ise) | Guilbault and Montalvo, 1969 |
| Field Effect Transistor (FET)  | Mello and Kubota, 2007       |

Source: Sources: Monošík R. *et al.*, Biosensors - classification, characterization and new trends. 2012

**Table.6** Inventors of various conductometric biosensor

| <b>Works and contributions</b>  | <b>Inventors</b>                 |
|---|----------------------------------|
| <b>Impedance biosensor is used as commonly a functional part of the Wheatstone bridge</b> | Pohanka and Skládál 2008         |
| <b>Double layer charging and concentration polarization invented</b>                      | Mohanty and Kougiannos 2006      |
| <b>Impedimetric biosensors were reviewed and modified</b>                                 | Guan <i>et al.</i> , 2004        |
| <b>Use conductometric biosensors for biosecurity</b>                                      | Muhammad-Tahir and Alocilja 2003 |

Source: Subramanian Viswanathan, Hanna Radecka, Jerzy Radecki; Electrochemical biosensors for food analysis. 2009

**Table.7** Commercial Food biosensors and corresponding companies

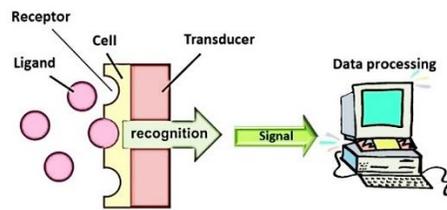
| <b>Company</b>                | <b>Biosensors</b>   |
|-------------------------------|---|
| <b>Chemel AB</b>              | Glucose, lactose, saccharose, ethanol                         |
| <b>Gwent sensors</b>          | Glucose   |
| <b>Analox Instruments</b>     | Ethanol, Methanol, Lactate, Glycerol                          |
| <b>BIAcore AB</b>             | Water soluble vitamins, Mycotoxins                            |
| <b>Texas Instruments</b>      | Peanut allergens, Antibiotics                                 |
| <b>Universal sensors</b>      | Ethanol, Methanol, Glucose, Sucrose, Glutamine, Ascorbic Acid |
| <b>Research International</b> | Protein, toxins, virus, spores and fungi                      |
| <b>Biomerieux</b>             | Microorganism   |
| <b>Motorola</b>               | Microorganism and genetically modified organism               |
| <b>IVA Co, ltd</b>            | Heavy metals  |
| <b>The Answer 8000</b>        | Sucrose, L-Glutamate, Alcohol                                 |
| <b>Oriental electric</b>      | Fish deterioration tracking                                   |
| <b>FAIZA 110-P</b>            | Glucose, Galactose, Lactate, L-Glutamate                      |

Source: B.D. Meshram<sup>1</sup>, A.K. Agrawal, Shaikh Adil<sup>1</sup>, SuvartanRanvir and K.K. Sande; Biosensor and its Application in Food and Dairy Industry: A Review, 2018

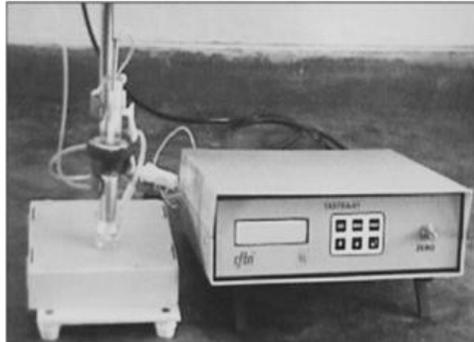
**Table.8** Various developer and their on line determination of milk constituents

| <b>Developer</b>                         | <b>Application</b>   |
|--|--|
| <b>Ashkenazi <i>et al.</i>, 2000</b>     | Multi-enzymatic amperometric biosensor for lactose in fresh raw milk |
| <b>Velasco- Garcia and Mottram, 2003</b> | Determine fat in milk  |
| <b>Schmidt <i>et al.</i>, 1999</b>       | Free fatty acids detection   |

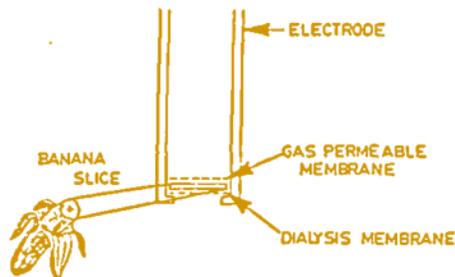
Source: B.D. Meshram<sup>1</sup>, A.K. Agrawal, Shaikh Adil, SuvartanRanvir and K.K. Sande; Biosensor and its Application in Food and Dairy Industry: A Review. 2018



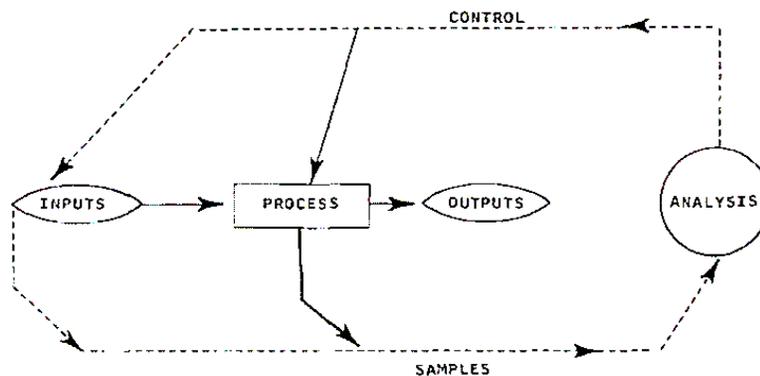
**Figure.1** A cell based bioreceptor attached with the target analytes and through transducer the signal passes through towards data processing unit



**Fig.2** Tea biosensor designed and developed in CFTRI, Mysore



**Figure.3** Schematic diagram of banana tissue electrode. Source: Sidwell and Rechnitz, 1986



**Figure.4** Desired feedback control of a process. Adopted from McMurdo and Whyard, 1984

## Advantages of biosensors

Rapid and continuous monitoring could help the food processor both reduce wastage from poorly controlled processes and increase productivity. This will increase microbial safety and also a more cost-effective control of food processing. The data generated should be used for process control as shown in Figure 3.

The first advantage of biosensors is its rapid action. Results came out in minutes rather than days. Second, biosensors do not require a large amount of sample preparation; their specificity allows direct measurement of particular analytes. A biosensor can be used by unskilled personnel. Another advantage is versatility. The biosensors being developed range from small, inexpensive, hand-held devices, for continuous, on-line monitoring of various food and industrial processes.

## Future scope

In the manufacturing processes of beer, wine, bread, and some dairy products the microbial growth must be kept within certain limits. For regulate both the component and microbial levels of these Biosensors could be used.

Multifunctional and versatile analytes (like raw materials, trace compounds, sugars, alcohols, amino acids, vitamins, flavour additives, and contaminants, e.g. antibiotics, microorganisms and their enzymes, toxins etc.) sensing system is needed in one device and that must be easy to handle that without any skilled professional we can use that in practical area.

Without compromising specificity, sensitivity and workability a small sized in hand device is required. Biosensor is a good area of investing funds for using nanotechnology and nanobiotechnology.

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