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Food Chemistry 77 (2002) 237–256

Food Chemistry

www.elsevier.com/locate/foodchem

Analytical, Nutritional and Clinical Methods

Review of the use of biosensors as analytical tools in the food and drink industries

Lucilene Dornelles Mello, Lauro Tatsuo Kubota*

Instituto de Química—Unicamp, PO Box 6154, 13083-970, Campinas, SP, Brazil

Received 1 August 2001; received in revised form 2 December 2001; accepted 2 December 2001

Abstract

The food and drink industries need rapid and affordable methods to assure the quality of products and process control, where the use of analytical methods such as high performance liquid chromatography (HPLC) or specific enzymatic methods may be costly or laborious. Application of the biosensor technique in the field of food processing and quality control is promising. Biosensors offer advantages as alternatives to conventional methods due to their inherent specificity, simplicity and quick response. This article presents a review about the potential application of biosensor technology in drink and food industries, its current situation and potential. Some biosensors recently described in the literature are also listed.

Keywords: Biosensors; Food analysis; Enzyme electrodes; Immunosensors.

Contents

* Corresponding author. Tel.: +55-19-3788-3127; fax: +55-19-3788-3023.
E-mail address: kubota@iqm.unicamp.br (L.T. Kubota).

0308-8146/02/$ - see front matter
PII: S0308-8146(02)00104-8

1. Introduction

The conformity of the industrial products regarding maintenance and warranty of their main features has a great economic importance. The control of food quality and freshness is of growing interest for both consumer and food industry. In the food industry, the quality of a product is evaluated through periodic chemical and microbiological analysis. These procedures conventionally use techniques as, chromatography, spectrophotometry, electrophoresis, titration and others. These methods do not allow an easily continuous monitoring, because they are expensive, slow, need well trained operators and in some cases, require steps of extraction or sample pretreatment, increasing the time of analysis. The food and drink industries need rapid and affordable methods to determine compounds that have not previously been monitored and to replace existing ones (Wagner & Guilbault, 1994). A non-destructive approach is desirable, which correlates information available outside the product with the stage of freshness. The use of a probe which penetrates into the samples such as sonic signals could be a method with these characteristics. For cheap and continuos monitoring with fast response time, sensors may be used with advantages (AOAC International, 1995; Ohashi & Karube, 1993).

An alternative to ease the analysis in routine of industrial products is the biosensors development. Biosensors are a sub group of chemical sensors in which are analytical devices composed of a biological recognition element (such as enzyme, antibody, receptor or microorganisms) coupled to a chemical or physical transducer (electrochemical, mass, optical and thermal). These devices represent a promising tool for food analysis due to the possibility to fullfil some demand that the classic methods of analysis do not attain. Original characteristic turns the biosensors technology a possible methodology to be applied in real samples. Some advantages as high selectivity and specificity, relative low cost of construction and storage, potential for miniaturization, facility of automation and simple and portable equipment construction for a fast analysis and monitoring in platforms of raw material reception, quality control laboratories or some stage during the food processing (Luong, Groom, & Male, 1991).

The development of biosensors is described in several works, the majority restricted to other areas of application, as: clinical, environmental, agricultural and biotechnology (Bourgeois, Burgess, & Stultz, 2001; Scheper et al., 1999; Tothill, 2001; Wang, 1999). Developments involving the use of this type of sensor could be employed in foods, 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. Despite the enormous diversity of research involving biosensors for the food industry, its application in this area, for any analyte is still restricted. On the other hand, tests of prototype in real samples have critical stages such as the immobilization of the biocomponent during the construction of the device and sample preparation for analysis. The biosensors need mild conditions of temperature and pH to maintain active the biological element (Gibson, 1999; Guilbault, 1970), therefore, in some cases, a pretreatment of the sample is recommended to remove interfering species such as ascorbic acid, tyrosin and others. Procedures that include neutralization, dilution or extraction are made when the food is acidic or hydrophobic. Methods of correction to reduce the analysis time, in foods, include acidic or alkaline hydrolysis, microwave digestion, supercritical fluid extraction, evaporation and filtration (Deng & Dong, 1996; Kotsira & Clonis, 1998; Luong, Brown, Male, Cattaneo, & Zhao, 1995; Marconi, Panfili, Messia, Cubadda, Campagnone, & Palleschi, 1996; Panfili, Manzi, Campagnone, Scarciglia, & Palleschi, 2000; Zhang & Wilson, 1998).

In the food industry an attractive area for the biosensor application is the detection of pathogens, pesticides, microorganisms and toxins. Traditional methods to identify contaminants include physicochemical, biological and serological tests. However, many of these require long sample-preparation, analysis time and lack sufficient sensitivity and selectivity and some of the analyses takes days. Thus, immunoanalytical methods are good alternatives because antibodies can be developed not only for recognizing proteins, but also for surface antigens of microorganisms and low-molecular weight compounds.

Biosensor or immunosensors reduce assay time and cost or increase the product safety. These methods have been adapted to detect or measure analytes in *on-line* systems (Rasooly, 2001). Hazard analysis and critical control points (HACCP) systems that is, generally accepted as the most effective system to ensure food safety, can utilize biosensor to verify that the process is under control. The high sensitivity of enzymatic biosensors or immunosensors enabled detection of microorganisms like *E. coli*, Salmonella, *S. aureus*, pesticides, herbicides etc, in hours or minutes (Fitzpatrick et al., 2000; Killard & Smyth, 2000).

The aim of this article is to review the development and application of some biosensors in the food technology, its current situation and future possibilities, as well as a brief commentary on the aspects of biosensors construction.

2. General aspects of biosensors construction

2.1. Classification of biological recognizers

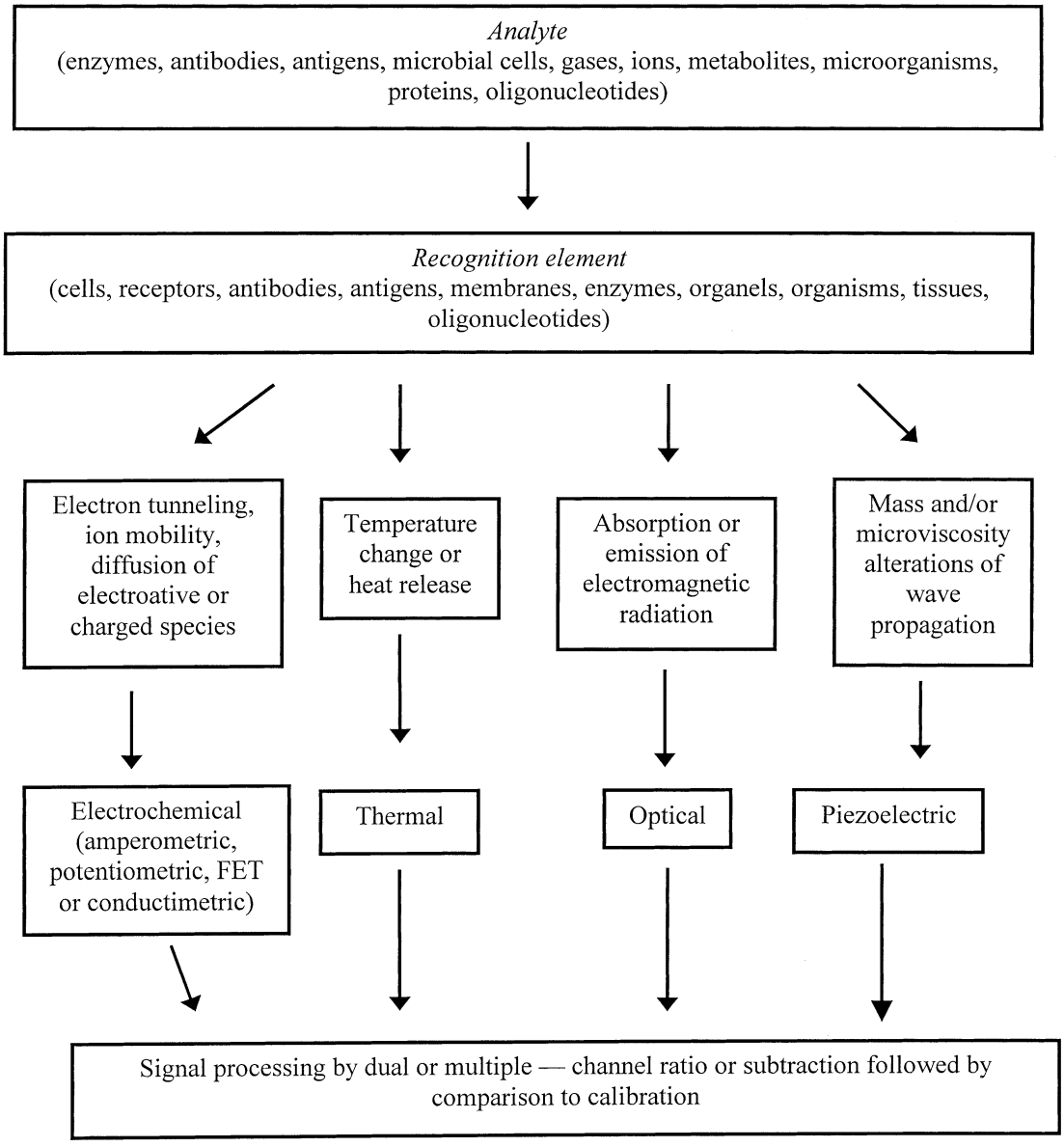
Biosensors can be classified in agreement to the type of involved active biological component in the mechan-

ism or the mode of signal transduction or combination of these two aspects. Scheme 1 shows some analytes (substrate) possible to be analysed immobilizing the biological components, separately, in several transducers. The choice of the biological material and the adjusted transducer depends on the properties of each sample of interest and the type of physical magnitude to be measured. The type of the biocomponent determines the degree of selectivity or specificity of the biosensor. Thus, the biological recognizers are divided in three groups: biocatalytic, bioaffinity and hybrid receptors.

2.1.1. Biocatalytic receptors

The biocatalytic recognition element can be systems containing enzyme (mono or multi enzyme), whole cells (microrganisms, such as bacteria, fungi, eukaryotic cells, yeast), cells organelles and plant or animal tissue slice (Davis, Vaughan, & Cardosi, 1995)

Biosensors that use microorganisms, plant or animal tissue, as biocomponents, have the advantage of unnecessary tedious procedures of extraction and purification, while the enzyme is used as an active component. Microbial sensors are less sensitive to the inhibition for other compounds present in the sample, are more tolerant to the pH variations, temperature and generally has a longer lifetime. These devices are based on the contact of electrodes and immobilized living cells, and they are easily regenerated, for immersion in a solution of nutrients. On the other hand, biosensors with these characteristics present a slow response and low selectivity of that gotten with isolated enzymes, due to a variety of metabolic processes occurring in an living cell (Phadke,



Scheme 1. Biocomponent and transducers employed in construction of biosensors.

1992). These sensors are generally based on the detection of organic compounds assimilated by the microorganisms or monitoring changes occorring in respiration activity during metabolism. Some microbial biosensors have been used for food analysis, but principally, in biological oxygen demand (BOD) measurements (Nisshin Electric Corp., Japan; Aucoteam GmbH, Germany; Medingen GmbH, Germany)

Problems like selectivity and the slow response characteristic of microbial sensors can be overcome by the use of enzymes which, not surprisingly, respresent the most commonly used sensing agents due to their selectivity (Davis et al., 1995). Enzyme sensors fall into various classes including those that are potentiometric, amperometric, optoelectric, calorimetric and piezoelectric. Basically, all enzyme sensors work by immobilization of the enzyme system onto a transducer. Among the enzymes commercially available, the oxidases are the most often used. This type of enzyme offers the advantages of being stable, and in some situations does not require coenzymes or cofactors (Davis et al., 1995; Phadke, 1992). Some examples of commercial biosensors based on enzyme available for industrial markets are PM-1000 and PM-1000DC (Toyo Joso); OLGA (On-line general analyzer; Eppendorf).

2.1.2. Bioaffinity receptors

The affinity-based biosensors may be chemoreceptors, antibodies or nucleic acids. Affinity-based biosensors provide selective interactions with a given ligand to form a thermodynamically stable complex. The potential use of immunosensors is due to their general applicability—any compounds can be analysed as long as specific antibodies are available—and to the specificity and selectivity of the antigen–antibody reaction and the high sensitivity of the method, depending on the detection method used. The antigen–antibody complex may be utilized in all types of sensors. The physichochemical change induced by antigen–antibody binding do not generate an electrochemically detectable signal. Therefore, enzymes, fluorescent compounds, electrochemically active substrates, radionuclides or avidin–biotin complexes are used to label either the antigen or the antibody (Fitzpatrick et al., 2000; Wilchek & Bayer, 1988). The most common transducers to immunosensors are acoustic and optical systems. The use of affinity-based biosensors, particularly immunosensors, in the identification and measure of food analytes and contaminants for the improvement of food safety was reviewed by Bilitewski (2000).

2.1.3. Hybrid receptors

The hybrid receptors such as DNA and RNA probes have shown promising application in food analysis as in microorganism detection. The principle of selective detection is based on the detection of a unique sequence of nucleic acid bases through hybridization. The nucleic acid structure is a double helix conformation of two polynucleotide strands. Each strand is constituted of a polymeric chain that contain bases: Adenine, Thymine, Cytosine, Guanine. These bases are complementary by two through three hydrogen bonds in the C–G base pair and two in the T–A base pair. This base-pairing property gives the ability of one single strand to recognize its complementary strand to form a duplex. DNA sensors consist to immobilize, onto a solid support, well-defined sequences of single strands as a biological receptor. A DNA probe is added to DNA or RNA from an unknown sample. If the probe hybridizes (combines) with the unknown nucleic acid because of pairing of complementary base recognition, detection and identification are possible. DNA-based analytical methods seems to be the only method for detecting genetic modifications and is the most sensitive approach for detecting microorganisms. Commercially, biosensing DNA probes exist for the detection of foodborne pathogens such as Salmonella, Listeria, *E. coli* and *S. aureus* (Boer & Beumer, 1999; Wolcott, 1991).

2.2. Immobilization procedures

Biological transducers can be immobilized on a solid support in a variety of ways. Methods for immobilization of the biological component include adsorption, cross linking, covalent bonding, entrapment, encapsulation and others as use of solid binding matrices. The immobilization matrix may function purely as a support or may also be concerned with mediation of the signal transduction mechanism. The purpose of any immobilization method is to retain maximum activity of the biological component on the surface of the transducer. The selection of an appropriate immobilization method depends on the nature of the biological element, type of the transducer used, physicochemical properties of the analyte and operating conditions for the biosensor (Luong, Mulchandani, & Guilbault, 1988).

The most common methods for immobilization of biocomponents are adsorption and covalent bonding.

Physical adsorption of the biocomponent based on van der Waals attractive forces is the oldest and simplest immobilization method. In this case a solution of enzyme, a suspension of cells or a slice of tissue is immobilized by an analyte permeable membrane as a thin film covering the transducer. The adsorption method does not require chemical modification of the biological components and it is possible to regenerate the matrix membrane. The advantage of this method is the simplicity and the great variety of beads that could be used. However, loss of adsorbed biological components is possible if changes in pH, ionic strength or temperature occur during measurements. Entrapping the biocomponent in matrices such as gels, polymers,

pastes, or inks considerably improves its stability and consequently the biosensor performance it may be essential to covalently link the biological recognizer to the solid support (Wagner & Guilbault, 1994; Zhang, Wright, & Yang, 2000).

Covalent bonding may be used to achieve the immobilization of biological components to a membrane matrix or directly onto the surface of the transducer. These methods are based on the reaction between the same terminal functional groups of the protein (not essential for its catalytic activity) and reactive groups on the solid surface of the insoluble bed. Functional groups available in the enzymes or protein mainly originate from the side chain of the amino acid. They include, for example, the ε-amino groups from lysine, carboxyl groups from aspartate and glutamate, sulfhydryl groups from cysteine and phenolic hydroxyl groups from tyrosine. Beds as membranes with different active functional groups are able to immobilize biocomponents with great efficiency and facility.

Bifunctional reagents (homo or hetero functionals) have also been used in the immobilization of enzymes and or proteins. The method is based on the macroscopic particle formation as a result of the formation of covalent binding between molecules of inert bed with functional reagents. Some of the most used homofunctionals reagents, include glutaraldehyde, carbodiimide and others; while the heterofunctionals include trichloro triazine, 3-metoxidifenil methane-4,4′ diisocianate (Bartlett, Booth, Caruana, Kilburn, & Santamaría, 1997; Zhang et al., 2000).

Other procedures to modify the surface of the transducer involves the incorporation of the biocatalyst within the bulk of a carbon composite matrix. These modified biosensors offer several advantages such as the close proximity of the biocatalytic and sensing sites; possibility to incorporate other components (cofactors); an easy renewing of the surface, economy of fabrication and a high stability of the incorporated biocatalysts. Biosensors with these features can be the carbon paste electrodes (Boujtita & Murr, 2000; Mullor, Cabezudo, Ordieres, & Ruiz, 1996), screen-printed biosensors (Capannesi, Palchetti, Mascini, & Parenti, 2000; Ge, Zhang, Zhang, & Zhang, 1998) and solid binding matrices (SBMs) of defined molecular structure (Miertus, Katrlík, Pizzariello, Stred'ansky, Svitel, & Svorc, 1998; Stred'anský et al., 1999).

2.3. Transducers

The activity of the biological component for a substrate can be monitored by the oxygen consumption, hydrogen peroxide formation, changes in NADH concentration, fluorescence, absorption, pH change, conductivity, temperature or mass. Thus, the biosensor can be classified in several types according to the transducer (see Scheme 1): potentiometric [ion-selective electrodes (ISEs), ion-sensitive field effect transistors (ISFETs)], amperometric, impedimetry, calorimetric, optical and piezoelectric transducers. Many biosensors used for food analysis are based on oxidase systems like an aerobic microorganism in combination with electrochemical transducers, in particular, amperometry devices.

2.3.1. Electrochemical transducers

An electrochemical biosensor according to the IUPAC definition, is a self-contained integrated device, which is able to provide specific quantitative or semi-quantitative analytical information using a biological recognition element (biochemical receptor) which is retained in direct and spatial contact with the transduction element (Thévenot, Toth, Durst, & Wilson, 2001). Biosensors based on electrochemical transducer have the advantage of being economic and present fast response; the possibility of automation allows application in a wide number of samples (Luong et al., 1988). The electrochemical biosensors can be classified in conductimetric, impedimetric, potentiometric and amperometry.

2.3.1.1. Conductimetric and impedimetry transducers. Conductimetric biosensors are based on the principle of change of conductivity of the medium when microorganisms metabolize uncharged substrates, such as carbohydrates, to intermediates, such as lactic acid. This measurable change to detect small changes in the conductivity of the medium between two electrodes. The amount of charged metabolites is directly proportional to the growth rate of the organism and is easily quantifiable. Many biological membrane receptors may be monitored by ion conductometric or impedimetric devices using interdigitated microelectrodes. Conductimetric biosensors are usually non specific and have a poor signal/noise ratio, and therefore have been little used.

The impedance principle was accepted by the Association of Official Analytical Chemists, Intl. (AOAC) as a first action method (Gibson, Coombs, & Pimbley, 1992) and is most indicated to monitor quality and detect specific food pathogens, detection of bacteria and sanitation microbiology (Feng, 1992). These biosensors are based on the principle that microbial metabolism results in an increase in both conductance and capacitance, causing a decrease in the impedance. Impedance is usually measured by a bridge circuit. Often a reference module is included to measure and exclude nonspecific changes in the test module. The reference module serves as a control for temperature changes, evaporation, changes in amounts of dissolved gases and degradation of culture medium during incubation. Commercial analytical devices based on the use of impedance technology for detection of microorganisms

are on the market, such as Bactometer and Malthus M1000s.

2.3.1.2. Potentiometric transducer. In biosensors based on potentiometry a membrane or sensitive surface to a desired species generates a proportional potential to the logarithms of the concentration of the active species, measured in relation to a reference electrode. The potentiometric devices can measure changes in pH and ion concentration. It is possible to use transistors as electric signal amplifiers coupled to ISE, called ISFET. These biosensors are based on the immobilization of a biological active material, in general, enzymes, antigen or antibodies, on a membrane, on the surface of a transducer as ISE that answers for the species formed in the enzymatic reaction or the formation of antigen–antibody immunocomplex. Fig. 1 shows a semiconductor immunosensor that detect potential changes associated with the formation of an antibody-antigen complex in minutes. The conductivity of the n-channel region in the p-type silicon is controlled by the strength of the electrical field at the membrane surface and is measured by application of a voltage between the source and drain electrodes. For proper functioning, the solution-membrane interface should remain ideally polarized and thus impermeable to the passage of charge. Failure to meet this criterion results in poor sensitivity (Deshpande & Rocco, 1994).

Currently the research in this field has been aimed at getting better limits of detection and selectivity of the ISE, with the purpose to supply the necessary requirements for its application in the industry. New developments include sensor arrays, new ionophores, improvement of the detection limit and new electrodes for miniaturization (Buhlmann, Pretsch, & Bakker, 1998; Karube & Suzuki, 1992; Koncki, Glab, Dzimulska, Palchetti, & Mascini, 1999).

The importance of the ISFET can be attributed to its capacity of miniaturization and the possibility to use the processes of microelectronics in its micromanufacture (Krull, 1990). The potentiometric biosensors based on enzyme, have applications (ENFET) in the field of industrial processes monitoring and in hygienical-sanitary quality control of products (Taylor, Marenchic, & Spencer, 1991; Wan, Chovelon, & Renault, 2000; Wan, Chovelon, Renault, & Soldatkin, 1999). When these devices are constructed in systems of channels of sensors, its application can be even more effective (Stefan, Van Staden, & Aboul-Enein, 1999).

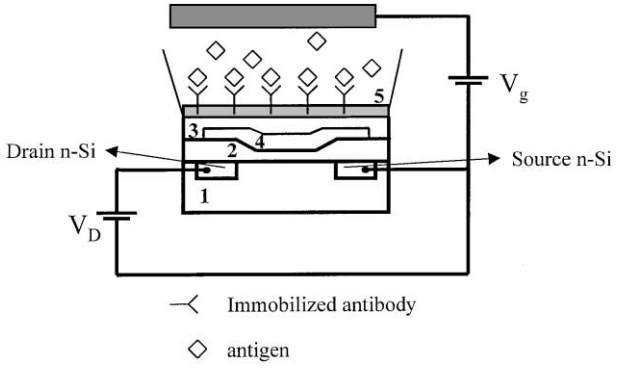


Fig. 1. Schematic diagrams of a Immuno-FielD-Effect transistor sensor. (1) Substrate p-Si; (2) insulator SiO_2/Si_3N_4; (3) Furrow metals; (4) Lacune (gap); (5) Selective coating; V_g and V_D are gate voltage and drain voltage, respective, for generation and an initial current flow.

2.3.1.3. Amperometric transducer. The amperometric biosensors measure the current produced for the chemical reaction of an electroative species to an applied potential, which is related to the concentration of the species in solution. The amperometric biosensor is fast, more sensitive, precise and accurate than the potentiometric ones, therefore is not necessary to wait until the thermodynamic equilibrium is obtained and the response is a linear function of the concentration of the analyte. However, the selectivity of the amperometric devices is only governed by the redox potential of the electroative species present. Consequently, the current measured by the instrument can include the contributions of several chemical species.

The first amperometric biosensor (Updike & Hicks, 1967) for glucose analysis using the glucose oxidase enzyme with the Clark oxygen electrode was based on the oxygen consumption monitoring. The formation of the product or consumption of reagent can be monitored to measure the analyte concentration. These biosensors are called as the *first generation*.

Amperometric biosensors modified with mediators are referred as the *second generation* biosensors. Mediators are redox substances that facilitate the electron transfer between the enzyme and electrode. The direct enzyme-electrode coupling or mediatorless biosensors based on direct electron transfer mechanisms are called *third generation*. In this case, the electron is directly transferred from the electrode to enzyme and to the substrate molecule (or vice versa). In this mechanism the electron acts as a second substrate for the enzymatic reactions and result in the generation of a catalytic current. The substrate transformation (electrode process) is essentially a catalytic process (Ghindilis, Atanasov, & Wilkins, 1997; Habermüller, Mosbach, & Schuhmann, 2000).

On food analysis, the majority of the electrochemical biosensors are based on the amperometric in combination with oxidases. Amperometric electrodes and oxidases enzymes have shown good results because the enzymatic react with their substrates and the facility to measure, associated with high sensitivity. Among the amperometric, transducers that are based on the monitoring of hydrogen peroxide present a higher sensitivity than those with detection of the oxygen consumption.

However, these are more suitable when the biological components are microbial cells, vegetables or animal tissues.

Other amperometric biosensors are used for indirect detection of microbial contamination in foodstuffs. Several microorganisms can be detected amperometrically by their enzyme-catalyzed electrooxidation/electoreduction or their involvement in a bioaffinity reaction (Boer & Beumer, 1999; Fitzpatrick et al., 2000). In this systems are utilized an enzyme-linked amperometric immunosensor for the detection of bacteria by means of the antigen/antibody combination. In this case, a heat-killed bacteria, such *S. typhimurium*, is sandwiched between antibody-coated magnetic beads and an enzyme-conjugated antibody (Brooks, Mirhabibollahi, & Kroll, 1992). Other amperometric immunoassays include; enzyme-channeling reactions and electrochemical regeneration of mediators within the membrane layer of an anion-exchange enzyme–antibody modified electrode (Rishpon & Ivnitski, 1997). Other biosensors sensing the microorganisms are based on partially immersed immunosensors in a solution resulting in the formation of a supermeniscus on the electrode surface. This supermeniscus plays a role in providing optimal hydrodynamic conditions for the current generation process in hydrodynamic conditions for the current generation process (Hamid, Ivnitski, Atanasov, & Wilkins, 1998). All these immunoassays cited have a relatively short assay time.

2.4. Optical transducers

Biosensor with optical transducers are receiving considerable attention nowadays, with advances in optical fibers and laser technology. These sensors had extended the limits of application of the spectrophotometric methods in analytical chemistry, specially, for miniaturized systems.

The optical biosensors are based on methods such as UV–Vis absorption, bio/chemiluminescence, fluorescence/phosphorescence, reflectance, scattering and refractive index, caused by the interaction of the biocatalyst with the target analyte. Optical sensors, initially, developed for oxygen, carbon dioxide and pH using acid-base indicators (Seitz, 1988) have been extended for the construction of fluorescent and luminescent optrodes. Optrodes are constructed with an immobilized selective biocomponent at one end of an optical fiber, with both the excitation and detection components located at the other end. The change in the intensity of absorbed or emitted light from an indicator dye that can in turn interact with the selective biocomponent is the principle the pH, pO_2 and pCO_2 fiber-optic probes that achieve transduction via the indicator dye alone. This change is directly proportional to the amount of analyte present in the sample. The principle of these fiber-optic probes is the total internal reflection (TIR) phenomenon in a light guide using evanescent waves, an electromagnetic wave that exists at the surface of many forms of optical waveguides, to measure changes in refractive index at the sensor surface. TIR-based biosensors make use of the evanescent wave penetrating only a fraction of a wavelength into the optically rarer medium when light coming from an adjacent denser medium is incident on the interface at an angle above the critical angle. Changes in the surface refractive index or absorptivity reduce the transmission of light through the guide. Systems of $NAD(P)^+$/NAD(P)H dependent dehydrogenase enzymes are indicated for use in optical devices as NAD(P)H absorbs light strongly at 340 nm (ultraviolet) and emits fluorescent light in the blue range (at 460 nm). These coenzymes have been used for analysis of acetaldehyde, alanine, malate, glucose, glycerol, ethanol, galactose, but show restriction because a high instability and high cost (Dremel, Schaffar, & Schmid, 1989; Mehrvar, Bis, Shrarer, Mao-Young, & Luong, 2000; Wangsa & Arnold, 1988).

Optical sensors make use of bioluminescent bacteria as *Vibrio fischeri* or *Vibrio harveyi* or chemiluminescent substances as luminol in combination with oxireductases for direct measurement of ATP, NAD(P)H or H_2O_2. Optical luminescent biosensors have application in the control of fermentative processes, alcohol and in the determination of carbohydrates (Bataillard, 1993; Blum, Gautier, & Coulet, 1988, 1991; Caselunghe & Lindeberg, 2000; Grate, Rosepehrsson, Venezky, Klusty, & Wohltjen, 1993; Latif & Guilbault, 1988; Mehrvar et al., 2000; Sternesjo, Mellgren, & Bjorck, 1995; Xie, Mecklenburg, Danielsson, Ohman, Norlin, & Winquist, 1995; Xing et al., 2000).

Another optical TIR-based biosensor that internal reflection in a light guide is SPR (surface plasmon resonance). SPR devices combine an evanescent wave detector with a biocomponent, generally, an antibody. Maybe SPR is a further important sensing technique that allows non-labelled immunoassay.

The SPR method is a charge-density oscilation that may exist at the interface of two media with dielectric constants of opposite sign, for instance, a metal and a dielectric. An SPR optical sensor, generally, comprises an optical system, a transducing medium which interrelates the optical and (bio)chemical domains, and an electronic system supporting the optoelectronic components of the sensor and allowing data processing. SPR is a quantum electro-optical phenomenon; energy carried by photons of light can be coupled or transferred to electrons in a metal. This coupling results in the creation of a plasmon, a group of excited electrons on the surface of the metal. The intensity of the plasmon is influenced by the type of metal and the environment of the metal surface. Changes in chemical properties within the range of the plasmon field (such as the protein interaction in

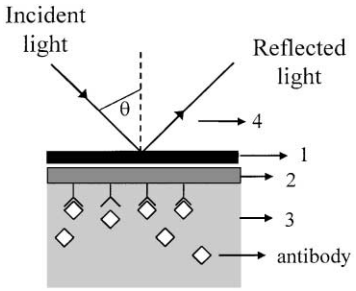


Fig. 2. Schematic diagrams of a biosensor based on surface plasmon resonance principle. (1) metal (Gold); (2) sensitizing layer; (3) sample solution (antigen) and (4) glass substrate. The devices measures changes in the refractive index upon antigen-antibody binding.

antibody–antigen binding) cause changes in plasmon resonance. These changes can be measured as a change in the angle of incidence or shift in the wavelenght of light absorbed and can be measured as a change in the SPR signal (expressed in resonance units, RU). Most SPR instruments measure changes in the angle of incidence. A SPR-based biosensor specimen is tested for its adsorption to a covalently immobilized molecule by surface sensitive optical techniques. The amount of adsorption is measured as a function of time and results are generated in the form of a sensogram that shows the response units measured as a consequence of the adsorption (Homola, Yee, & Gauglitz, 1999).

SPR biosensors are potentially useful for environmental and food safety analysis because they are relatively easy to use, do not require labeling of either molecule in the reaction, and can assay crude samples without purification (Homola et al., 1999). Fig. 2 shown an SPR immunosensor that consists of a prism on a glass slide carrying a thin metal layer. The sensitizing antibody layer is in direct contact with the antigen or analyte to be determined. The changes in the refractive index can be monitored as a shift in the angle of the total absorption of incident light on a metal layer carrying the antibody. This type of immunosensor requires no prior incubation or separation step (Caselunghe & Lindeberg, 2000; Deshpande & Rocco, 1994; Mehrvar et al., 2000; Rasooly & Rasooly, 1999; Sternesjo et al., 1995; Xing et al., 2000).

2.4.1. Thermal and acoustic wave transducers

Although the electrochemical and the optical biosensors dominate, other forms of transducer such as thermal and acoustics are used, which can be sufficiently effective in analytical applications. Despite the lack of selectivity, which is a characteristic problem of these transducers, they present the advantage of miniaturization and the possibility of construction of arrays of sensors for simultaneous determination of several compounds (Grate et al., 1993; Xie et al., 1995).

2.4.1.1. Thermal transducer. Biosensors with thermal transducers are based on the monitoring of the energy changed, under the heat form, over time, that occurs in a chemical reaction catalyzed by enzymes or microorganisms. However, the heat cannot be perfectly

Table 1
Types of transducers, their characteristics and application

Transducer	*Advantages*	*Disadvantages*	*Application*
Ion-selective electrode (ISE)	Simple, reliable, easy to transport.	Sluggish response, requires a stable reference electrode, susceptible to electronic noise.	Amino acids, carbohydrates, alcohols and inorganic ions
Amperometric	Simple, extensive variety of redox reaction for construction of the biosensors, facility for miniaturize.	Low sensitivity, multiple membranes or enzyme can be necessary for selectivity and adequate sensitivity.	Glucose, galactose, lactate, sucrose, aspartame, acetic acid, glycerides, biological oxygen demand, cadaverine, histamine, etc.
FET	Low cost, mass production, stable output, requires very small amount of biological material, monitors several analytes simultaneously.	Temperature sensitive, fabrication of different layer on the gate has not been perfected.	Carbohydrates, carboxylic acids, alcohols and herbicide
Optical	Remote sensing, low cost, miniaturizable, multiple modes: absorbance, reflectance, fluorescence, extensive electromagnetic range can be used.	Interference from ambient light, requires high-energy sources, only applicable to a narrow concentration range, miniaturization can affect the magnitude of the signal.	Carbohydrates, alcohols, pesticide, monitoring process, bacteria and others...
Thermal	Versatility, free from optical interferences such as color and turbidity.	No selectivity with the exception of when used in arrangement	Carbohydrates, sucrose, alcohols, lipids, amines
Piezoelectric	Fast response, simple, stable output, low cost of readout device, no special sample handling, good for gas analysis, possible to arrays sensors.	Low sensitivity in liquid, interference due to non specific binding.	Carbohydrates, vitamins, pathogenic microorganisms (e.g. *E. coli*, Salmonella, Listeria, Enterobacter), contaminants (e.g. antibiotics, fungicides, pesticides), toxic recognition as bacterial toxins.

confined in an adiabatic system and always presents a loss of information since the produced heat is partly wasted by irradiation, conduction or convection. The thermal biosensors can be based on thermistors or stacks. The use of thermal biosensors in food analysis is still limited, probably due to tradition and the relative complex instrumentation involved.

Despite this, several important compounds for the quality control of foods have been determined using thermal transducers, including ascorbic acid, glucose, lactate, galactose, ethanol, sucrose, penicillin G, cephalosporin and oxalic acid (Bataillard, 1993; Mosbach, 1995; Ramanathan, Jonsson, & Danielsson, 2001; Ramanathan, Rank, Svitel, Dzgoev, & Danielsson, 1999).

As well as enzymes, microbial cells and antibodies have been also used in these devices in thermometric enzyme-linked immunosorbent assays (TELISAs). This technique has been applied to assays for microbial contamination in food products (Mosbach, 1995).

2.4.1.2. Piezoelectric transducers. The piezoelectric transducers (surface acoustic wave) are more applied in immunosensors. In these devices, an antigen or antibody is immobilized in the surface of a crystal (O'Sullivan, Vaughan, & Guilbault, 1999). The interaction of these elements with the analyte highly specific can be monitored through the oscillation of the immersed crystal in a liquid, which will produce a modification of mass in the crystal, perceptible by means of its frequency of oscillation. The immunosensors with wave acoustics principles, among others types, can be used for detection of pathogenic microorganisms, gases, aromas, pesticides, hormones and others (Abad, Pariente, Hernandez, Abruña, & Lorenzo, 1998; Horacek, Garnett, Skládal, & Morgan, 1998; Bizet, Gabrielli, & Perrot, 1999; Ivnitski , Hamid, Atanasov, & Wilkins, 1999; Wu, 1999; Babacan, Pivarnik, Letcher, & Rand, 2000). Research in this field is directed to improve the sensitivity and selectivity of these transducers. Character-

Table 2
Application of the biosensors for glucose

Analyte	*Application*	*Biocomponent*	*Transducer*[a]	*Detection range*	*Ref.*
Glucose	Soft drinks, juices and milk	Glucose oxidase (GDO)	Amp.	50–500mM	Centonze, Zambonin, & Palmisano, 1997
Glucose	Musts and wine	Glucose oxidase (GDO)	Amp.	1×10^{-5}–8×10^{-4} mol/l	Del Cerro, Cayuela, Reviejo, Pingarrón, & Wang, 1997
Glucose	Juices and honey	Glucose oxidase (GOD)	Amp.	0.5–10 mM	Gavalas, Fouskaki, & Chaniotakis, 2000
Glucose and maltose	Synthetic samples	Glucose oxidase (GDO) and amyloglucosidase (AG)	Amp.	$\leqslant$35 mol/l(glucose) $>$25 mmol-L(maltose)	Ge et al., 1998
Glucose and lactose	Milk	Glucose oxidase (GDO), β-galactosidade and mutarotase	Amp.	4.44g/100g (lactose)	Liu, Li, Ying, Sun, Qin, & Qi, 1998
Glucose	Biscuits, juices and milk	Glucose oxidase (GDO)	Amp.	100–10,000 ppm	Mannino, Brenna, Buratti, & Cosio, 1997
Glucose and galactose	Yoghurt and milk	Glucose oxidase (GDO), galactose oxidase and peroxidase	Amp.	250–4.000 mg/l	Mannino, Cosio, & Buratti, 1999
Glucose, fructose, ethanol, L-lactate, L-malate and sulfite(simultan.)	Wine	Glucose oxidase (GDO), D-fructose dehydrogenase, alcohol dehydrogenase,L-lactate dehydrogenase,L-malate dehydrogenase, sulfite oxidase and diaphorasc	Amp.	0.03–15 mM (glucose) 0.01–10 mM (fructose) 0.014–4 mM (ethanol) 0.011–1.5 mM (L-lactate) 0.015–1.5 mM (L-malate) 0.01–0.1 mM (sulfite)	Miertus et al., 1998
Glucose and Glutamate	Beverages	Glucose oxidase (GDO) and glutamate oxidase (GLOX)	Amp.	10 μM-3 mM(glucose) 3 μM-0.5 mM(glutamate)	Mizutani , Sato, Hirata, & Yabruki, 1998
Glucose and lactate	Tomato juice	Glucose oxidase (GOD)	Amp.	20–100 mM	Palmisano, Rizzi, Centonze, & Zambonin, 2000
Glucose	Wine	Glucose oxidase (GDO), cholesteryl myristate (CM) and cholesteryl oleate (CO)	Amp.	0.2–47 g/L	Svorc, Miertus, Katrlík, & Stred'anský, 1997
Glucose, ascorbic acids and citric acids	Fruit drinks	Glucose oxidase (GDO), horseradish peroxidase (HRP) and Urease	ENFET	1–10 mM (glucose) 0.25–2 mM (ascorbic acids) 5–100 mM (citric acids)	Volotovsky & Kim, 1998
Glucose	Synthetic samples	Glucose oxidase (GOD)	Amp.	$\leqslant$40 mmol/l	Zhang & Dong, 1999
Glucose	Beverages	Glucose oxidase (GDO)	Optical	0.06–30 mmol/dm^3	Wu, Choi, & Xiao, 2000
Glucose	Fruit juice and coca-cola	Glucose oxidase (GDO)	Thermal	0.2–30 mM	Ramanathan et al., 2001

[a] Amp., amperometric.

istics of the transducers and principal application for the relevant analytes are listed in Table 1.

3. Potential applications

Since the pioneering work of Updike and Hicks, (1967) for the determination of glucose and the enzymatic electrodes to this analyte in particular, the amperometric have dominated the literature about biosensors. The principal reason is that glucose is an analyte of great importance in biotechnology.

Tables 2–8 present some of the most important biosensors, described during the last 5 years in the literature (1997–2001). The tables start with glucose and other carbohydrates and end with complex parameters such as contaminants and additives compounds. As most works cited are prototypes they are not fully optimized for a defined application in real samples. Some applications are synthetic samples and can be applied in food samples. Some biosensors listed in the tables are used to determine more than one analyte. These are either suitable for determining more than one substrate or are used in combination for simultaneous measurements. The tables show the detection range of the biosensors and the most researchers define detection range as the linear part of the calibration curve of the particular equipment that was used during the experiments. Normally the response of the biosensor extends beyond both the upper and lower ends of the linear range.

4. Commercial biosensors

In spite of the great number of publications on biosensors applied in food analysis, only a few systems are commercially available. Drawbacks that have to be overcome are the limited lifetime of the biological components, mass production as well as practicability in handling. However, this problem will be managed in the near future, since biosensors offer unique solutions to food analysis in terms of specificity and time saving.

Very few biosensors are presently used in the food industry for *on-line* analysis, although in principle they can be combined with flow-injection analysis for on-line monitoring of raw materials, product quality and possibly the manufacturig process. Commercial biosensors are available in several forms, such as autoanalysers,

Table 3
Application of the biosensors in food analysis (carbohydrates)

Analyte	Application	Biocomponent	Transducer[a]	Detection range	Reference
D-amygdalin	Synthetic samples	β-Glucosidase	Potent.	–	Merkoci, Braga, Fàbregas, & Alegret, 1999
Fructose	Honey	D-fructose dehydrogenase (FDH)	Amp.	<1.0 mM	Bassi, Lee, & Zhu, 1998
Fructose	Juice	D-fructose dehydrogenase (FDH)	Amp.	<1.0 mM	Boujtita & Murr, 2000
Fructose	Dietetic jelly and sweetener	D-fructose dehydrogenase (FDH)	Amp.	0.1–0.8 mmol/l	Garcia, Neto, & Kubota, 1998
Fructose	Juice	D-fructose dehydrogenase (FDH) and n-octyl β-D-glucopyranoside (n-octyl glucoside)	Amp.	$\cong$ 0.5 mM	Kinnear & Monbouquette, 1997
Fructose and lactulose	Milk	D-fructose dehydrogenase (FDH) and β-galactosidase(β-gal)	Amp.	1×10^{-6}–5×10^{-3} mol/l (fructose) 1×10^{-5}–5×10^{-3} mol/l (lactulose)	Moscone, Bernado, Marconi, Amine, & Palleschi, 1999
Fructose	Honey, juice and cola	D-fructose dehydrogenase (FDH)	Amp.	0.5–15 mM	Paredes, Parellada, Fernández, Katakis, & Domínguez, 1997
Fructose	Honey, milk, juice and wine	D-fructose dehydrogenase (FDH)	Amp.	50×10^{-6}-10×10^{-3} mol/l	Stred'anský et al., 1999
Fructose	Synthetic samples	Fructose dehydrogenase (FDH)	Amp.	<0.5 mM	Yabuki & Mizutani, 1997
Galactosidase conjugates and glycerol	Foods	Galactose oxidase (GalOD)	Amp.	0.2–2 mM (galactose) 0.5–6 mM (raffinose) 25–250 mM (lactose) 2–200 mM (glycerol)	Vega, Núñez, Weigel, Hitzmann, & Ricci, 1998
Lactose	Milk	β-Galactosidase, lactozym and Saccharomyces cerevisiae	Potent.	–	Amárita, Fernández, & Alkorta, 1997
Lactulose	Milk	D-fructose dehydrogenase (FDH) and β-galactosidase (β-gal)	Amp.	1–30 μM	Sekine & Hall, 1998
Starch	Wheat flour samples	α-Amilase, amyloglucosidase (AMG) and glucose oxidase (GOD)	Amp.	5×10^{-6}–5×10^{-4} mol/l	Marconi, Baldino, Messia, Cubadda, Moscone, & Palleschi, 1998

[a] Potent., Potentiometric; Amp., amperometric.

manual laboratory instruments and portable (hand-held) devices. Commercially devices for the food industry are listed in Table 9 (Ramsay, 1998). They are based on similar technology, either an oxygen electrode or a hydrogen-peroxide electrode in connection to an immobilized oxidase as Apec Glucose Analyser, ESAT Glucose Analyser, Glucoprocesseur, Amperometric Biosensor Detector, ISI Analysers and Oriental Freshness Meter.

The electrochemistry principle is also applied to microorganism monitoring in commercial analytical systems such as Malthus 2000 that use conductance technology to estime microbial populations including coliforms, lactic acid and bacteria, fungi and yeasts. This analyzer detects changes in the electrical conductance of the media caused by the growth and metabolism of the microorganism and the analysis time of

Table 4
Application of the biosensors in food analysis (alcohols, fenols and carboxylic acids)

Analyte	Application	Biocomponent	Transducer[a]	Detection range	Reference
Ethanol	Beer	Alcohol oxidase	Amp.	0.12–2.00 mM	Boujtita, Hart, & Pittson, 2000
Ethanol	Wine	Alcohol dehydrogenase (ADH) and diaphorase (DP)	Amp.	0.2–40 mM (non linear)	Katrlík, Svorc, Stred'anský, 1998
Ethanol	Alcoholic beverages	Alcohol dehydrogenase (ADH) and NaDH oxidase	Amp.	3×10^{-7}–2×10^{-4} M	Leca & Marty, 1998
Ethanol	Synthetic samples	Alcohol dehydrogenase (ADH)	Amp.	0.1–4.0 mM	Tobalina, Pariente, Hernández, Abruña, & Lorenzo, 1999
Ethanol	Synthetic samples	Alcohol oxidase	Amp.	0.05–10 mM	Morozova, Ashin, Trotsenko, & Reshetilov, 1999
Aldehydes	Monitoring fermentation	Alcohol oxidase (AOX), methylotrophic yeast hansenula polymorpha	ENFET	5–200 mM	Korpan et al., 2000
Acethaldehyde	Alcoholic beverages	Aldehyde dehydrogenase	Amp.	0.5–330 μM	Noguer & Marty, 1997
Glycerol	Monitoring fermentation	Glycerokinase and glycerol–3 phosphate oxidase	Amp.	2×10^{-6}–10^{-3} mol/l	Campagnone, Esti, Messia, Peluso, & Palleschi, 1998
Glycerol	Wines	Glycerophosphate oxidase (GPO) and glycerol kinase (GK)	Amp.	2–160μ mol/l	Kiranas, Karayannis, & Karayanni, 1997
Polyphenols	Olive oil	Tyrosinase	Amp.	1–37 μM (hexane) 10–350 μM (chloroform)	Campanella, Favero, Pastorino, & Tomassetti, 1999
Polyphenols	Olive oil	Tyrosinase	Amp.	0.3–30.0 μM	Dall'Orto, Danilowicz, Rezzano, Del Carlo, & Mascini, 1999
Polyphenols	Wines	Horseradish peroxidase (HRP)	Amp.	<25 mM	Imabayashi et al., 2001
Polyphenols	Green tea, grape and olive extracts	Tyrosinase	Amp.	10–100μ mol/l	Romani, Minunni, Mulinacci, Pinelli, Vinceri, Del Carlo, & Mascini, 2000
Catechol	Synthetic samples	Catechol oxidase	O_2 electrode	5×10^{-7}–30×10^{-5} M	Dinçkaya, Akyilmaz, Akgöl, Önal, Zihnioglu, & Telefoncu, 1998
Catechol	Beer	Polyphenol oxidase	Amp.	2×10^{-6}–10^{-5} M	Eggins, Hickey, Toft, & Zhou, 1997
Ascorbic acid	Juices	Ascorbate oxidase	Amp.	5.0×10^{-5}–1.2×10^{-3} M	Alkyilmaz & Dinçkaya, 1999
Citric acid, pyruvate acid and oxaloacetic acid	Synthetic samples (fruits)	Citrate lyase (CL), pyruvate oxidase (POD) and oxaloacetate descarboxylase (AOCD)	Amp.	<100 mM (citric acid) <6 mM (pyruvate) <6 mM (oxaloacetate)	Maines, Prodromidis, Karayanni, Karayannis, Ashworth, & Vadgama, 2000
Citric acid	Juices and sport drinks	Citrate lyase (CL),	Amp.	0.015–0.5 mM	Prodromidis, Karayanni, Karayannis, & Vadgama, 1997
Folic acid	Fortified food	Anti-folic acid antibody	SPR	–	Caselunghe & Lindeberg, 2000
Biotin and folate	Infant formula and milk	Anti-biotin antibody and anti-folic acid antibody	SPR	2–70 ng/ml	Indyk et al., 2000

[a] Amp., amperometric; SPR, surface plasmon resonance.

this device is 8–24 h. Midas Pro devices are based on amperometric detection technique and can detect microorganisms in the range of 10^6 cells/ml in 20 min. More details of biosensors for microorganism and contamisnts may be found in reviews and articles cited by Fitzpatrick et al. (2000) and Ivnitski et al. (1999).

The BIACORE device is based on SPR (surface plasmon resonance) technology for microorganism detection. Swedish BIACORE AB (originally Pharmacia Biosensor AB) offers several models of SPR biosensor: BIACORE©2000™ (vitamins analysis), BIACORE© 1000™ (assays for organophosphate-based pesticides), for more details see http://www.biacore.com/.

The Lumac Biocounter and the Unilite are developed for the estimation of microbial biomass based upon the bioluminscence principle. Both analyzers can detect microorganism in the range of 10^3 cells/ml in 10 min.

5. Commentary and future trends

The quantitative *on-line* determination of the composition and properties of the raw materials that are being industrialized and the final products is a trend for the future. Factors such as stability, storage and sensitivity are still not equated in its totality, but they can be modified in the materials of electrodes, techniques of immobilization of the biocomponent, use of different mediators, addition of stabilizers and a pre-treatment of the sample, when necessary.

Based on optical detection, the surface plasmon resonance (SPR) technique allows monitoring of the molecular interactions at interfaces in real time without interferences from the bulk solution and the need for a special label. Surface plasmon is an eletromagnetic wave associated with the longitudinal oscillation of the free electron gas on the interface of the metal and dieletric. In SPR biosensors, the target analyte binds to its receptor immobilized on a sensor chip surface. This binding gives rise to a change in the refractive index at the surface where the interaction occurs and where polarized light is focused, thus registering the amount of the analyte bound (Homola et al., 1999). The potential of SPR as a highly sensitive probe characterizing the optical structure of the interface has been recognized for some years (Nice & Catimel, 1999).

Associated to this, progresses that have been made in the development of new methods of immobilizing biological recognition elements are the entrapment or covalent bonding of proteins, enzymes, antibodies and their receptors on self assembled monolayers (SAMs) or bilayer lipid membranes (BLMs). Many physical and chemical methods for immobilizing enzymes and other biological recognition elements like adsorption and entrapment within membranes, in many cases, have problems. Problems such as conformational change

Table 5
Application of the biosensors in food analysis (amino acids)

Analyte	Application	Biocomponent	Transducer[a]	Detection range	Reference
L-amino acids	Synthetic samples	L-Amino acid oxidase (L-AAO) and horseradish peroxidase (HRP)	Potent.	–	Lee & Huh, 1999
L-amino-acids	Milk and fruit juices	D-Amino acid oxidase(D-AAO)	Amp.	0.47–2.5 mM (L-leucine) 0.20–2.0 mM (L-glycine)	Sarkar, Tothiel, Setford, & Turner, 1999
L- glutamate	Soy sauce	L-Glutaminase oxidase	Amp.	<1.6 mM	Kwog, Gründig, Hu, & Renneberg, 2000
L-glutamate	Food seasonings	L-Glutamate oxidase (GluOD) and NaDH oxidase (NOD)	Amp.	0.05–1.00 mM	Matsumoto, Asada, & Murai, 1998
L-lactate	Cider	Glutamic pyruvic transaminase (GPT) and L-lactate dehydrogenase (LDH)	Amp.	6×10^{-7}– 8.5×10^{-5} M	Castañón, Ordieres, & Blanco, 1997
L-lysine	Milk and pasta	L-Lysine-α-oxidase	Amp.	10^{-5}– 10^{-3} mol/l	Curulli, Kelly, O'Sullivan, Guilbault, & Palleschi, 1998
L-lysine	Milk	Lyase oxidase	Amp.	2–125 μM	Kelly, O'Connell, O'Sullivan, & Guilbault, 2000
L-lysine	Samples fermentation	L-Lysine-α-oxidase	Amp.	10–250 μM	Olschewski, Erlenkötter, Zaborosch, & Chemnitius, 2000
L-malate	Wine, juices and soft drinks	L-Malate dehydrogenase (MDH) and pyruvate oxidase (POP)	Amp.	1μmol/dm^3–0.9 mmol/dm^3	Gajovic, Warinske, & Scheller, 1997
L-malate	Wine, juice and cider	L-Malate dehydrogenase (MDH) and salycilate hydroxylase (SHL)	Amp.	0.01–1.2 m mol/l	Gajovic, Warinske, & Scheller, 1998
L-malate and L-lactate	Wine	L-Malate dehydrogenase, diaphorase andL-lactate dehydrogenase (LDH)	Amp.	<1.1 mM (L-malate) <1.3 mM(L-lactate)	Katrlík, Pizzarielo, Mastihuba, Svorc, Stred'anský, & Miertus, 1999
L-malate	Synthetic samples (fruits)	L-Malate dehydrogenase	Potent.	10^{-2}–10^{-5} mol/l	Kwun, Lee, & Lim, 1999

[a] Potent., Potentiometric; Amp., amperometric.

Table 6
Application of the biosensors in food analysis (biogenic amines and heterocyclic compounds)

Analyte	Application	Biocomponent	Transducer[a]	Detection range	Reference
Amines	Fish	Diamine oxidase (DOO)	Amp.	<6 mM	Bouvrette, Male, Luong, & Gibbs, 1997
Amines	Anchovy samples	Diamine oxidase (DAO)	Amp.	1×10^{-6}–5×10^{-5} mol/l	Draisci, Volpe, Lucentini, Cecília, Frederico, & Palleschi, 1998
Amines	Fruit and vegetables	Diamine oxidase (a) and polyamine oxidase (b)	Amp.	2×10^{-6}–2×10^{-3} mol/l (a) 2×10^{-6}–1×10^{-3} mol/l (b)	Esti, Volpe, Massigan, Campagnone, La Notte, & Palleschi, 1998
Amines	Meat	Xanthine oxidase (XOD)	O_2 electrode	<4 mM	Park, Choi, & Kim, 2000
Amines	Prawn freshness	Ornithine carbamyl transferase, nucleoside phosphorylase and xanthine oxidase (XOD)	Amp.	0–40 mM	Shin, Yamanaka, Endo, & Waranabe, 1998
Amines	Fish freshness	Hypoxanthine oxidase and xanthine oxidase (XOD)	Amp.	1×10^{-7}–1×10^{-5} mol/l	Qiong, Tuzhi, & Liju, 1998
Biogenic amines	Fish freshness	Amine oxidase and peroxidase	Amp.	1–100 μM (histamine and putrescine)	Niculescu, Frebort, Pec, Galuska, Mattiasson, & Csöregi, 2000
Biogenic amines	Fish	Diamine oxidase (DAO)	Amp.	1–100 μM	Tombelli & Mascini, 1998
Histamine	Sea foods	Histamine oxidase	Amp.	$<9.5\times10^{-7}$ M	Hibi & Senda, 2000
Histamine	Fish	Amine oxidase	Amp.	10–20 μM	Niculescu, Nistor, Frebort, Pec, Mattiasson, Csöregi, 2000
Histamine	Synthetic samples (fish)	Methylamine dehydrogenase (MADH)	Amp.	25 μM–4 mM	Zeng, Tachikawa, Zhu, & Davidson, 2000
Hypoxanthine	Fish frehness	Xanthine oxidase (XOD)	Amp.	0–20 μM	Hu & Liu, 1997
Hypoxanthine	Fish	Xanthine oxidase (XOD)	Amp.	1 μM–0.4 mM	Liu, Xu, Luo, Luo, & Cui, 2000
Hypoxanthine	Fish	Xanthine oxidase (XOD) and horseradish peroxidase (HRP)	Amp.	0.5–30 μM	Mao & Yamamoto, 2000
Hypoxanthine and xanthine	Synthetic samples	Hypoxanthine oxidase and xanthine oxidase (XOD)	Amp.	5×10^{-7}–2×10^{-4} M (hypoxanthine) 6×10^{-7}– 2×10^{-4} M (Xanthine)	Pei & Li, 2000
Xanthine	Synthetic samples	Xanthine oxidase (XOD)	Amp.	1–15 mM	Kilinc, Erdem, Gokgunnec, Dalbasti, Karaoglan, & Ozsoz, 1998

[a] Amp., amperometric.

Table 7
Application of the biosensors in food analysis (inorganic and organic compounds)

Analyte	Application	Biocomponent	Transducer[a]	Detection range	Reference
Nitrate	Synthetic samples	Nitrate reductase (NR)	Amp.	<100 μM nitrate	Moretto, Ugo, Zanata, Guerriero, & Martin, 1998
Oxalate	Spinach samples	Oxalate oxidase (OXO)	Amp.	0.12–100 μM	Milardovic, Grabaric, Grabaric, & Jukic, 2000
Oxalate	Spinach, sesame seed, tea leaves and strawberries samples	Oxalate oxidase (OXO)	Amp.	2.5–400 μM	Milardovic, Grabaric, Rumenjak, Jukic, 2000
Oxalate	Spinach samples	Oxalate oxidase (OXO) and horseradish peroxidase (HRP)	Amp.	0.1–2.0m mol/l	Perez, Neto, & Kubota, 2001
Phosphate	Drinking water	Polyphenol oxidase and alkaline phosphatase	Amp.	–	Cosnier, Gondran, Watelet, De Giovani, Furriel, & Leone, 1998
Sulfite	Wine	Sulfite oxidase	Amp.	0.002–0.3 mM	Situmorang, Lubbert, & Gooding, 1999

[a] Amp., amperometric.

Table 8
Application of the biosensors in food analysis (contaminants and additives compounds)

Analyte	Application	Biocomponent	Transducer[a]	Detection range	Reference
Antibiotics	Milk	Antibodies	SPR	–	Baxter, Ferguson, O'Connor, & Elliot, 2001
Antibiotics	Milk	Antibodies	SPR	–	Bergstrom, Sternesjo, Bjurling, & Lofar, 1999
Antibiotics	Foods	Antibodies	SPR	20–35 ng/ml	Haasnoot & Verheijen, 2001
Antibiotics	Milk	Antibodies	SPR	–	Mellgren & Sternesjö, 1998
Antibiotics	Milk	Antibodies	SPR	–	Gaudin & Maris, 2001
Bacteria	Chicken carcass	Anti-Salmonella antibody	Amp.	10^3–10^7 CFU/ml	Che, Li, Slavik, & Paul, 2000
Bacteria	Beef	Anti-*Escherichia coli* O157:H7	Fiber-optic	3–30 CFU/ml	DeMarco, Saaski, McCrea, & Lim, 1999
Bacteria	Foods	Anti-*E.coli* and anti-salmonella antibodies	Amp.	50–200 cells/ml	Hamid, Ivinitski, Atanasov, & Wilkins, 1999
Bacteria	Ckicken and egg	*S. enteritidis* proteins	Piezoelectric quartz crystal	–	Su, Low, Kwang, Chew, & Li, 2001
Bacteria	Foods	Anti-Salmonella spp antibody	Piezoelectric quartz crystal	5×10^5–1.2×10^9 CFU/ml	Ye, Letcher, & Rand, 1997
Herbicide	Vegetables	Antibodies	ISFET	5–175 ng/ml	Starodub, Dzantiev, Starodub, & Zherdev, 2000
Herbicide	Foods	Antibodies	Potent.	0.5–5μg/ml	Yulaev, Sitdikov, Dmitrieva, Yazynina, Zherdev, & Dzantiev, 2001
Herbicide	Drinking water	Antibodies	Piezoelectric quartz cristal	–	Steegborn & Skládal, 1997
Pesticides	Synthetic samples	Acetylcholinesterase (AchE)	piezoelectric quartz cristal	5×10^{-8}–1.0×10^{-5}M (paroxon) 1.0×10^{-7}–5.0×10^{-5} M (carbaryl)	Abad et al., 1998
Pesticide	Synthetic samples	Acetylcholinesterase (AChE)	Fiber-optic	5×10^{-8}–5×10^{-7} M (carbofuran) 5×10^{-7}–5×10^{-6}M (paroxon)	Andres & Narayanaswamy, 1997
Pesticide	Synthetic samples	Butyrylcholinesterase (BChE) and choline oxidase	Amp.	3.3–209 μ mol/l	Campanella, De Luca, Sammartino, & Tomasseti, 1999
Pesticide	Synthetic samples	Acetylcholinesterase (AChE)	Fiber-optic	0.5–20 mM	Dong & Tsai, 2001
Pesticide	Synthetic samples	Acetylcholinesterase (AChE) and butyrylcholinesterase (BChE)	Potent.	1.5×10^{-5}–2.5×10^{-3} mol/l	Ivanov, Evtogyn, Gyurcśanyi, Tóth, & Budnikov, 2000
Pesticide	Synthetic samples	Acetylcholinesterase (AChE)	Amp.	1.8×10^{-7}– 5.4×10^{-5} M	Li, Zhou, Feng, Jiang, & Ma, 1999
Pesticide	Milk	Cholinesterase (ChE)	Amp.	1×10^{-11}– 5×10^{-7} M	Medyantseva, Vertlib, Budnikov, & Tyshlek, 1998
Pesticide	Vegetables	Acetylcholinesterase (AChE) and butyrylcholinesterase (BChE)	Amp.	5×10^{-5}–50mg/kg	Nunes, Skládal, Yamanaka, & Barceló, 1998
Pesticide	Fruit and vegetables juices	Acetylcholinesterase (AChE) and butyrylcholinesterase (BChE)	Amp.	0.5–2500μg/L (carboryl)	Nunes, Barceló, Grabaric, Diaz-Cruz, & Ribeiro, 1999
Pesticides	Fruit and vegetables	Choline oxidase, acetylcholinesterase (AChE) and acetylcholine	Amp.	$1\times10^{-8-}$ 4×10^{-7} M	Palchetti, Cagnini, Del Carlo, Coppi, Mascini, & Turner, 1997
Pesticides	Spiked apple samples	Tyrosinase	Amp.	0.2–2.2μ mol/l	Pita, Reviejo, Villena, & Pingarrón, 1997
Toxin	Foods	Anti-aflatoxin antibody	Fiber-optic	–	Carter, Jacobs, Lubrano, & Guilbault, 1997
Toxin	Synthetic samples	Anti-Staphylococcal enterotoxin B (SEB) antibody	Piezoelectric quartz crystal	1– 10μg SEB/ml	Harteveld, Nieuwenhuizen, & Wils, 1997
Toxin	Synthetic samples	Antibodies	SPR	–	Mullet, Lai, & Yeung, 1998
Toxin	Foods	Anti-Staphylococcal enterotoxin A (SEA) antibody	Optic	10–100 ng/g	Rasooly & Rasooly, 1999
Toxin	Foods	Anti-Staphylococcal enterotoxin B antibody	SPR	1–10 ng/ml	Rasooly, 2001
Aspartame	Foods	Alcohol oxidase,α-chymotrysin and catalase	Amp.	–	Campagnone et al., 1997

[a] SPR, surface plasmon resonance; Amp., amperometric; Potent., Potentionmetric.

Table 9
Commercials biosensors for food industry

Companies (country)	Biosensors	Target compounds
Danvers (USA)	Apec glucose analyser	Glucose
Biometra Biomedizinische Analytik GmbH (Germany)	Biometra Biosensors for HPLC	Glucose, ethanol and methanol
Eppendorf (Germany)	ESAT 6660 Glucose Analyzer	Glucose
Solea—Tacussel (France)	Glucoprocesseur	Glucose and lactate
Universal Sensors (USA)	Amperometric Biosensor Detector	Glucose, galactose, L-amino acids, ascorbate and ethanol
Yellow Springs Instruments (USA)	ISI Analysers	Glucose, lactose, L-lactate, ethanol, methanol, glutamate and choline
Toyo Jozo Biosensors (Japan)	Models: PM-1000 and PM-1000 DC (*on line*), M-100, AS-200 and PM-1000 DC	Glucose, lactate, L-amino acids, cholesterol, tryglicerides, glycerin, ascorbic acid, alcohol
Oriental Electric (Japan)	Oriental Freshness Meter	Fish freshness
Swedish BIACORE AB (Sweden)	BIACORE	Bacteria
Malthus Instruments (UK)	Malthus 2000	Bacteria
Biosensori SpA (Italy)	Midas Pro	Bacteria
Biotrace (UK)	Unilite	Bacteria

affecting the functional activity, adsorption with random orientation, detachment of the protein and fragility on the membrane resulting in less sensitivity and short longevity, still exist (Gooding et al., 2001). Thus, the self-assembled monolayer or BLMs have been used as new strategies for the immobilization, orientation and molecular organization of biomolecules at interfaces. The stability of the bond between the specific functional group of a reagent and the electrode surface over a wide range of applied potentials and the well-defined microenvironment mimicking biological membranes makes the use of self-assembled monolayer suitable for proteins orientation without denaturation becoming easier the electron transfer of proteins (Imabayashi, Kong, & Watanabe, 2001).

Among the alternatives to improve the stability of biosensors is the possibility of the *enzymeless biosensors* development (Berchmans, Gomathi, & Rao, 1998). This concept is used by some groups of research that are developing this type of biosensors (Berchmans, Gomathi, & Rao, 1995; Berchmans et al., 1998; Casella, Desimoni, & Salvi, 1991, 1993), where the electrode is modified with a redox substance that can be an enzyme active site of biological importance. This modification would provide a better electron transfer of the enzyme active site for the electrode surface (Casella et al., 1993).

A developing field is microbiosensor technology. Microbiosensors for several compounds were contructed with immobilized biocatalysts and micro transducers, such as ion sensitive field effect transistors, amorphous silicon ion sensitive field effect transistors, micro oxygen electrodes, micro hydrogen peroxide electrodes, and planitized carbon fiber electrodes. Microbiosensors have many advantages over the conventional biosensors, such as: they can easily be integrated into one chip, simultaneous determination of multiple components of food, disposable-type biosensors can be fabricated and applied for on-site monitoring of food processes.

Another field in growing is the DNA technology (Souteyrand, 1999). This type of technology is considered as a new and powerful tool combining the large integration ability of microelectronic devices with the properties of biological interactions of foodborne pathogens because this microorganisms are susceptible to DNA probes, but their application depends on the future advances in term of miniaturization, specificity and sensitivity.

The sensitive potentiometric sensors for gases have shown good applications in the determination of aromas, food freshness through odor, when used in systems of multiple channels. Other specific applications would be aroma monitoring in wines, brandies, gin, liquors and volatile compounds of deterioration in fish. These sensors for gases coupled to a ISFET, sensitive to pH, equipped with a mycrodyalise membrane to the gas that it is collected in an aqueous solution where an acid-base balance involves the dissolution of gases. Devices with these characteristics involving a biosensor, could become more effective for application of this type of device, in these analyses.

The detection of contaminants is another active area of research. These devices make use of irreversible receptors based on, e.g. the antigen–antibody reaction. Based on its high specificity and low detection limits (10^{-11}–10^{-9} M), these elements have been used in the detection of pesticides, herbicides, microorganisms and microbial toxins. In this field SPR emerges as a powerful tool for new biosensor development.

In this context the treatment of the experimental data using chemometrics models has great perspectives in food analysis (Bailey & Rohrback, 1994). The use of these methods provides an increase in the rapidity and

economy in the analysis. The models cited in the literature (neural networks, PCR, PCA and PLS) had assisted in the diagnostic of volatile compounds, amino acid mixtures and detection of contaminants in products as fish, vegetables and others.

Acknowledgements

The authors thank FAPESP for financial support, Prof Heloise O. Pastore for the English revision of the manuscript and LDM is also indebted for a fellowship.

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