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Review

Analyte Recognition and Signal Conversion in Potentiometric and Optical Chemical Sensors

A. Dybko, W. Wróblewski

Department of Analytical Chemistry, Warsaw University of Technology,
Noakowskiego 3, 00-664 Warsaw, Poland

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Abstract

The process of analytical signal generation in chemical sensors such as ion-selective electrodes, ion-sensitive field effect transistors and fibre optic sensors is described. The principle of operation of these sensors is explained with respect to the signal conversion from the concentration of the analyte into the changes in analytical signal obtained from the sensor. Some general considerations about chemical sensor design are also given.

Keywords: analyte recognition, signal conversion, chemical sensor, ion-selective electrode, chemically modified field effect transistor, fibre optic chemical sensor

Introduction

Chemical sensors are finding more and more applications in chemical analysis, environmental monitoring, medicine, industry, etc. A great number of chemical sensors have been developed and commercialized over the last decades [1-4]. Everyday clinical analyses are based on the use of ion-selective electrodes (ISE): pH-sensitive glass electrodes are probably the most popular chemical sensors used in analytical chemistry, and industrial ion-sensitive field effect transistors (ISFETs) are applied in food tests, to name a few of the successfully introduced sensors. The fast growing market and requirements such as small sample consumption are the driving force of microsensors and micro total analysis systems (so-called μTAS).

Many classifications and definitions of a chemical sensor can be found in the literature. According to the Cambridge definition, a chemical sensor is a miniaturised analytical device which can deliver real-time and on-line information on the presence of specific compounds or ions in the complex samples. A broader definition given by IUPAC [5] claims that a chemical sensor is a device which converts chemical information, ranging from the concentration of a specific sample component to total composition analysis, into an analytically useful signal. Receptor and transducer are the main parts of a chemical sensor. The receptor part converts chemical information into a form of energy acceptable by the transducer and then the analytical signal is generated. Other more general or more specific definitions have been given for chemical sensors and can be found in the literature [1-3].

These definitions, however, cannot be applied to every type of chemical sensor because sometimes it is very difficult to distinguish between the receptor and the transducer. The situation is more complicated if so-called reagent-less optical sensors are considered [6, 7]. They still are named sensors nevertheless in the principle of operation they can be regarded as remote spectrophotometric measurements where fibre optics are used only for light transmission from a light source to a sample and from a sample to a detector. A certain group of sensors (for

Correspondence to: Dr. A. Dybko

example biosensors) does not fulfil the requirement of thermodynamic reversibility, considered in most definitions [3]. Moreover, many definitions of chemical sensors include classical detectors used in analytical devices based on efficient separation techniques (chromatographic systems). In such a case the non-selective detection system does not require any recognition sites (layers).

The aim of this paper is to explain the principle of operation of a chemical sensor based on the analyte recognition and signal conversion processes occurring in the chemical interface and the transducer of the sensor. The paper also presents principles of the design and laboratory measurements of various types of chemical sensors, i.e. ion-selective electrodes, ion-sensitive field effect transistors and fibre optic chemical sensors (FOCS).

Signal Conversion in a Chemical Sensor

A typical structure of a chemical sensor is presented in Fig. 1.

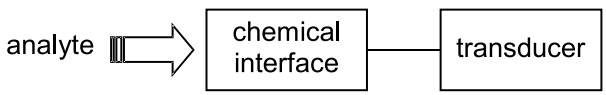

Fig. 1. Signal conversion in a chemical sensor.

An analyte to be measured interacts with the chemical interface whose primary task is to recognise the analyte and deliver this information to the transducer. In the case of fibre optic sensors, a chemical interface can be called a chemooptical because the analyte changes the optical properties (absorbance, fluorescence, polarisation) of receptor molecules; this information is then guided by fibre optics to a detector. Potentiometric sensors (i.e. ISE and ISFET) are based on the use of an electrochemical interface where the conversion from ion/molecule concentration to the potential changes takes place.

There are several steps in signal conversion occurring in the FOCS, which are shown in Fig. 2.

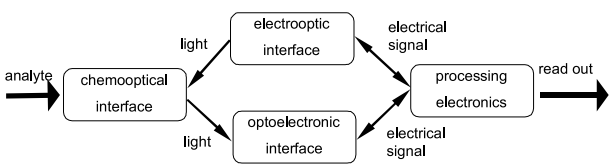

Fig. 2. Signal conversion in a fibre optic chemical sensor.

Since the number of analytes exhibiting their own spectral changes is very limited, it is necessary to match an appropriate reagent. The reagent should recognise the analyte and convert information on its concentration into changes of optical properties (e.g. absorbance, fluorescence, reflectance). The reagent is immobilised in the chemooptical interface, which is in contact with the sample under the test. The principle of operation and performances (sensitivity, selectivity etc.) of an optical sensor depend on the chemooptical interface. This interface can be designed as a separate layer – membrane, which contains reagent molecules, held against the end of a single fibre optic or bundle (a so-called extrinsic sensor) [7]. In the second group, the reagent phase is directly incorporated into the structure of a fibre optic, e.g. it replaces the removed cladding (so-called intrinsic sensors) [7] or it is immobilised in the porous sol-gel cladding. The exciting beam of light is delivered by the electrooptic interface (there is no such interface in the case of a chemiluminescent sensor). Its main part is an appropriate light source, which is spectrally matched to the maximum of absorbance or excitation of the reagent. After having interacted with the chemooptical interface, this light is converted into an electrical signal by the optoelectronic interface containing a photodetector (e.g. photodiode) and an amplifier. Both optoelectronic and electrooptic interfaces can be driven by the processing electronics. Their work can be synchronised by clock pulses or homodyne detection of low light signals can be used. Contemporary measuring systems are based on the use of microprocessors (microcomputers) and they give a direct readout after applying a calibration of the sensor and/or additional signal processing.

The process of signal conversion in a potentiometric sensor is presented in Fig. 3.

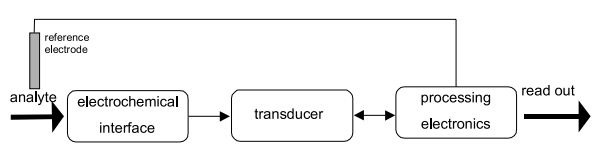

Fig. 3. Signal conversion in a potentiometric sensor.

The role of the electrochemical interface is to change the information about the analyte into changes of the charge on the surface of the transducer, which results in the changes of the transducer potential. These changes are measured against a reference electrode dipped into a sample. A silver/silver chloride electrode is frequently used in potentiometric measurements [8]. ISE and ISFET differ in the type of transducer used. In the case of ISE, this is Ag/AgCl wire usually delivered in a set with a body of the electrode e.g. Philips IS 561 [9]. This wire is surrounded by the internal electrolyte. The analyte to be measured causes the ion exchange between the electrode membrane and the internal electrolyte, the internal electrolyte and the AgCl layer, and finally the AgCl layer exchange electrons with the silver wire. As a result of these interactions, the ionic conductance of the electrolyte is converted into charge transfer in the metal conductor, i.e. an analytical electrical signal is generated.

CHEMFETs are based on the use of a field effect transistor as a transducer. This type of transducer developed in early 1970s [10] is pH sensitive and recently industrial pH-meters based on ISFET have been commercialised [1]. The principle of the operation of the CHEM-

FET is quite similar to ISE. The analyte reaches the membrane where it is complexed by an appropriate ionophore. This causes ion changes in the layer deposited on the gate of the transistor (the role of this layer is similar to the internal electrolyte in ISE and is usually made from polyHEMA) and thus the changes in the surface charge on the gate are induced. As an effect the drain current changes and can be measured as an analytical signal proportional to the concentration of the analyte.

The necessity of a reference electrode in potentiometric sensors is the main difference between these sensors and optical ones. It becomes a crucial problem when a miniaturised sensor should be developed, e.g. for medical applications. The reference electrode has to be equipped with the junction between the internal electrolyte and the sample under the test. A problem with the fabrication of the miniature junction, the leakage of the electrolyte, and the internal resistance of such an electrode should be overcome. One of the possible solutions of a miniaturised reference electrode was the design of the so-called REFET (reference field effect transistor) but up to now none of the constructions were put into practice mainly because of material and technological problems.

In any type of chemical sensor, the chemical interface governs its characteristics such as selectivity, lifetime, and long-term drift. Typically special chemical compounds sensitive to the analyte are immobilised in this interface. It is very important to apply an efficient and reproducible procedure of immobilisation giving a chemical interface from which no receptor molecules will be washed out. Such an interface should be compatible with an environment, an analyte under the test and a transducer. Technology of a sensor producing is a key factor in commercialisation of the sensor. Usually a chemical interface is created in a form of a polymeric matrix containing, besides receptor molecules, a plasticizer, an ion excluder, a wetting agent etc. These additional compounds can make the interface more compatible with the environment and enhance measuring properties.

Analyte Recognition in a Chemical Sensor

The recognition processes (host-guest interactions) of any analyte occurring in the receptor part govern the selectivity of the chemical sensors. Analyte recognition is based on selective complexation reaction of a guest molecule and synthetic or biological molecules [1-3]. The target chemical components include ions as well as neutral molecules. The driving force of these reversible processes can be ion-dipole, dipole-dipole and hydrogen bond interactions. In certain cases, the analyte recognition process can be based on the formation of covalent bonds. The recognition of the guest molecules is achieved by the combination of complementary cavity shape and appropriate arrangement of the binding sites (functional groups) of the receptor (key-lock configuration).

In a potentiometric chemical sensor, a synthetic receptor molecule is immobilised in a polymeric membrane. One side of the membrane is in contact with the studied analyte solution. The reversible exchange of the ions between the analyte solution and the membrane phase (and the complexation reactions in the membrane) causes the formation of the membrane potential i.e. signal generation [11]. The potential difference across the selective membrane depends on the molar free analyte concentration. In the case of molecular recognition of an ion, the receptor is capable of extracting ions from an aqueous solution and acts as an ionophore or an ion-carrier. The complexation of the analyte ion by the ionophore results in the charge separation at the boundary of the solution/membrane interface. The transfer of the ion complexes through the aqueous solution/membrane boundary occurs due to the relatively high potential energy of dipole-ion interactions in a lipophilic membrane phase. The overall ion-selectivity of the membrane is defined by the selectivity of the ion-ionophore complex formation as well as by the partition coefficients of different species (i.e. target and interfering ions) between the aqueous sample and less polar membrane phase.

A similar mechanism of ion recognition occurs in the ion-sensitive layer of the fibre optic chemical sensors. In this case, the process of the mass transport between two phases, based on the maintenance of the electroneutrality, leads to changes in optical properties (e.g. absorbance or fluorescence) of the ion-sensitive membrane [6, 7, 12]. The ion recognition process is achieved by the incorporation of an appropriate reagent: chromogenic ionophore (chromoionophore or fluoroionophore). The reagent molecules include an ion-recognising complexing centre (ionophoric moiety) coupled with a chromogenic group, which transduces the chemical information into the changes in optical signal. The selectivity of the optomembrane is governed by the selectivity of the ion-chromoionophore complex formation.

The optical signal of the optomembrane can be generated directly or indirectly [12]. The application of a chromoionophore results in a direct signal generation. The selective complexation of the analyte by this type of the reagent is coupled with changes in its optical properties. An indirect signal generation occurs when an ionophore selectively interacts with an analyte and this reaction gives changes in optical properties of another, chromogenic reagent. The mechanism of the indirect signal generation is also based on the equilibrium of the complexation reaction and on the maintenance of the electroneutrality of the bulk ion-sensitive membrane. One of the frequently used configurations is based on a neutral ion-selective carrier and a lipophilized hydrogen-selective indicator (pH chromoionophore) entrapped in a plasticized PVC bulk membrane [12]. The complexation and the extraction of the analyte into a reagent phase give the protonation or the deprotonation of the pH chromoionophore, which drastically change its optical properties.

Chemical Sensor Design

A sensor suitable for measurements of an analyte in a given situation can be useless if different composition of the sample will be tested or the sensor will be used in a different environment. It is very difficult to design a versatile chemical sensor suitable for measurements in

any environment and any conditions. The environment determines appropriate materials and transducing principle utilised in a sensor. Thus the very first step in a sensor design is to determine its working conditions, required measuring range, response time, resolution of measurements, lifetime, etc. Expected temperature changes, possible chemical interferences, and electromagnetic interactions should also be considered as well as size of the sensor, its weight, cost, safety of operation, and reliability.

Potentiometric Sensor Design

Fig. 4 shows the design process of a potentiometric sensor.

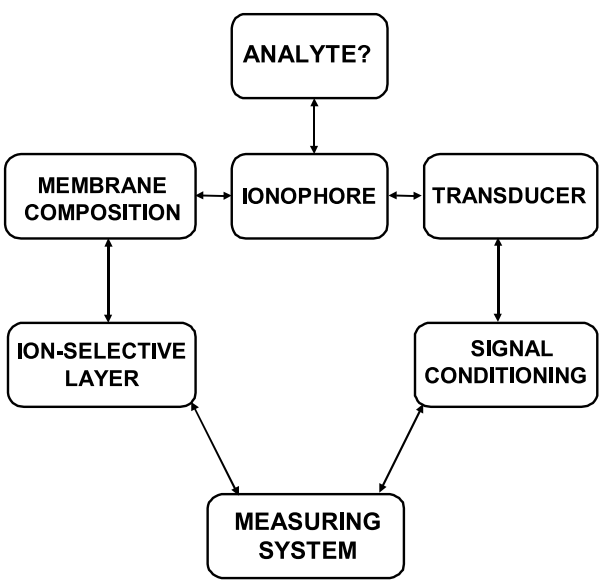

Fig. 4. Steps in the design of a potentiometric chemical sensor.

The presence of the ionophore molecules is responsible for chemical sensing and signal generation in the electrochemical interface of a potentiometric sensor. The first step in the design of a potentiometric sensor involves the choice of an appropriate ionophore (electrically neutral or charged). In many cases this leads to the synthesis of a new ionophore structure dedicated to the ion to be measured. A new ionophore should exhibit high selectivity towards the target ion and sufficient lipophilicity to ensure durable electrochemical interface.

The following step is the fabrication of an ion-selective layer based on the carefully matched membrane composition. The ionophore molecules should be incorporated into the bulk of a polymeric membrane. Plasticized PVC, the commonly used polymeric matrix in membranes of ISEs, functioned well with the ISFETs but the durability of such a sensor was not good because of the poor adhesion of the membrane to the FET surface [13]. The application of polysiloxane or polyuretane based membranes with intrinsic elastomeric properties improved the adhesion properties of the obtained sensing layers. Most of the ion-sensitive membranes contain, besides the ionophore, lipophilic ionic sites [9, 14]. The addition of these additives is required to obtain proper performances, i.e. a wide linear range with theoretical slope and stable sensor signals. The theoretical Nernstian response of the potentiometric sensor is measured if the presence of lipophilic counter ions maintains the constant concentration of the free target ions in the membrane, due to the ion buffering mechanism of the ionophore (establishment of a constant ratio between the concentration of the ion-ionophore complex and the free ionophore) [9, 14-16]. The constant free ionophore-complex ratio is achieved when the concentration of ionic sites is approximately 50% mol. with respect to the ionophore (for monovalent ions). The presence of ionic sites in the membrane is also necessary to improve the selectivity of the potentiometric sensors [17-19]. In cation-selective electrodes with neutral receptors, tetraphenylborate salts are added to the membrane composition (tetraalkylammonium salts for anion-selective membranes containing neutral ionophore). Recently, it has been shown that the presence of ionic sites is also required in the case of ion-selective membranes with charged ionophores [19, 20].

A parallel pathway of the sensor design is focused on the appropriate choice of the transducer (i.e. ISE or ISFET). In the case of the sensors based on field effect transistors, it is necessary to apply an intermediate layer between the polymeric membrane and the surface of the transducer (for example polyHEMA). Both ISE and ISFET require the use of an internal electrolyte in order to convert the ionic signal into the electrical one. The choice of the transducer used in the sensor influences the construction of the measuring system. Extremely high internal resistance of ISE leads to the construction of a high input-resistance amplifier usually in a typical voltage follower configuration. In the case of ISFET, a special driving circuit should be applied to allow proper functioning of the field effect transistor as a transducer. Such a driver can be done as a constant drain follower with drain current I_D = 0.1 mA and U_{DS} = 0.5 V [21].

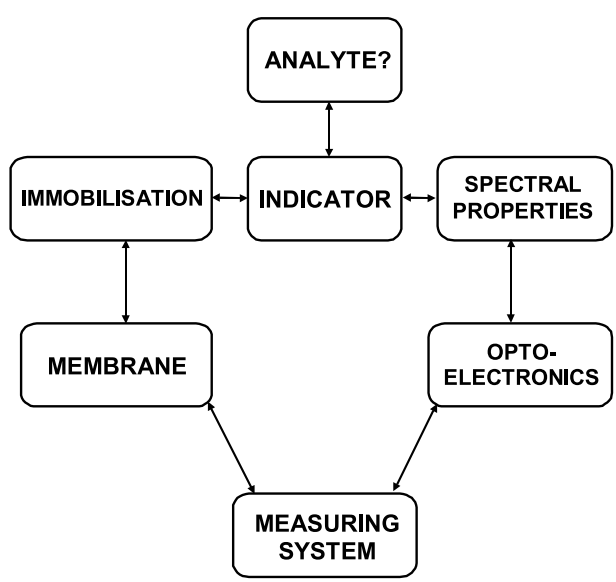

Fig. 5. Steps in design of a fibre optic chemical sensor.

Fibre Optical Sensor Design

The design process of a fibre optic chemical sensor is presented in Fig. 5.

The chemical sensing and the signal processing of the chemooptical interface are achieved by the incorporation of an appropriate reagent i.e. indicator. Selective complex-forming indicator dyes (chromoionophores) or acid-base indicators are frequently used. The reagent molecules include an ion-recognising complexing centre coupled with a chromophoric group. The chemical interactions between the reagent and the analyte are based on an acid-base, complexation or redox reaction [12]. The first step in the design of FOCS is the chemical matching of the reagent molecules (chromoionophore) to the analyte to be measured. The design of a new chromoionophore can be based on the well-known ionophores studied in the electrochemical sensors. The problem is in the appropriate attachment of the chromophoric group to the receptor molecule e.g. to the crown ether or calixarene derivative. Classic spectrophotometric indicator dyes may also be applied as chromoionophores incorporated in a support matrix. The recognition reaction must be followed by the change in optical properties of the reagent depending on the concentration of the analyte. The performances of the sensor (sensitivity, selectivity, dynamic range, response time, etc.) are affected by the reagent properties. The selectivity is governed by the recognition ability of the reagent towards the analyte. The reagent used should exhibit large changes in spectral properties in dependence on small changes in the concentration of the analyte. In this way, wide dynamic range and sensitivity can be obtained.

The following step includes the attachment of the reagent phase to the fibre optic by producing chemooptical interface. The chemooptical interface may consist of a reagent solution separated from the sample by a semipermeable membrane [6, 7, 12]. The membrane retains the reagent phase and, in addition, its permeability can exclude interfering substances, thus improving the selectivity of the sensor. Another solution is based on the incorporation of the reagent molecules on a support membrane. The reagent can be immobilised either directly on the surface or in the bulk of the membrane. Physical (entrapment, formation of lipophilic ion-pairs) and chemical (covalent binding of the chromoionophore) procedures of the reagent immobilisation in the chemooptical interface are used [12]. Also there is possible to immobilise the reagent phase directly on the fibre. In all cases, the efficiency of the reagent immobilisation governs the durability of the designed sensor. It is important to point out that during the process of immobilisation spectral properties of the indicator can be changed.

A parallel part of the sensor design is focused on the sensor as an optoelectronic device. Having immobilised the indicator, it is necessary to determine spectral properties of the optrode and choose wavelengths that should be used in the system. For sensors based on the absorbance indicators these are analytical wavelength and reference, i.e. where no absorbance changes occur, for the fluorescence sensors – excitation and emission wavelengths. These investigations allow to match an appropriate light source and photodetector. The choice of optical fibre is more flexible. The essential factor in matching the fibre is the attenuation at a given wavelength. A custom-made circuit with optical power stabilisation can be used as an LED driver if the intensity based sensor is designed. Optical sensors often deal with low-light signals and thus very sensitive photodetectors should be used (e.g. photomultiplier, avalanche photodiode) allowing to obtain high value of signal to noise ratio.

The whole measuring system for testing of chemical sensors is constructed in stages, with strong feedback between specialists from various science disciplines. The work of the contemporary system is governed by a personal computer where very important is software governing the work of the system and data acquisition process (according to National Instruments, the software is the instrument). User-friendly software should allow modifications during measurements (voltage ranges, sampling frequency, etc.) as well as a calibration process of the sensor. Additional advantage of the system will be computer controlled chemical equipment (e.g. burette, pump, stirrer, valves, etc.) for sample dosing and the sensor calibration allowing automatic tests of the sensor.

Summary

A proper design of a chemical sensor requires understanding of its principle of operation and which parts of the sensor are crucial from the measurement point of view. Each of the sensors described in this paper has its own specific requirements concerning the transducer, membrane, analyte recognition, immobilisation process, etc. The instrumentation used for sensor measurements is also different. The contemporary system for testing chemical sensors should allow the use of various types of sensors in order to confirm and verify the results obtained from different analytical methods.

The process of chemical sensor design was depicted symbolically in Figs. 4-5. In fact, the following steps in sensor design and the relationships between various disciplines of the science are more sophisticated, with strong feedback between the stages. Sometimes the reagent showing excellent analytical performances in the laboratory cannot be used in a sensor since during the immobilisation process its functioning groups are blocked or destroyed. Then the designer has to modify this process, optimise it or change the reagent, reaching the compromise between analytical properties and sensor metrology.

Acknowledgements

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