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# Frontiers in Chemical Sensors

## Novel Principles and Techniques

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# Frontiers in Chemical Sensors

## Novel Principles and Techniques

Volume Editors:
Guillermo Orellana · Maria C. Moreno-Bondi

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# Preface

With their similarity to the organs of the most advanced creatures that inhabit the Earth, sensors are regarded as being the "*senses of electronics*": artificial eyes and ears that are capable of seeing and hearing beyond the range of human perception; electronic noses and tongues that can recognise odours and flavours without a lifetime training; touch that is able not only to feel the texture and temperature of the materials but even to discern their *chemical* composition. Among the world of chemical sensors, *optical* devices (sometimes termed "optodes", from the Greek "the optical way") have reached a prominent place in those areas where the features of light and of the light-matter interaction show their advantage: contactless or long-distance interrogation, detection sensitivity, analyte selectivity, absence of electrical interference or risks, and lack of analyte consumption, to name just a few. The introduction of optical fibres and integrated optics has added more value to such sensing since now light can be confined and readily carried to difficult-to-reach locations, higher information density can be transported, indicator dyes can be immobilised at the distal end or the evanescent field for unique chemical and biochemical sensing (including multiplexed and distributed measurements), optical sensors can now be subject to mass production and novel sensing schemes have been established (interferometric, surface plasmon resonance, fluorescence energy transfer, supramolecular recognition ...).

This third volume of Springer Series on Chemical Sensors and Biosensors aims to enable the researcher or technologist to become acquainted with the latest principles and techniques that keep on enlarging the applications in this fascinating field. Chapter 1 deals with the well-established absorption spectrometry but based on miniaturised integrated optics. Novel luminescence lifetime-based techniques for interrogation of sensor arrays in high-throughput screening are described in Chapter 2, while a modern use of the exotic cataluminescence is the topic of Chapter 3. Going from the uv-vis spectral region into the infrared allows chemical sensing with hollow waveguides (Chapter 4). Chapters 5 and 6 discuss new ways of succeeding in sensor design and fabrication by means of either combinatorial methods or engineered indicator/support couples, respectively. Frontiers in analytical biosensing is the common theme of Chapters 7 to 9, the hot topics of which are the design of DNA optosensors, gold nanoparticle-based assays and reverse symmetry waveguides. The book ends with three chapters concentrating on applications – dealing with pressure-sensitive luminescent paints, optical sensing of enantiomers and the amazing use of digital colour analysis for ions and protein monitoring. All these novel optosensing principles and techniques dramatically increase the analytical power of the current chemical sensors allowing us to predict a promising future for such devices in the years to come.

This monograph is aimed at graduate students in chemistry, physics, biology, engineering, and material science, as well as researchers and technologists in academic and industrial environments who want to keep abreast of the latest trends in chemical sensing and biosensing with photonic devices. The contributing authors are recognised experts in their respective fields so that, in addition to providing an authoritative overview of each selected topic and the advances therein, they have been able to convey to the reader first-hand information and experimental results from their own research and developments. Therefore, the Editors would like to acknowledge and gratefully thank the effort and enthusiasm of all the authors who have provided outstanding, exquisite manuscripts to constitute the present new volume of Springer Series on Optical Chemical Sensors and Biosensors. In Spanish, there is a saying which says it is impossible to make a gate to the countryside, in the same way, it is certainly difficult to define frontiers in the optical sensing field. However, we hope the contents of this book will guide the reader through the novel principles and techniques that are setting the pace in the advances in our continuously evolving field.

September 2005

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Maria C. Moreno-Bondi

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# Absorbance-Based Integrated Optical Sensors

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**Abstract** Optochemical sensors have had a huge expansion and in recent years interesting sorts of optical sensor have been developed which make use of the integrated circuit microelectronic technology and the optical technological advances achieved in the telecommunications industry. These devices are based on optical fibers, planar waveguides or the combination of both supports as light-guiding structures and offer an enhanced performance thanks to a miniaturized size, a feasible mass production at low cost, the possibility to measure at large distances and the capability of reaching places hard to access for the in situ monitoring of environmental or medical parameters. In this chapter, we provide an overall view of integrated chemical sensors based on absorbance measurements, describing their main characteristics, advantages and drawbacks. In order to focus on these types of devices, first of all, a brief classification is given, in terms of the interaction mechanisms and the reactive phases or membranes that are involved in the response, and the radiation transmission medium. Next, different waveguide configurations are briefly described because of to the relevancy of these structures as the main constituent of integrated optodes and, finally, some absorbance-based integrated sensors are detailed.

**Keywords** Absorbance · Antiresonant reflecting optical waveguide · Core-based optodes · Integration · Ion-selective optodes

**Abbreviations**

| | |
|---|---|
| $A$ | Absorbance |
| ATR | Attenuated total reflection |
| ARROW | Antiresonant reflecting optical waveguide |
| AU | Absorbance units |
| $C$ | Concentration (M) |
| CMOS | Complementary metal oxide semiconductor |
| CVD | Chemical vapor deposition |
| $d$ | Membrane thickness |
| $D_{\mathrm{m}}$ | Diffusion coefficient ($cm^2\ s^{-1}$) |
| DOS | Bis(2-ethylhexyl)sebacate |
| DRIE | Deep reactive ion etching |
| $\varepsilon$ | Molar absorptivity ($kg\ mol^{-1} cm^{-1}$) |
| FIA | Flow injection analysis |
| IOC | Integrated optic circuit |
| IWAO | Integrated waveguide absorbance optode |
| KtpClPB | Potassium tetrakis(4-chlorophenyl)borate |
| $L$, $l$ | Path length (cm) |
| LPCVD | Low-pressure chemical vapor deposition |
| $\lambda$ | Wavelength (nm) |
| $n$ | Refractive index |
| NIR | Near IR |
| PECVD | Plasma-enhanced chemical vapor deposition |
| PIN | p-n photodiode |
| RIE | Reactive ion etching |
| RSD | Relative standard deviation |
| TIR | Total internal reflection |
| SPR | Surface plasmon resonance |
| $t_{95\%}$ | 95% response time (min) |
| $t_{\mathrm{r}}$ | Response time (min) |

## 1 Introduction

The chemical sensor area has proved to be one of the most dynamic fields in analytical chemistry. During the last few years, an enormous effort has been made in order to design sensors that show appropriate features such as selectivity, low detection limits, reversibility, robustness, portability and easy handling. However, this continuously evolving field is improving to achieve the goals of the conceptual term of sensor and most of the existing ones still present clear limitations.

The collaboration of diverse groups allows conjugating the knowledge of different research fields such as electronics, optics, analytical, inorganic and organic chemistry, biochemistry and materials science, and then adapts sensor technology to industrial, medical or environmental needs. Despite the hindrance of combining such multidisciplinary groups, a great variety of chemical sensors which are designed for very concrete applications and which would not have much utility [1, 2] have been commercialized and show their potentiality and usefulness in the real world.

Optochemical sensors have had a huge expansion during the last few years, and surely the main reason is the wide range of optical phenomena that one can take advantage of for the design of different sensing schemes.

Recently, the greatest improvements have been based on the productive merger of integrated circuit microelectronics and telecommunications technology. This has provided new instrumental platforms and the possibility to apply new optical phenomena, like the evanescent field, in the design of new chemical sensing setups. Miniaturized optical components, such as light sources, photodetectors and light guiding structures (cylindrical and planar waveguides), also offer an enhanced performance and a feasible mass production at low cost, with the possibility to measure at large distances, reaching places hard to access for the in situ monitoring of environmental or medical parameters.

In this chapter, we present an overall view of integrated chemical sensors based on absorbance measurements, explaining their main characteristics, advantages and drawbacks. In order to focus on such devices, first of all, the main sensor components are briefly described and after that a brief explanation is given in terms of the most suitable reactive phases depending on the sensor format to be constructed or the radiation transmission medium employed. Next, because of the relevancy of waveguide structures as the main constituents of integrated optodes, details of some configurations are given and, finally, some absorbance-based integrated sensors are detailed.

## 2
## Design of Optochemical Sensors

The fundamental operation of an optochemical sensor consists of three main steps: the analyte-recognizing element interaction by means of any of the different mechanisms that are schematized in Fig. 1 [3]; the detection and transduction of any physical or chemical variation caused by the recognizing reactions; and the signal processing and the acquisition of results.

Concerning the required instrumentation, usually conventional active and passive optical components are employed; however, their complexity can vary according to the proposed objectives. Two main parts can be distinguished: the *recognition element*, which includes the selective reagents, the intermedi-

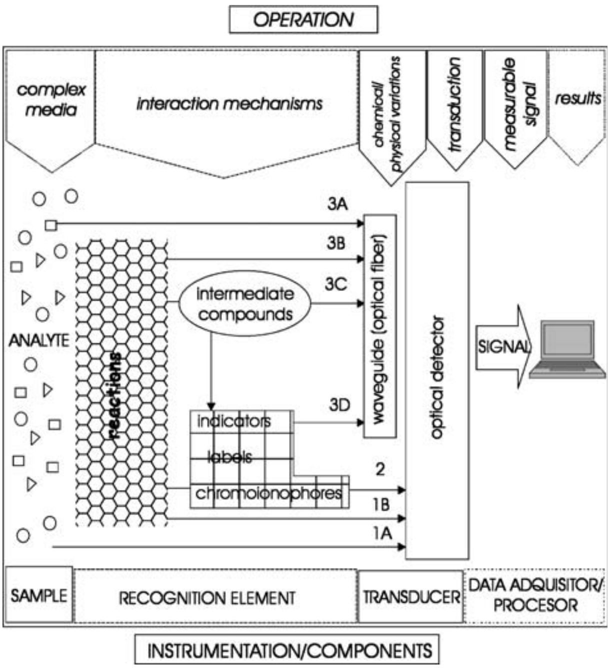



**Fig. 1** Chemical interaction mechanisms, basic components of the optical sensor instrumentation and their operation. Mechanisms: direct measurement of chemical compounds that exhibit spectroscopic properties (1*A*) and measurement of light originating from a chemical or a biological reaction in chemiluminescent or bioluminescent phenomena (1*B*); 2 optodes based on the interaction of indicators and labels with light, which are immobilized in a support; and sensors that modify the intrinsic physical or chemical properties of a waveguide (refractive index, phase, etc.) as a result of the presence of the analyte (3*A*), a recognition element (3*B*), an intermediate analyte (3*C*) or an indicator (3*D*)

ate analytes, the indicators or labels, and sometimes a matrix as a support or a membrane, and the *transducer*. The instrumentation in the latter includes the light source, the wavelength selectors, the waveguides and the detector. Finally, amplifiers and processors are used for the signal treatment.

An integrated optical sensor is one including all the different constituents for the signal transduction, amplification and processing in the same substrate. However, the concept of integration is usually employed to designate miniaturized devices, whose main parts (the recognition element and waveguides) lie in the same substrate, and whose waveguides are fabricated with common microelectronic techniques.

From the diversity of the analytical methods and the availability of the instrumentation and possible configurations that can be found, one can infer that the design, the formulation and the integration of the recognition element in the transducer are crucial because quality parameters such as sensitivity, selectivity, lifetime and dynamic range directly depend on them. The initial stages of the development of an integrated optical sensor, based on the direct or the indirect analyte recognition by means of a reactive phase, involve the study and selection of the response mechanism, the choice of the reagents implicated in the recognizing process, the matrix formulation and sometimes the selection of appropriate membrane deposition techniques over the waveguides.

## 2.2
## Reagents and Indicators

When an analyte lacks measurable optical properties by itself, spectroscopically active intermediate molecules are needed. Indicators modify their optical properties when they interact with the analyte and usually are neutral or ionizable dyes.

A great number of indicators are known, but only a few of them are really useful in the optochemical sensor field owing to their properties. As the main characteristics, they must have high molar extinction coefficients and be specific for a certain analyte. Moreover, they must be photochemically stable to be applied in real situations, making viable the development of simple, rugged and low-cost devices. Other operational limitations arise from the use of optical fibers (with low transmission capability in the UV spectral region), from the chosen immobilization conditions and from the low-cost available light sources and detectors (usually LEDs and p-n photodiode, PIN, photodiodes), which are only adequate for a particular spectral range. For instance, indicators with absorption bands located at wavelengths shorter than 500 nm are only appropriate for classical optical instrumentation in absorbance-based systems. Some new blue and violet diode lasers can be found in the market [4, 5]. However, the first ones need an umbral intensity of 500 mA to emit and, moreover, both sources are not optimized for common telecommunication optical fibers. They might be suited if fluorescence is to be measured but they are not optimal for integration in compact systems based on integrated optics.

For the development of new miniaturized and mass-production devices, dyes presenting absorption bands between 550 and 650 nm are needed, because they can be activated with low-cost light sources of high intensity and can work with optical fibers.

A great variety of reagents which fulfill all or part of the requirements mentioned have been employed. Depending on the analytical goal, we face a given recognition principle that is mediated by a certain reagent or indicator. pH indicators (absorbent or fluorescent proton exchangers) have been extensively employed for acidity determinations [6], and when they are combined with ionophores, for indirect measurements of cations and anions [7–13]. On the other hand, for the direct detection of such ions, various types of chromoionophores (metal-chelating agents or ion-pairing formers) have been used [14–18] and different fluorophores have been used to perform indirect measurements based on the quenching effect [6, 19–28].

## 2.3
## Supports and Matrices

Reagents and indicators are immobilized, occluded or dissolved in supports which are formed by cross-linked polymers, plasticized polymers or organic and inorganic activated surfaces. The waveguide itself, the cladding of an optical fiber or any other optical element can be the support. However, it must obey two basic functions: act as a liquid–solid or gas–solid interface and, if radiation crosses through it to allow the signal transmission, be an optically transparent material.

On the other hand, it must stay inert while facing the chemical reactions that are involved in the recognizing process and it must assure an efficient radiation coupling with the light source, if optical fibers are used. In addition, the matrix sometimes plays the role to improve selectivity and regulates the charge transference.

A large variety of different support materials can be used. The preferred ones are often organic polymers even though they sometimes swell significantly as a function of the external medium and are less resistant to abrasion and mechanical shock than the inorganic ones. The main reasons are that indicators and labels are frequently organic compounds and that a great variety of organic supports are available. The selection depends on the affinity towards the reagents, the stability, and the permeability to the analyte, the compatibility towards other materials employed for the sensor construction (e.g., in cases where it is the cladding of an optical fiber) and the compatibility with the sample. The polymeric material has a great influence on the sensor performance.

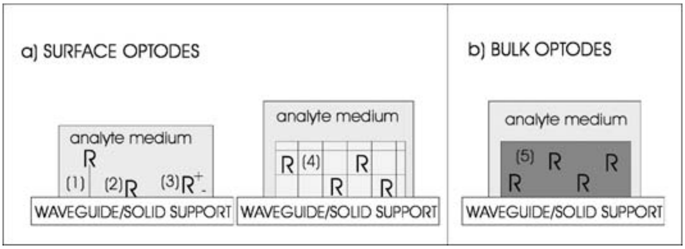



**Fig. 2** Schematic representation of optochemical sensors depending on the arrangement of the optically active reagents. **a** Surface optodes: reagents are directly immobilized over a solid support by (1) covalent bonding, (2) adsorption or (3) electrostatic interactions or a waveguide or are trapped in a porous matrix (4). **b** Bulk optodes: reagents are dissolved in a plasticizer (5)

Other inorganic polymers, such as silicones, have excellent optical and mechanical properties for optical membranes. A great number of easily handled commercial silicone prepolymers are available but they have some disadvantages towards other materials. The surface is not easily modifiable to covalently immobilize indicators, they are not suited to combine with the customarily used support structures, owing to hard adhesion, and they are bad solvents for most of the indicators.

Other types of common inorganic supports are silicon gels, quartz/glasses or sol–gels. They are rigid materials and play an important role in the optical transmission when acting as waveguides. In that sense, indicators are usually covalently immobilized in the surface or are trapped in the porous material. Depending on the arrangement of the reagents and indicators in the reactive phase, we can make a distinction between two types of optical sensors which follow different response mechanisms. Reagents are directly immobilized over the support or the waveguide in surface-phenomena-based optical sensors, while in bulk optodes they are dissolved in a polymeric membrane. In Fig. 2 both schemes are depicted and the nature of the interaction concerning the indicators and the matrix or the waveguide is indicated.

### 2.3.1 Surface Optodes

Their main characteristic is that the optically active reagents are immobilized over the surface of an optical component (waveguide, metallic plate, glass, prism, etc.) or in a porous matrix in a way that they are in direct contact with the analyte in the sample solution. This immobilization can be carried out by covalent bonding [29], by mechanical interactions such as physical adsorption [30], by physical entrapment or by electrostatic interactions [31].

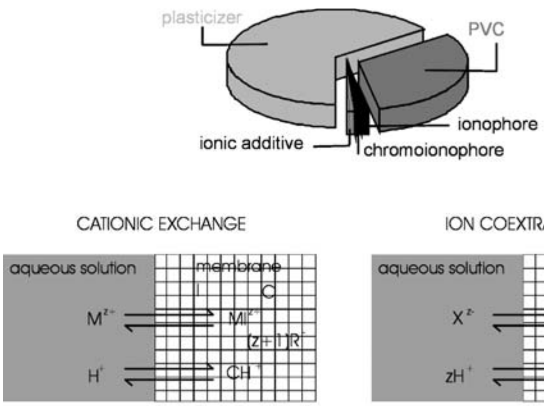
The selective recognizing reactions take place only in the surface that is in contact with the solution. Then, the response time depends on the equilibrium rate in the surface of the reactive phase and the signal relies on the superficial charge density as well as on the ionic strength of the solution. In these conditions, both parameters must be maintained constant.

### 2.3.2
### Bulk Optodes

The reagents are dissolved in an immiscible phase that is held up to an inert polymeric matrix in bulk optodes. The whole constitutes the sensing membrane, and the signal relies on concentration changes within the bulk.

They are often plasticized PVC matrices, which occlude an ionophore as the key selective element, a chromoionophore or a fluoroionophore as the chemical-optical transducer and, sometimes, ionic additives to maintain electroneutrality. Such optodes follow ion-exchange mechanisms between the membrane and the aqueous solution and the analytical response originates from the ratio of the concentration of ions in the solution or from their product (Fig. 3). Moreover, selectivity is ruled by the ion distribution coefficients between both phases and by the formation constants of complexes within the membrane.

The main advantages of using this approach are that response is not affected by the ionic strength of the solution and that the development of specific ion-selective optodes is easily adapted from their analogous well-studied ion-selective electrodes [32–34], because the same selective reagents and membrane constituents are employed. Most of the ion-selective optodes




$$\frac{a_M}{(a_H)^z} = K\frac{\alpha^a}{(1-\alpha)^b}$$

$$(a_{H^+})^z a_{X^{z-}} = K\frac{(1-\alpha)^a}{\alpha^b} \qquad a_{H^+} = \frac{1}{Ka_{MBM}}\frac{(1-\alpha)^a}{\alpha^b}$$

**Fig. 3** Basic composition of ion-selective bulk optodes and extraction mechanisms. This type of sensor follows an extraction equilibrium between the aqueous solution and the membrane and the signal is related to the analyte activity in the aqueous solution described belong to this class of sensors. Table 1 shows some organic compounds employed as near-IR (NIR) chromoionophores in optical sensors based on bulk optodes [35].

## 2.4 Sensor Configuration

The optical sensor construction is more or less complex depending on its design, the type of formulated membrane, the optical phenomenon that generates the signal and how this signal is measured. Taking into account whether radiation transmission structures are employed or not, we can distinguish two different basic configurations: non-guided radiation devices (conventional configurations) and waveguide-based sensors (Fig. 4).

### 2.4.1 Non-Guided Radiation Devices

The main characteristic of non-guided radiation devices is that the recognition element or the chemical membrane is not physically integrated in any waveguide structure. Variations of the membrane optical properties lead to variations of the transmission of a non-guided light beam (Fig. 4a).

This class of sensors is the easiest to build but prevents the development of miniaturizable sensors for in situ applications. In general, this conventional configuration represents an easy and rapid way to optimize the response characteristics of any recognition element, before any possible integration in

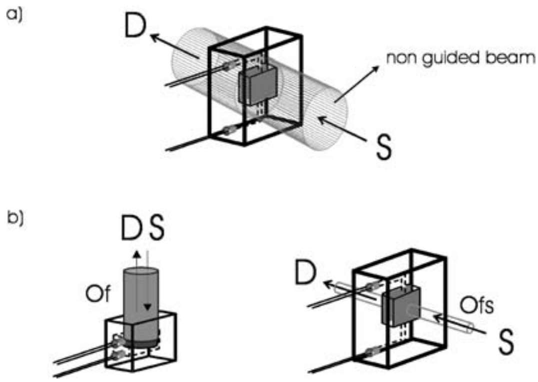



**Fig. 4** Different optochemical configurations for flow-cell-based sensors. Notice that flow cells are expendable. *S* source, *D* detector, *Of* optical fiber. **a** Non-guided sensors: the transmission of a non-guided collimated radiation beam is measured. **b** Radiation is guided though optical fibers from the source to the recognition element and from this position to the detector

**Table 1** Near-IR chromoionophores applied in bulk optodes. The absorption maxima, the type of matrix employed, the sensor configuration, the optical properties measured, the analyte and year of publication are listed

| Type of dye | Name | λ (nm) | Matrix | Configuration optical property | Analyte | Year (Ref.) |
|---|---|---|---|---|---|---|
| Structure 1 polymethinic dyes | Crococyanine | $815_{EtOH}$ | PVC/DOS | Flow cell/A | $H^+$ | 1997 [36] |
| | Squarocyanine | $819_{PVC/DOS}$ | PVC/DOS | Flow cell/A | $H^+$ | 1997 [36] |
| | | $821_{PVC/oNPOE}$ | PVC/o-NPOE | | | |
| | Streptopolymethine cyanine | – | PVC/DOS | Flow cell/A | $H^+$ | 1996 [11] |
| | | $810_{Nafion}$ | Nafion | Flow cell/A | $H^+$ | 1996 [11] |
| | Carboxyheptamethine Cyanine | $780_{Nafion}$ | Nafion | Flow cell/A | $H^+$ | 1996 [11] |
| | Styrylcyanine | $660_{MeOH:H_2O}$ | PVC/DBS | Flow cell/A | $H^+$, $K^+$, $Na^+$, $Li^+$, $Ca^{2+}$, $Mg^{2+}$, $Ba^{2+}$, $NH_4{}^+$ | 1999 [17] |
| | | $670_{ISP:H_2O}$ | PVC | OF/A | $H^+$ | 1995 [37] |
| | | $680, 720_{PVC/TOP}$ | PVC/TOP | Flow cell/A | $H^+$ | 1994 [9] |
| | Asymmetric trimethinecyanine | $826_{ISP:H_2O}$ | PVC | OF/A | $H^+$ | 1995 [37] |
| | | $850_{PVC/TOP}$ | PVC/TOP | OF/A | $H^+$ | 1994 [9] |
| | Ketocyanine | $727–770_{PVC/TOP}$ | PVC/TOP | Flow cell, IOS/A | $H^+$ | 2002 [38] |
| | | $768_{PVC/TOP}$ | PVC/TOP | Flow cell, IOS/A | $Cd^{2+}$ | 2002 [39] |
| Structure 2 diphenyltriphenyl methane | Benzophenoxazine | $690_{PVC/DOS}$ | PVC/DOS | IOS/R | $Ca^{2+}$ | 1995 [40] |
| | ETH 5294 (Fluka) | – | PVC/DOS | Flow cell/A | $Pb^{2+}$ | 1992 [41] |
| | | – | PVC/DOS | Flow cell/A | $NH_3$ | 1991 [42] |
| | Benzophenoxazine | 660 | PVC/DOS | Flow cell/A, F | $NO_2$ | 1997 [43] |
| | ETH 2439 (Fluka) | – | PVC/DOS | Flow cell/A | $Pb^{2+}$ | 1992 [41] |
| | | – | PVC/DOS | Flow cell/A | $NH_3$ | 1991 [42] |

**Table 1** (continued)

| Type of dye | Name | λ (nm) | Matrix | Configuration optical property | Analyte | Year (Ref.) |
|---|---|---|---|---|---|---|
| | Benzophenoxazine ETH 5418 (Fluka) | 665 | PVC/DOS | Flow cell/A | $Pb^{2+}$ | 1992 [41] |
| | Benzophenoxazine ETH 5350 (Fluka) | 640 | PVC/DOS | Flow cell/A | $NH_3$ | 1991 [42] |
| Structure 3 mixed chromophoric system | Dicyanovinyl alkylated dye ETH 5003–5009 (Fluka) | $576–759_{MeOH}$ | PVC/DOS | Flow cell/A | $H^+$, $Ca^{2+}$ | 1998 [44] |
| | Dicyanovinyl | $755_{PVC/DOS}$ $768_{PVC/oNPOE}$ | PVC/DOS PVC/o-NPOE | Flow cell/A | $H^+$ | 1997 [36] |
| Structure 4 metal complexes | Copper complexes | $760_{PVC/DOS}$ | PVC/DOS | OF/ev. | $NH_3$(g) | 1998 [45] |

*OF* optical fibers, *IOS* integrated optical sensors, *A* absorbance, *R* reflectance, *F* fluorescence, *ev* evanescent wave, *ISP* isopropyl alcohol, *DOS* bis(2-ethylhexyl)sebacate, *o – NPOE ortho*-nitrophenyl octyl ether, *TOP* tris(2-ethylhexyl)phosphate waveguide structures. That is why a large number of the reported optodes were firstly assayed in such a configuration using different conventional spectroscopic techniques (absorbance, luminescence, reflectance, etc.).

### 2.4.2 Waveguide-Based Devices and Integrated Optochemical Sensors

Optical fibers and planar waveguides are the main components of waveguide-based sensors, where the recognizing element is directly integrated (Fig. 4b). Waveguides were developed for and by the telecommunications industry and have been widely applied for the procurement of chemical sensors in the field of analytical chemistry because they offer optimum characteristics concerning their dimensions, flexible geometry, immunity to electric interferences and the possibility to transmit light over large distances. The recognition element–waveguide contact can occur by means of a chemical activation of the waveguide surface (covalent immobilization of the reagents) or by physical deposition of homogeneous reactive phases, such as bulk optodes and sol–gel matrices.

Different situations can be distinguished depending on the waveguide configuration. Devices can give discrete information as probes or continuous information, if they are incorporated in flow cells and, from a spatial point of view, measurements can be punctual or distributed all along the guiding structures such as in optical time domain reflectometry [46, 47]. In order to understand their operation, it is essential to learn the waveguide characteristics and optical properties.

#### 2.4.2.1 Light Propagation in Waveguides and Light Coupling

Optical waveguides generally confine light by means of the total internal reflection (TIR) effect, which is accomplished at the interfaces of a high refractive index dielectric medium (core) surrounded by a lower refractive index medium (cladding and substrate) (Fig. 5) [48, 49].

Light propagates inside a waveguide under some restricted conditions. The propagation characteristics of optical fibers are well known and can be found in the literature [50]. In contrast, the analysis of light propagation characteristics in planar waveguides is much more complicated and a theory of propagation is not well established yet. The preferred analysis tool is the simulation of their behavior by means of beam propagation methods [51] and taking into account several approximations. In any case, it is usually necessary to overcome some cycles by trial and error before relatively fair featured waveguides can be fabricated and used to develop integrated sensors on a chip.

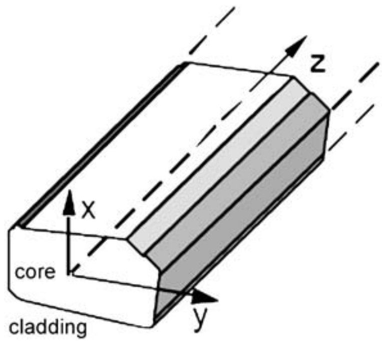



**Fig. 5** Elementary parts of a waveguide, propagation and confinement directions

Moreover, to thoroughly study the propagation characteristics of a given waveguide it is important to previously know how light is coupled into it. Light is frequently coupled into integrated waveguides by means of optical fibers, as there are a great number of commercially available ones which have been designed for all the existing optical sources and detectors. Other coupling alternatives are prisms and grating couplers [52], but their application is restricted to planar waveguides and they are not suitable if the goal is to achieve a total integration level or to develop small and compact devices, because bulky optical components such as the light sources and detectors are required.

On the other hand, there are some sensor configurations such as Mach–Zehnder [53–55] interferometers or even evanescent waveguide-based devices [56] that require a single-mode behavior. Such waveguides are difficult to fabricate and require very thin cores to attain low insertion losses with the coupling to standard optical fibers. The only way to prevent such losses is by using more complex coupling configurations as lensed fibers, spot transformers or grating couplers [57].

Optical waveguides can be very different depending on the application they are designed for, and so their light propagation properties will also be very different. For instance, optical fibers are used whenever information is needed to be transported far away from any position, but integrated waveguides are used when designing photonic circuits on a chip. More often, variations in their intrinsic guiding properties are exploited as the measured signal.

#### 2.4.2.2
#### Waveguide Designs

Waveguide-based devices can take on different configurations depending on the guiding structures employed: cylindrical (optical fibers and capillary waveguides) or planar.

A great number of different optical fibers exist depending on the structure, geometry and fabrication materials. Each of these parameters determines the performance (attenuation, dispersion), physical properties (refractive indexes) and optical properties (propagation range wavelengths). The main materials for fabrication of optical fibers for use in the IR range are $SiO_2$ glasses and metallic fluoride glasses such as $MF_3 - AlF_3$ and $MF_3 - ZrF$, where $M$ can be Ca, Sr, Ba or Pb. For medical applications plastic fibers of polycarbonate, polystyrene or poly(methyl methacrylate) are employed. They are commonly used in fluorescence and evanescent field applications or for illumination of samples [58, 59]. Multimode glass fibers are also used for fluorescence [60] and single-mode glass fibers for evanescent sensors and surface plasmon resonance (SPR) [61].

Standard single-mode fibers are often 10-μm-thick and multimodal ones 50- and 62.5-μm-thick. The latter are the easiest to apply in the optochemical sensor field, because they allow a proper light transmission at medium and short distances and can be employed with a great number of commercial optical components.

The recognition element can be set out at the distal end of the fiber or sidelong between the core and the cladding.

Capillary waveguides are a special type of guiding structures as they not only transmit light but can also act as flow cells and as the mechanical support for the chemical immobilization of the recognition element [62]. They are multilayered structures, where a liquid or a gas, which is in direct contact with a reactive layer that is deposited in the inner wall or in an extra coating layer, can flow inside. Light can propagate through the capillary cladding if a reflective layer of lower refractive index than the core is used. Then, an evanescent wave optode can be developed. On the other hand, core-based op-

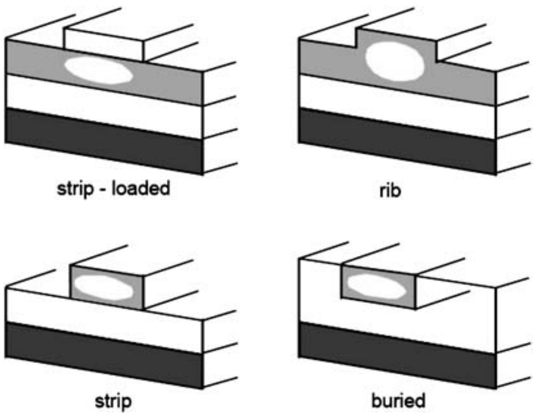



**Fig. 6** Types of planar waveguides depending on the processes employed for their fabrication

todes can be developed by using membranes with higher refractive indexes than the surrounding layers, as light propagates though the membrane.

Planar waveguides can be differentiated depending on the fabrication techniques employed: those fabricated by the deposition of layers onto a substrate (such as silica on silicon waveguides) and those fabricated by means of diffusion techniques, by generating an area of a higher refractive index than the rest of the substrate, such as titanium:lithium niobate waveguides (Fig. 6).

The so-called buried waveguides have squarelike or cylindrical geometry depending on the fabrication method. If diffusion or ionic exchange is used, they are often cylindrical, but if they are fabricated by deposition techniques, they can be square. The diffusion of materials in the substrate gives rise to a refractive index gradient in the core and a smooth core–cladding interface. Figure 6 schematically shows the square geometry, whose waveguiding characteristics are similar to that of optical fibers [63].

On the other hand, deposition-based waveguides usually have a squarelike geometry in a strip, a strip-loaded or a rib configuration (Fig. 6). They are fabricated by depositing several layers onto a planar substrate by means of microelectronic processes, covering and etching them until the final geometry is obtained.

### 2.4.2.3 Waveguides in Integrated Optical Circuits

During the last 50 years, research on microelectronics has overcome the most optimistic expectations regarding achievements as well as new equipment. Integrated optical circuits (IOCs) are still far from microelectronics, but the technology is expected to progress much faster since, instead of developing new equipment, the existing systems can be adapted so as to provide good results in integrated optics.

In order to develop an integrated optical sensor, it has to be taken into account that the main material used in microelectronics is silicon, which absorbs at wavelengths below 1.12 μm. Then, the first step would be the design of waveguides that could operate in the visible region with acceptable absorption losses while keeping their single-mode behavior.

Integrated guiding structures can be based on several optical principles. Among the most interesting, TIR and antiresonant reflecting optical waveguides (ARROW) configurations are highlighted, since they are more versatile, simpler and more robust than the others. The simplest TIR waveguides consist of two layers with different refractive indexes but their main problems arise during the fabrication process and the structure characterization [64].

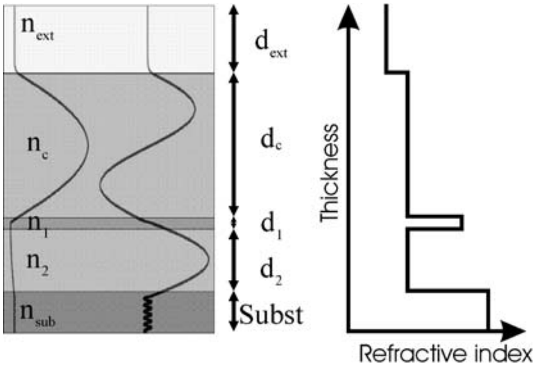



**Fig. 7** Fundamental and first mode of an antiresonant reflecting optical waveguide (*AR-ROW*) waveguide. Layer thickness *d* and refractive indexes *n* are detailed for the external medium (*ext*), the core (*c*), the first cladding (1), the second cladding (2) and the substrate (*sub*)

### 2.4.2.4 ARROW Structures

ARROW waveguides were firstly developed in 1986 [65]. Their layered structure is presented in Fig 7. As a distinction from TIR waveguides, two different layers are placed just below the core. The refractive index and thickness have to be chosen, for a given working wavelength, so as to provide very high reflections. At the upper air-core interface there is still a TIR. But in the antiresonant pair ($d_1$ and $d_2$), a high reflection happens at the antiresonant wavelengths. It could be thought that the fabrication conditions of these structures are extremely strict and that they only work in a very narrow wavelength range. Nevertheless, since the layers are tuned in to antiresonance, the tuning region is broad, providing a high degree of robustness and tolerance to fabrication errors. The major advantage of ARROW structures is that, owing to their principle of operation, the modal properties do not depend on the core thickness, but on the antiresonant pair located just beneath the core. Hence, it is possible to obtain waveguides with a core thickness of the same magnitude as for coupling with optical fibers. Thus, insertion losses are reduced [73].

A brief review of the literature concerning the several materials employed in the fabrication of both TIR and ARROW structures is given in Table 2. The processes employed are completely different, ranging from molecular beam epitaxy to several chemical vapor deposition (CVD) systems, such as low-pressure CVD (LPCVD) or plasma-enhanced CVD (PECVD). As a rule, all suitable materials for ARROWs (and in general for IOCs) should have homogeneous refractive indexes, high mechanical and chemical stability, few

**Table 2** Different materials employed in the fabrication of total internal reflection (*TIR*) and antiresonant reflecting optical waveguide (*ARROW*) waveguides

| | Substrate | $d_c$ | $d_1$ | $d_2$ | λ (µm) |
|---|---|---|---|---|---|
| TIR | | | | | |
| [66] | Si | $As_2S_3$ | | | 1.3 |
| [67] | Si | SiN | | | 1.3 |
| [68] | Si | $Si_{1-x}Ti_xO_2$ | | | 1.3 |
| ARROW | | | | | |
| [69] | InP ($n = 3.16$) | InP ($n = 3.16$) | InGaAsP ($n = 3.553$) | InP ($n = 3.16$) | 1.55 |
| [70] | Si | $SiO_2$ ($n = 1.46$) | $TiO_2$ ($n = 2.3$) | $SiO_2$ ($n = 1.46$) | 0.633 |
| [71] | Si | Si | GeSi | Si | 1.33 |
| [72] | Si | $SiO_2$ ($n = 1.46$) | $TiO_2$ ($n = 2.3$) | $SiO_2$ ($n = 1.46$) | 0.633 |
| | Ge | NA45 ($n = 1.54$) | $Si_3N_4$ ($n = 2.0$) | NA45 ($n = 1.54$) | |
| | GaAs | C7059 ($n = 1.54$) | ZnO ($n = 1.98$) | C7059 ($n = 1.54$) | |
| | InP | | $Al_2O_3$ ($n = 1.65$) | | |
| | | | $ZrO_2$ ($n = 1.92$) | | |
| | | | $Ta_2O_5$ | | |

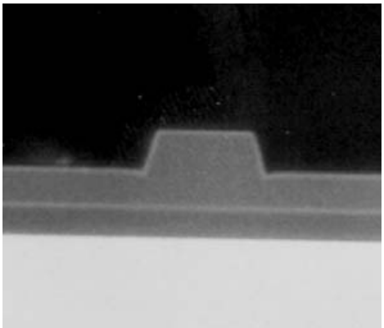


**Fig. 8** Photograph of the cross section of an ARROW structure obtained using the technological processes described in the text

defects and impurities and elastic properties compatible with further processing.

The main disadvantage of ARROWs is that the standard structure is polarization-dependent; however, this can be overcome by means of a proper tailoring of the layers. In any case, for sensing applications the advantages of the ARROW configurations outweigh the disadvantages and ARROW configurations are a very good choice for the fabrication of cheap and reliable integrated devices [65].

The structure of an ARROW has the shape of a slab waveguide, i.e., there is only light confinement in the direction orthogonal to the surface of the layers. On the other two axes light is able to propagate freely. This type of waveguide

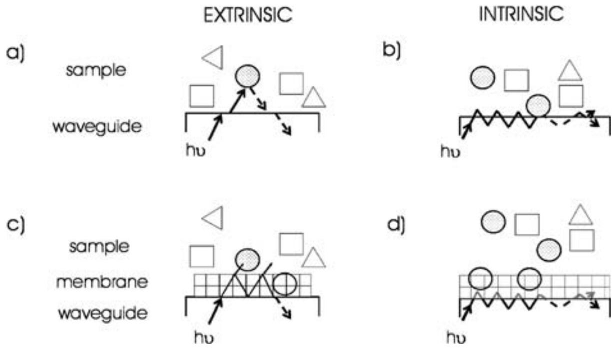



**Fig. 9** Four waveguide-based sensors. *Left* Extrinsic sensors **a** in direct analyte measurements or **c** in indirect measurements by means of indicators or other reagents immobilized in membranes. *Right* Intrinsic sensors for measurements of changes in the light guided though the waveguide by **b** the adsorption of the analyte into its surface or by **d** the interaction of the analyte with a recognition phase, which is in direct contact with the waveguide

is rarely used since it does not permit integration of several IOCs in the same substrate. But this drawback is solved by defining a lateral confinement, by way of partially etching the core of the waveguide by forming a rib structure (Fig. 8).

A final protective layer is necessary to insulate devices from the external medium and prevent scratches that could dramatically increase light losses.

## 2.5 Waveguide-Based Optochemical Sensors

A fundamental classification of optochemical sensors can be done depending on the area where the interaction of light with matter occurs and results in changes in the light guided towards the detector. Light can be allowed to exit the waveguide and be modulated in a separate zone before being directed into either the same or a different waveguide in *extrinsic sensors*. If it continues within the waveguide and is modulated in response to the analyte while it is still being guided, *intrinsic sensors* are developed. Figure 9 depicts four examples of chemical sensors based on waveguides, as well as in cases where the analyte exhibits optical properties such as in cases where immobilized indicators are employed.

### 2.5.1 Extrinsic Sensors

In terms of the interaction of light with matter, extrinsic sensors can be compared with non-guided radiation sensors because light temporally exits the waveguide to interact directly or indirectly with the analyte or with an active phase before being directed and guided again. This operation principle is derived from the conventional concept of an optochemical sensor. Therefore, waveguides are not really required but offer some advantages: easy miniaturization and the possibility of transmitting information over large distances, using, for instance, optical fibers for luminescence measurements [74, 75], for Raman spectrophotometry [76, 77] or for reflectance [78, 79]. In these situations, the waveguide only acts as the radiation transmission medium.

Other types of sensors are the so-called active waveguides [80] or integrated waveguide absorbance optodes (IWAOs) [81]. They are based on the radiation transmission through the core of a chemically active membrane yielding one part of a light-guiding planar structure. The response mechanism consists of the absorbance/transmittance phenomena of the recognition optode membrane as it interacts with the analyte in the sample and while light is guided through it. Sensors that make use of all the light transmitted though the core/membrane offer some remarkable advantages, such as high sensitivity and an adequate selectivity (regulated by the immobilized reagents), compared with other absorbance sensors derived from waveguides. Hence, they will be discussed in more detailed in due course.

### 2.5.2 Intrinsic Sensors

The interaction phenomenon of the analyte with radiation is governed or modifies the principle on which light is transmitted through the waveguide. Depending on that interaction, we can differentiate three basic types of intrinsic optical sensors [82]: refractive-index-type sensors, luminescence-based sensors and absorption-type sensors.

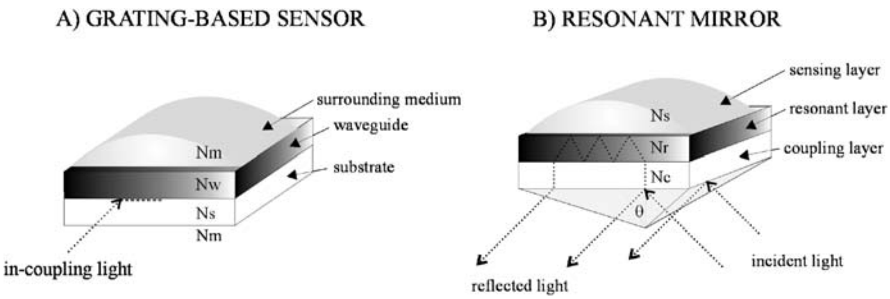



**Fig. 10** Different refractive-index-based sensors. **a** A grating coupler, where $N_s$, $N_w$ and $N_m$ are the refractive indexes of the substrate, the waveguide and the surrounding medium respectively. **b** A resonant mirror, where $N_m$, $N_r$ and $N_c$ are the refractive indexes of the medium, the resonant layer and the coupling layer

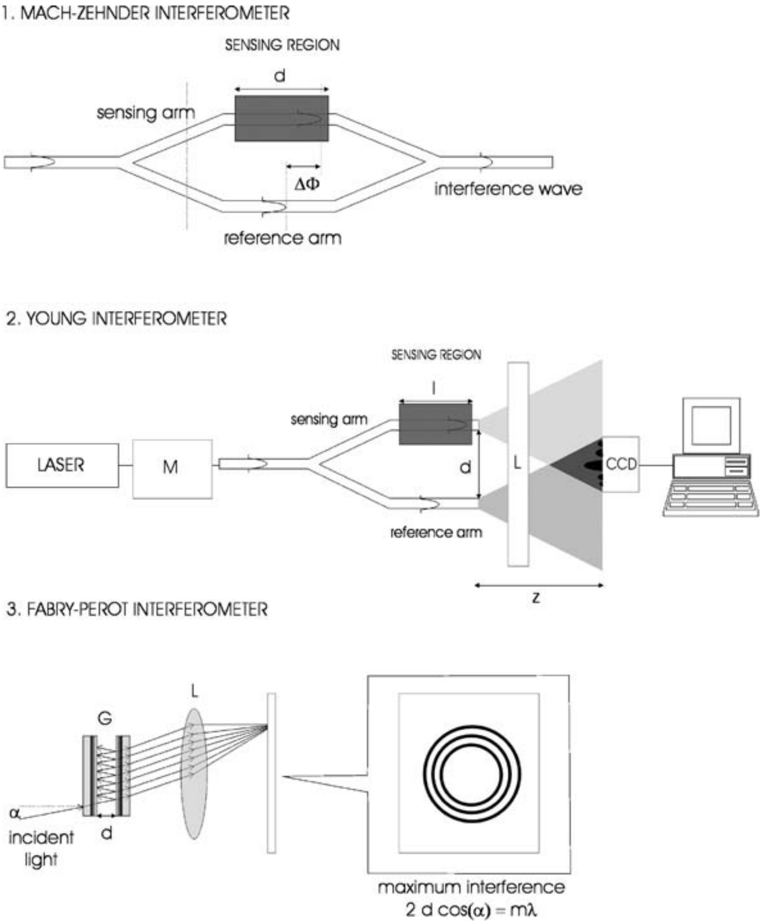



**Fig. 11** Geometry of interferometers and basic components. 1 Mach–Zehnder: *d* interaction distance of light and sensing region. 2 Young: *M* microscope objective, *l* length of the sensing window, *d* distance between the parallel channels, *L* lens, *Z* distance between the CCD camera and the end face of the interferometer. 3 Fabry-Perot: *G* parallel mirrors, *d* distance between mirrors or the medium filling the cavity, *L* lens

### 2.5.2.1 Refractive-Index-Type Sensors

For refractive-index-type sensors, the waveguide is intrinsically the sensing element, and then chemical processes are measured with the variations of the refractive index, *n*, of guided modes. The majority of the various sensor types and published configurations make use of grating couplers (Fig. 10a) [83, 84], resonant mirrors (Fig. 10b) [52, 86–89] or interferometric sensors (Fig. 11) as

Mach–Zehnder [53, 90–94], Young [95–97] and Fabry–Perot [98–100] interferometers.

One of the most widely studied refractive index sensor, especially for the detection of proteins and other bioanalytes, is the SPR-based evanescent-wave-type sensor. In comparison with evanescent-based sensors, the intensity of the field in the recognition layer deposited over the metal is 2 orders of magnitude higher than that deposited over the glass.

These sensors have been used in very concrete applications for gas analysis or analysis of liquid mixtures as well, but following up immunological reactions is an interesting field of application as the interaction of an antigen with an immobilized antibody leads to large changes in the resonance angle and real-time continuous monitoring of affinity reactions can be performed.

Integrated waveguides for SPR have to be manufactured in such a way that the propagation constant matches that of the surface plasmon, which is very difficult to achieve for a given range of refractive indexes, even if an optical fiber is used. Nevertheless some research groups [101, 102] have studied this possibility.

Refractive-index-type sensors present poor specificity in their response and instabilities due to temperature or pressure variations and on the other hand, interferometric sensors are complex, but more sensitive than other integrated chemo-optical evanescent-field-based sensors.

### 2.5.2.2 Luminescence-Based Sensors

The luminescence techniques can be more selective than the absorption ones as it is possible to distinguish between two different wavelengths (the emission and the excitation one) and because only few molecules are potentially capable of emitting light when relaxing. This fact and the high sensitivity are the reasons why they have been widely applied in the field of optical sensors. If the excitation energy comes from a (bio)chemical reaction, the phenomenon is called (bio)chemiluminescence, meanwhile if it comes from a light source, it is called fluorescence or phosphorescence, depending on whether the excited state where the emission is produced is singlet or triplet.

Different situations can be found: direct determinations, where the luminophore is the analyte itself, or indirect determinations, where the analyte interacts with a luminophore, changing its optical properties, the quenching effect. And different measurement possibilities can be followed: intensity or lifetime of emission.

Even though sensors based on the measurement of fluorescence intensity are the most numerous, the high-intensity light sources employed accelerate the possible photodecomposition of the active molecules. Fluorescence-lifetime-based sensors avoid this problem by the excitation of molecules with light pulses.

Luminescence core-based optodes have been reported as waveguide capillary flow cells in liquid-filled optical fibers [103] or with polymers attached to the inner surface of a glass capillary [104].

Luminescent evanescent wave-based sensors use optical fibers and planar waveguides [105, 106] as light-guiding structures, and they are more complex than the absorbance ones. However, such optodes have been satisfactorily applied to measure fluorescence of indicators or labels for the measurement of gas molecules, proteins or labeled antigen–antibody interactions as well as directly in solution [24, 107] when immobilized in matrices [23, 109].

#### 2.5.2.3 Absorption-Type Sensors

Core-based optodes, such as hollow fibers, and direct and coating-based evanescent wave spectroscopic optodes are included in the classification of absorption-type sensors.

## 3 Absorbance-Based Integrated Devices

Despite the fact that direct absorbance/transmittance measurements are well established in analytical chemistry owing to the simplicity of the instrumentation and their broad applicability and versatility towards a large number of analytes, most of the reported miniaturized optical devices are based on the measurement of variations of the real part of the refractive index, such as SPR sensors [84, 109–111] or interferometric sensors [94, 112].

Some optical sensors exploit light absorption phenomena and most of them are based on evanescent wave spectroscopy [113, 114]. To avoid problems related to the inherent reduced sensitivity, they require long interaction distances or a great amount of the field out of the waveguide, which in turn makes the response very dependent on variations of the real part of the sample refractive index. Although they have high sensitivity, only a few optical sensors which make use of the guided field in the core of a waveguide have been developed.

The most significant reported absorbance-based miniaturized devices are detailed next.

### 3.1 Intrinsic Core-Based Optodes

A hollow fiber directly uses the fiber core as the recognition element. This configuration allows much greater interaction of light and the sensing material, so this technique gives sensors with much greater sensitivity. Moreover the optical setup is simple as, once the hollow fiber is made, it can be coupled to commercial optical fibers. Doping the hollow fiber with different sensing materials permits the fabrication of selective and sensitive chemical sensors. Hollow fibers can be fabricated using metal, glass or plastic tubing.

In the previous section, the advantages of using ARROW structures for IOCs, which work in the visible range, were explained. However, for some applications, wavelengths located in the IR range are required. Several attempts have employed low molecular weight chalcogenide glasses ($As_2S_3$), heavy-metal fluorides, silver halides and sapphire but they have severe drawbacks, such as low laser-damage thresholds, poor chemical and mechanical stability and difficult and expensive fabrication processes [115].

Hollow waveguides have emerged as a very attractive alternative to solid-core IR waveguides because of the inherent advantage of their air core. However, only a few applications in medical and industrial fields have been reported.

They not only enjoy the advantage of high laser power thresholds (transmit wavelengths beyond 10 μm, and ultrashort laser pulses at intensities close to 1014 W cm$^{-2}$) [116], but they also have low insertion losses, no end reflection, ruggedness and small beam divergence. Their main disadvantages include additional losses on bends and a small numerical aperture. Nevertheless, nowadays they are one of the best alternatives for both chemical and temperature sensing as well as for power delivery in IR laser surgery or in industrial laser systems.

In such waveguides, the core can be simultaneously used for confining the light and the fluid/gas to be measured, thus achieving a high interaction between them. As an example, in optical gas detection, hollow waveguides have already improved the detection limits [117].

Hollow fibers have been tried as liquid-core fibers in spectrophotometry [118] and porous fibers have been well adapted for gas measurements [119, 120]. The latter are made of porous polymers, which can trap indicators or reagents in the matrix with a very high permeability of gases and liquids. For liquid applications, porous silica gel has also been used [121].

Propagation into a hollow waveguide has a high dependence on the geometrical parameters of the waveguide and on the reflection coefficient of the walls. It has to be noted that in order to obtain specular reflections in the waveguide walls the roughness must be as low as possible, reaching values below the working wavelength. Generally, hollow waveguides can be grouped in two categories: if the fiber walls have a refractive index higher than unity (e.g., metallic or dielectric films deposited on the inside of metallic, plastic or gas tubing), they are called leaky hollow waveguides. In contrast, if the material in the inner walls has a refractive index lower than unity (e.g., using a dielectric material that matches this condition at the working wavelength) they are called attenuated total reflection (ATR) hollow fibers.

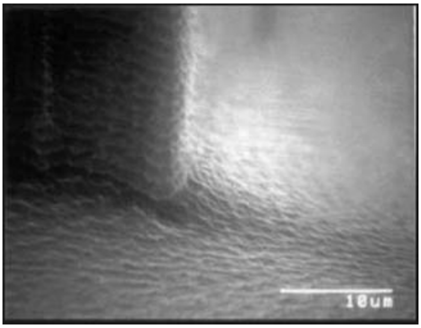



**Fig. 12** Scanning electron microscopy (*SEM*) microphotographs of the walls and bottom of a hollow waveguide after the deep reactive ion etching process

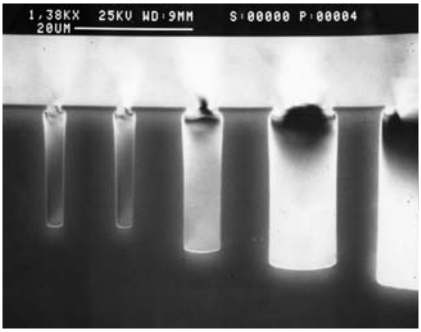



**Fig. 13** SEM microphotographs of Si-based hollow waveguides

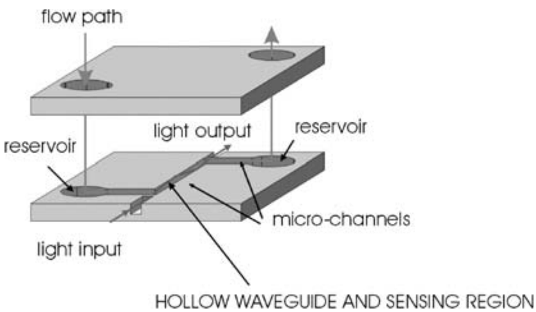



**Fig. 14** Standard configuration of hollow-based sensors. Flow is injected from a reservoir to the microchannel that also forms the hollow waveguide. Light interacts with the flow after crossing the input membrane and the signal is read after the output membrane

Hollow planar waveguides have been fabricated by several techniques, including physical vapor deposition and CVD of silver and dielectric layers on metallic substrates. Nevertheless, better results can be obtained by taking advantage of silicon micromachining techniques. Perhaps the most important advantage of silicon hollow waveguides over other hollow structures is the simplicity of the fabrication process. Moreover, hollow planar waveguides do not need a polishing step. Silicon confers a high chemical and mechanical durability to the structure. Then, the combination of the hollow fiber features with the silicon micromachining capability offers an outstanding flexibility for the development of integrated optical devices.

The most important process in the fabrication of silicon hollow fibers is deep reactive ion etching (DRIE). This process is very similar to the standard reactive ion etching (RIE) [122] process but permits us to achieve perfect vertical structures with low roughness. The results shown in Figs. 12 and 13 clearly confirm the required verticality of the walls to assure good confinement can be achieved.

Moreover, since the process is completely complementary metal oxide semiconductor (CMOS) compatible, more complex systems can be developed, with a large variety of components as different as valves, coolers, and photodetectors.

As an example, a proposed integrated sensor based on hollow waveguides is presented in Fig. 14. As can be observed, it consists of a silicon wafer into which the reservoirs (or fluid chambers), together with the fluid channel and the hollow fiber have been defined by a DRIE process. Leakage between these last two structures is prevented by defining a thin chemical membrane between them. The structure is completed by bonding on a second micromachined silicon chip, in such a way that only the input/output reservoirs are exposed to the external medium. Light is injected and crosses the chemically sensitive membrane, which interacts with the flow in the sensing region. After going through the second (output) membrane, light is collected again using an optical fiber or is directly pointed at a photodetector.

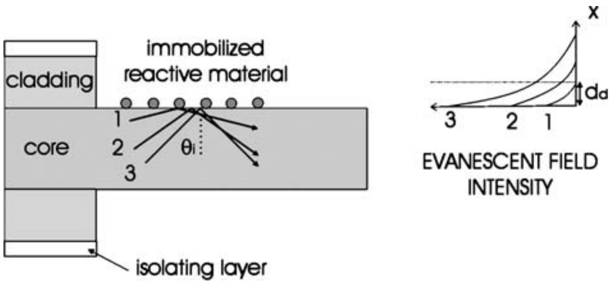



**Fig. 15** Light confined in the core interacts with the immobilized reactive material or with the sample though the evanescent field. It decays exponentially in the recognizing medium with the distance from the waveguide-coating interface and its maximum depth ($d_d$) is obtained at the light incident angle $\theta$i. 1, 2 and 3 are different light incident angles

## 3.2
## Intrinsic Direct or Coating-Based Evanescent Wave Spectroscopic Optodes

The evanescent wave phenomenon takes place in the core–cladding interface of a waveguide. Part of the radiation transmitted through the core permeates into the cladding a certain depth (between 50 and 12 000 nm for visible light), which depends on the transmitted wavelength, the incident light angle and the refractive indexes of the core and the cladding media. The evanescent field intensity decays exponentially with the interface distance (Fig. 15). Such sensors are usually obtained by removing a small longitudinal section of the cladding of a standard commercial fiber and replacing it by an absorbing medium. This can be the solution itself or reagents immobilized directly on its surface, in direct evanescent wave spectroscopic optodes, or reagents trapped in a chemically sensitive layer, in coating-based evanescent wave spectroscopic optodes [123].

Absorbance evanescent-based sensors are based on the absorption or dispersion of light outside the core. They rely on light attenuation in the evanescent field following the Beer–Lambert law (ATR sensors), but owing to the low intensity of the field, they offer poor sensitivity. This can be improved because the effective optical path length can be increased, especially when using optical fibers, capillary [62] or planar waveguides [114].

These techniques have usually been applied to the measurement of intrinsic absorptions of the analyte in direct evanescent-wave-based optodes [124], to follow absorption changes of immobilized indicators over the core of a waveguide [125] or as integrated NIR evanescent spectrophotometers [126]. In the latter, a broadband light source from the NIR range is coupled into a planar structure, via optical fibers, and the evanescent wave part of the light field penetrating into the a sensing layer, deposited on the structure, is absorbed at the characteristic frequencies of the molecules trapped on it. The spectral dispersion or absorption of the light coming from the waveguide is then coupled to a conventional NIR spectrometer or a diode array [127].

## 3.3
## Extrinsic Active Waveguides and IWAOs

From the transduction point of view, the optical phenomena that provide sensing in a waveguide configuration may occur in the core layer or outside it. Despite the fact that the former is the more sensitive one because the sensing area is probed by the major part of the energy, as has been stated before, the sensing region is located in the cladding in most optical sensors and is probed by the evanescent field. This kind of sensor requires long interaction distances or a great amount of field out of the waveguide, which in turn makes the response very dependent on variations of the real part of the refractive index.

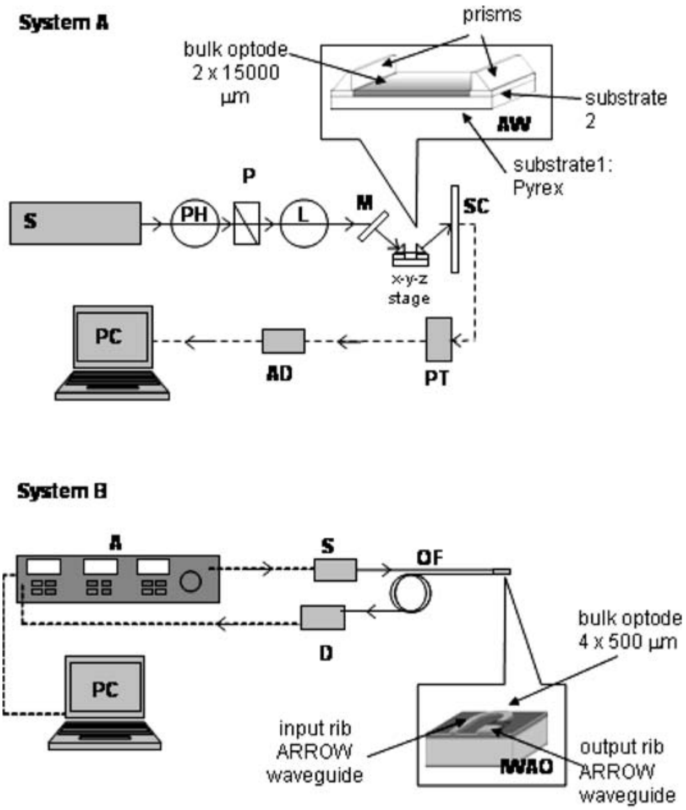



**Fig. 16** Optical setup of the extrinsic active waveguides and Integrated waveguide absorbance optodes (*IWAOs*). *System A*: *S* argon laser 488 nm, *PH* pin hole, *P* polarizer, *L* lens, *M* mirror, *SC* screen, *PT* photosensor/photometer, *AD* analog-to- digital converter, *PC* personal computer and *AW* active waveguide composed of a 15 000 µm × 2 µm bulk optode (PVC copolymer), deposited over a 26 mm × 76 mm × 1 mm substrate (Pyrex glass) and *substrate 2* corning 7059 and coupling and decoupling prisms. *System B*: *A* lock-in amplifier, *S* diode laser 778 nm, *OF* optical fibers, *D* p-n photodiode, *PC* personal computer and 30 mm × 20 mm × 0.6 mm IWAO composed of a 20-µm-input ARROW waveguide, a 500 × 4 µm PVC-selective membrane and a 50-µm-output ARROW waveguide

Very few extrinsic core-based sensors have been described. They are focused on polymeric active waveguides (bulk optodes) to develop planar sensors, which possess the advantages of the selective analyte determination and the optical signal propagation in the same structure. This new optical sensor concept consists of light propagation through the absorbing sensing layer, which incorporates a recognition element that leads to changes in the transmitted light. Light has no interaction with the solution matrix, so interference