

# Optical Chemical Sensors: Design and Applications

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## 1. Introduction

Optical sensors, or opt(ri)odes, represent a group of chemical sensors in which electromagnetic (EM) radiation is used to generate the analytical signal in a transduction element. The interaction of this radiation with the sample is evaluated from the change of a particular optical parameter and is related to the concentration of the analyte (Blum, 1997). Typically, an optical chemical sensor consists of a chemical recognition phase (sensing element or receptor) coupled with a transduction element (Fig. 1). The receptor identifies a parameter, e.g., the concentration of a given compound, pH, etc., and provides an optical signal proportional to the magnitude of this parameter. The function of the receptor is fulfilled in many cases by a thin layer that is able to interact with the analyte molecules, catalyse a reaction selectively, or participate in a chemical equilibrium together with the analyte. The transducer translates the optical signal produced by the receptor into a measurable signal that is suitable for processing by amplification, filtering, recording, display, etc. (Gründler, 2007; Nagl & Wolfbeis, 2008).

Sensors that have a receptor part based on a biochemical principle are usually called biosensors. The selectivity and sensitivity provided by Nature have been utilized in such sensors, frequently by immobilizing the biologically active compounds, such as enzymes and immunoglobulins, within a receptor part of the sensor (Patel et al., 2010). An effective way of obtaining the biological selectivity is a combination of cell cultures, tissue slices, organs and sometimes of whole living organisms with the transducer.

Optical sensors can be based on various optical principles (absorbance, reflectance, luminescence, fluorescence), covering different regions of the spectra (UV, Visible, IR, NIR) and allowing the measurement not only of the intensity of light, but also of other related properties, such as lifetime, refractive index, scattering, diffraction and polarization (Jerónimo et al., 2007). As an example, a luminescent sensor can be constructed by associating a sensing element, which emits light when in contact with a specific analyte, with a photodiode, which converts the energy of the incident light into a measurable signal.

Optical chemical sensors have numerous advantages over conventional electricity-based sensors, such as selectivity, immunity to electromagnetic interference, and safety while working with flammable and explosive compounds. They are also sensitive, inexpensive, non-destructive, and have many capabilities. Optrodes do not require a reference cell, as is

the case in potentiometry. Furthermore, they can easily be miniaturized and allow multiple analyses with a single control instrument at a central site (Lukowiak & Streck, 2009).

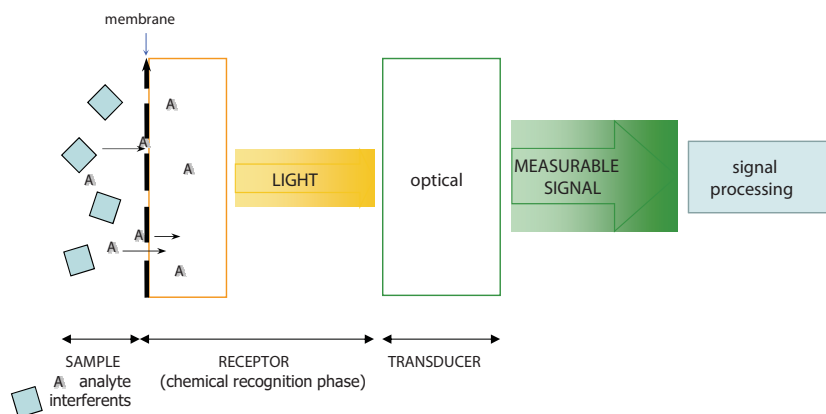


Fig. 1. Schematic representation of the composition and function of an optical chemical sensor

However, besides a number of advantages, optical sensors also exhibit disadvantages: ambient light can interfere with their operation, the long-term stability is limited due to indicator leaching or photobleaching, there may be a limited dynamic range, selectivity may be poor, and a mass transfer of the analyte from the sample into the indicator phase is necessary in order to obtain an analytical signal (Seitz, 1988).

Fiber-optic chemical sensors (FOCSs) represent a subclass of chemical sensors in which an optical fiber is commonly employed to transmit the electromagnetic radiation to and from a sensing region that is in direct contact with the sample. The spectroscopically detectable optical property can be measured through the fiber optic arrangement, which enables remote sensing. In addition to advantages in terms of cheapness, ease of miniaturization, obtaining safe, small, lightweight, compact and inexpensive sensing systems, a wide variety of sensor designs are possible (Jerónimo et al., 2007; Lukowiak & Streck, 2009; Seitz, 1988).

The most common classification of FOCs distinguishes between the intrinsic and extrinsic types of sensors (Seitz, 1988; Wolfbeis, 2008).

- In the intrinsic type of FOCs, the sensing principle is based on the change in light-transmission characteristics due to the change occurring in a fiber property (e.g., refractive index or length) upon the interaction with the analyte or the system being studied. The optical fibre itself has sensory characteristics. This type of sensor is mainly applied to measure physical or physicochemical parameters, such as the pressure, temperature, or enthalpy of reactions.
- In the extrinsic type of FOCs, the optical fiber acts as a transporting media by means of guiding the radiation from the source to the sample or from the sample to the detection system. Extrinsic sensors can be subdivided into a) distal and b) lateral types. The most common are distal-type sensors, in which the indicator is immobilized at the distal end (tip) of the optical fibre. Alternatively, in a lateral sensor, the sensing chemistry can be immobilized along a section of the core of the optical fibre to make an evanescent field sensor.

## 1.1 Optical detection principles

For sensor applications only part of spectroscopic wavelength range is useful. From the practical point of view the following ways (Fig. 2) in which radiation can interact with an analytical sample are the most useful (Gründler, 2007):

- absorption
- emission (fluorescence or phosphorescence)
- reflexion and refraction

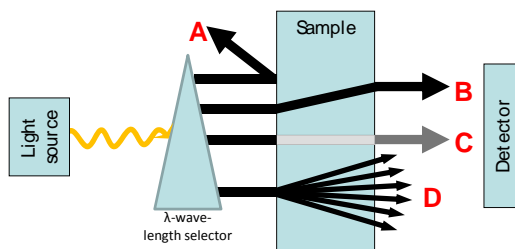


Fig. 2. General arrangement of spectroscopic measurements: A - light reflection, B - light refraction, C - light absorption, D - light emission.

However, the most commonly applied methods in optical sensing are those based on light absorption or light emission. Compared to absorption-based methods, molecular emission (fluorescence, phosphorescence, and generally speaking, luminescence) is particularly important because of its extreme sensitivity and good specificity. The sensitivity of luminescence methods is about 1000 times greater than that of most spectrophotometric methods. In addition, lower limits of detection for the desired analytes can be achieved (Guilbault, 1990; Schulman, 1988; Wolfbeis, 2005). Measuring the emission intensity is also the most popular because the instrumentation needed is very simple and cheap. Nevertheless, measuring the light emission intensity has some disadvantages compared to emission lifetime measurements, in which the sample is excited only by a pulse of EM rather than via continuous illumination, which is the case with intensity-based methods. The precision and accuracy of luminescence intensity-based schemes are greatly affected by fluctuations in the light-source's intensity, detector sensitivity, inner filter effects, indicator concentration (bleaching and leaching), sample turbidity, and sensing layer thickness. However, some of these problems can be minimized or even overcome by measuring luminescence lifetimes instead of intensities. But again, lifetime measurements also have some drawbacks, which are the instrumentation complexity and high costs, along with a limited number of indicator dyes available that show significant analyte-dependent changes in the lifetime (Lippitsch & Draxler, 1993).

Another way to reduce the problems associated with intensity as well as with lifetime detection principles is the use of ratiometric measurements. This technique employs dual-emission or dual-excitation indicators or mixtures of two luminophores, exhibiting separated spectral areas with different behaviour. For example, the ratio of two fluorescent peaks is used instead of the absolute intensity of one peak. The sensors therefore typically contain a reference dye; the advantage of this approach is that factors such as excitation source fluctuations and sensor concentration will not affect the ratio between the

fluorescence intensities of the indicator and the reference dye (Arduini et al., 2007; Buck et al., 2004; Cywinski et al., 2009; Doussineau et al., 2009; Frigoli et al., 2009; Sun et al., 2006).

Another important process that occurs in the excited state is the Förster or fluorescence resonance energy transfer (FRET). This process occurs whenever the emission spectrum of one fluorophore, which is the donor, overlaps with the absorption spectrum of another molecule, which is the acceptor. The acceptor must absorb the energy at the emission wavelength(s) of the donor, but does not necessarily have to reemit the energy fluorescently itself. The transfer of energy leads to a reduction in the donor's fluorescence intensity and excited state lifetime, and an increase in the acceptor's emission intensity. The rate of energy transfer from donor to acceptor is highly dependent on many factors, such as the extent of the spectral overlap, the relative orientation of the transition dipoles, and, most importantly, the distance between the donor and the acceptor. Due to its sensitivity to distance, FRET has been used to investigate molecular interactions (Demchenko, 2009; Frigoli et al., 2009; Kikuchi et al., 2004; Lakowicz, 2006).

## 2. Design of an optical sensor

The overall sensor quality is dependent on the total sensor system components, which are defined by the transduction, the sensitive layer, light source, data-acquisition electronics and evaluation software. In the next paragraphs the emphasis is devoted to the components when designing the sensitive sensor layer, namely, to the choice of suitable indicators, polymers, and immobilization techniques. Some selected, recently published applications using new nanomaterials are further presented.

An optical detection system may be based either on a) direct sensing or b) indicator-mediated sensing. In a direct optical sensor, the analyte is detected directly via some intrinsic optical property such as, for example, absorption or luminescence. In an indicator-mediated system, a change in the optical response of an intermediate agent, usually an analyte-sensitive dye molecule (indicator), is used to monitor the analyte concentration (McDonagh et al., 2008; Nagl & Wolfbeis, 2008). The principle of immobilized indicators relies on a large group of optical chemical sensors, because the measuring analytes mostly have no intrinsic optical property or this property is not convenient for their detection.

The reagent immobilised materials (sensitive layers) can be fabricated into several configurations, such as thin films, gels, to be interfaced with optical fibres (Gründler, 2007), in nanoparticles, etc. The most common are thin polymer films or membranes. This "smart" material responds to the species of interest by altering its optical properties (Seitz, 1988; Wolfbeis, 1991). For example, pH is measured optically by immobilizing a pH indicator on a solid support and observing the changes in the absorption or fluorescence of the indicator as the pH of the sample varies with time (Jerónimo et al., 2007; Lobnik, 1998,2006; Turel, 2008; Wolfbeis, 1991).

### 2.1 Indicators

The basic principle of the indicator chemistry (immobilized in or on the polymer matrix) in an optical chemical sensor is in transforming the measuring concentration of the analyte into a measurable analytical signal. The analyte concentration is measured indirectly, through the alteration of the indicator's optical properties. Various types of indicators are used in

optical chemical sensing, such as colorimetric - based on light absorption, and luminescent - based on light emission (Demchenko, 2009; Guilbault, 1990; Lobnik, 2006; Wolfbeis, 1991). However, the latter are of primary importance due to their high interdisciplinarity, great sensitivity, and applicability to different detection principles. A large number of fluorescent synthetic organic products are available nowadays so that a researcher can easily select the proper dye (indicator) corresponding to a particular sensing application in terms of spectroscopic properties and chemical reactivity. On the other hand, the basic organic chemistry also offers great potential as it enables synthesizing tailor-made indicators for specific applications.

### 2.1.1 Colorimetric indicators

Colorimetric sensing is accomplished using an indicator that changes its colour upon binding the analyte; this change is usually spectroscopically determined, but it is also visibly observed. Among the great variety of organic chromophores, such as azo dyes, nitrophenols, phthaleins, sulfophthaleins, aniline-sulfophthaleins, triphenylmethane dyes, the most popular applications using these materials is to measure the pH parameter. The  $pK_a$  of these indicators indicates the center of the measurable pH range, for example, cresol red, bromophenol blue, and bromocresol purple respond to acidic pH ( $pH < 7$ ), while cresol red, naphtholbenzene, and phenolphthalein respond at basic pH ( $pH > 7$ ) (Lobnik, 2006; Wolfbeis, 1991).

Redox indicators are the next example of colorimetric reagents. These are all organic dyestuffs, exhibiting reversible redox reactions. Examples include materials such as anilinic acid, diphenylamine, eriogreen, m-cresol-indophenol, methylene blue, Nile blue, etc. (Wolfbeis, 1991; Lobnik, 2006). For example, a redox indicator Meldola blue can be incorporated into a sol-gel layer for an optical sensor measuring hydrogen peroxide in the concentration range of  $10^{-8}$  to  $10^{-1}$  mol/L (Lobnik & Čajlaković, 2001).

Ion sensing is possible using metal indicators that form coloured complexes with metal ions (Kaur & Kumar, 2011; Kim et al., 2009). The so-called ionophores are ligands that selectively bind ions. Chromogenic ionophores are designed to bring about a specific colour change in the interaction with metal cations (Murković Steinberg, 2003). Typical representatives are macrocyclic molecules with an ion-binding cavity, crown ether dyes, etc.

Among the new nano-based materials, nanoparticles (NPs), the colorimetric ones are less common in comparison with the luminescent NPs. However, some examples have recently been reported where gold NPs for sensing  $Cd^{2+}$  (Ying et al., 2011),  $Fe^{3+}$  (Shu-Pao et al., 2011),  $Pb^{2+}$  (Nan et al., 2010), nitrite, nitrate ions were utilized (Weston et al., 2009), and carbon nanotubes were reported for sensing nucleic acids (Ai Cheng, 2007), and nanowires were used for  $Hg^{2+}$  (Tsao-Yen, 2011).

### 2.1.2 Luminescent indicators

The analyte concentration is determined by the change in the emission properties of a luminophore. Luminescence is intrinsically more sensitive than absorption as a sensing technique, so for many applications the literature more often reports on sensing with luminescent probes and sensors. A variety of fluorescent and luminescent materials in the form of molecules, complexes and NPs are available for implementation as the response

units into sensing technologies; among them, organic fluorescent dyes are of primary importance. However, there is an increasing application of other materials, such as luminescent metal-ion chelating complexes, fluorescent polymer molecules and especially, from different kinds of NPs (Demchenko, 2009; Basabe-Desmonts et al., 2007;).

As already mentioned, organic dyes are most commonly used in fluorescence sensing. Their advantages are easy availability, a low price, versatility. The best known are fluoresceins, rhodamines, cyanine dyes, Alexa dyes, and BODIPY dyes, which are frequently used for labelling. In addition to these, the environment-sensitive dyes (for example, Nile red), hydrogen-bond responsive dyes (ketocyanine dye), electric-field-sensitive dyes (styryl dyes), supersensitive multicolour ratiometric dyes (3-hydroxychromone dyes), phosphorescent dyes eosin and erythrosine derivatives, optimal FRET pairs (for example Pyrene/Coumarin) are known fluorescent reporters (Demchenko, 2009,2010; Lakowicz, 2006).

Luminescent metal complexes, with europium(III) ( $\text{Eu}^{3+}$ ) and terbium(III) ( $\text{Tb}^{3+}$ ) ions being the most used, represent advantages since they show longer lifetimes, large Stokes' shifts and, therefore, enable eliminating the light-scattering effects and short-lived background luminescence (Turel et al., 2009,2010), thus significantly increasing the sensitivity of the analysis. Transition-metal complexes that exhibit phosphorescence are also formed by ruthenium (Balzani et al., 2000), osmium, and rhenium ions and there are those based on porphyrin complexes (with Pt and Pd ions) (Papkovsky & O'Riordan, 2005).

Interesting alternatives to fluorescent indicators are represented by the dye-doped NPs, NPs made of organic polymer, silica-based NPs, dendrimers, quantum dots, noble metal NPs, fluorescent conjugated polymers and visible fluorescent proteins (Borisov&Klimant, 2008; Demchenko, 2010; Wolfbeis, 2005).

## 2.2 Immobilization techniques

A method for indicator immobilization into a suitable polymer matrix also has an important influence on the sensing characteristics. The following possibilities are usually applied:

- Impregnation - the indicator is immobilized in the polymer matrix through physical adsorption, chemisorption or electrostatic bonding. The polymer thin film is dipped into a saturated indicator solution and the solvent is then left to evaporate (Wolfbeis, 1991).
- Covalent bonding - the indicator is covalently bonded to the polymer matrix. This may be achieved by a) choosing the indicator that contains a functional group for covalent bonding to the polymer, which is at the same time insensitive for the target analyte, or b) polymerizing the indicator to certain monomers to form a copolymer (Baldini et al., 2006; Lobnik et al., 1998).
- Doping - the indicator is entrapped in the matrix during the polymerization process, where the indicator is simply added to the starting polymer solution (Lobnik et al., 1998).

Covalent immobilization enables the sensor having good stability (no leaching, crystallization and evaporation of components) and a longer operational lifetime. The disadvantage is that the covalent bonding often lowers the sensitivity for the analyte and

prolongs the response time of the sensor (Lobnik et al., 1998). Although the impregnation technique is widely used and lowpriced, it is used first of all for test strips and in gas sensors due to its low stability (indicator leaching). Doping is one of the most used immobilizations as it is not restricted to certain indicators and polymers. The sensor stability (in terms of indicator leaching) is better compared to impregnation and worse compared to covalent bonding. The response time is better than in covalent immobilization.

### 2.3 Polymers

Polymer chemistry is an extremely important part of optical sensor technology. Both the light guide (including its cladding and coating) and the sensing chemistry of indicator-mediated sensors are made from organic or inorganic polymers (Baldini et al., 2006; McDonagh et al., 2008; Orellana et al., 2005; Wolfbeis, 1991). The choice of polymer is governed by the permeability of the polymer for the analyte, its stability and availability, its suitability for dye immobilization, its compatibility with other materials used in the fabrication of optrodes, and its compatibility with the sample to be investigated. The polymer micro-environment has a strong effect on the spectral properties of the immobilized indicator, pKa value, luminescence lifetime, binding constant, etc. (Lobnik & Wolfbeis, 2001; Wolfbeis, 1991). Consequently, the choice of polymer material has a pronounced influence on the sensor performance and its characteristics, such as selectivity, sensitivity, working range, calibration, response time, (photo)stability (Orellana et al., 2005; Korent et al., 2007). The response time, for example, will be governed by the diffusion coefficients of the gases or liquids, and the quenching efficiency by the solubility of the gas in the polymer.

However, although most authors have compiled a considerable amount of data on various polymers, numerous new materials are available for which no data exist. It is also known that copolymers and polymer mixtures do not necessarily display the properties that may be expected from averaging the data of the pure components.

On the other hand, nano-sized (polymer) materials pose new technological and analytical challenges in many different sensor designs to improve industrial process monitoring (air and water quality), food-quality surveillance, and medical diagnostics, and to provide the reliable, real-time detection of chemical, biological, radiological and nuclear hazards for military and anti-terrorism applications – all this by enabling improved sensor characteristics, such as sensitivity, selectivity and response time, along with dramatically reduced size, weight and power requirements of the resulting monitoring devices compared to the conventional, macroscaled alternatives (Basabe-Desmots et al., 2007; Borisov & Klimant, 2008; Demchenko, 2010).

#### 2.3.1 Hydrophobic polymers

Silicones have excellent optical and mechanical properties, and unique gas solubility. The main applications of silicone materials is in sensors for oxygen and other uncharged quenchers, such as sulfur dioxide and chlorine, and as gas-permeable covers in sensors for carbon dioxide or ammonia. Silicones cannot be easily plasticized by conventional plasticizers, but form copolymers, which may be used instead. Blackened silicone is a most useful material for optically isolating gas sensors in order to make them insensitive to the optical properties of the sample (Baldini et al., 2006; Wolfbeis, 1991).

Poly(vinyl chloride) (PVC), poly(methyl methacrylate) (PMMA), polyethylene, poly(tetrafluoroethylene) (PTFE), polystyrene (PS), and ethylcellulose comprise another group of hydrophobic materials that efficiently reject ionic species (Amao, 2003). Except for polystyrene, they are difficult to chemically modify so that their function is confined to that of a "solvent" for indicators, or as a gas-permeable cover. For example, PMMA and PDMS have been selected as the optimum matrix for oxygen sensing.

### 2.3.2 Hydrophilic polymers

Hydrophilic polymers provide a matrix that corresponds to an aqueous environment. Hydrophilic supports are characterized by a large number of hydrogen-bridging functions, such as hydroxyl, amino, or carboxamide groups, or by anionic groups (mainly carboxyl and sulfo) linked to the polymer backbone. Typical examples are the polysaccharides (cellulose), polyacrylates, polyacrylamides, polyimines, polyglycols, and variety of so-called hydrogels. Depending on the degree of polymerization and cross-linking, they are water-soluble or water-insoluble. The ions can diffuse quite freely, but the possible water uptake (10-1000%) can cause significant swelling of the polymer. Swelling of the matrix affects the optical properties of the sensors and, consequently, the signal changes. They display poor compatibility with hydrophobic polymers, such as silicone and polystyrene. Most hydrophilic polymer membranes are easily penetrated by both charged and uncharged low-molecular-weight analytes, but not by large proteins, and have found widespread application as support for indicators (Baldini et al. 2006; Wolfbeis, 1991). Hydrophilic matrices have been widely used for pH sensing.

### 2.3.3 Hydrophobic/hydrophilic polymers

Glass is widely used for manufacturing optical fibres. Its surface may be made either hydrophilic or hydrophobic by treatment with a proper surface-modification reagent. Surface derivatization is usually performed with reagents, such as amino-propyl-triethoxysilane, which introduces a free amino group onto the surface of the glass to which dyes or proteins may be covalently attached. Glass does not measurably swell, but is difficult to handle because of its brittleness.

Sol-gel forms an attractive alternative to conventional glass (Baldini et al. 2006; Lobnik & Wolfbeis, 2001). By changing parameters, such as the sol pH, precursor type and concentration, water content, and curing temperature, materials of the desired porosity and polarity can be produced. The versatility of the process facilitates tailoring of the physicochemical properties of the material in order to optimize sensor performance. The basic process involves the hydrolysis and polycondensation of the appropriate metal alkoxide solution to produce a porous glass matrix. The reagent is entrapped in such a matrix and the analyte can diffuse to it. By altering its polarity, the sol-gel matrix makes it possible to sense either ions or gas molecules (Lobnik & Wolfbeis, 1998; Lobnik & Čajlaković, 2001; Murković, 2003; Pagliaro, 2009; Turel et al., 2008).

## 2.4 Effect of nanodimensions on sensor characteristics

The sensor characteristics can be tuned not only by the choice of the indicator and polymeric support but also by merely reducing the size (< 100 nm). This is because materials that are



smaller than the characteristic lengths associated with the specific phenomena often display new chemistry and new physics that lead to new properties that depend on size. Perhaps one of the most intuitive effects is due to the change in the surface-to-volume ratio. When the size of the structure is decreased, this ratio increases considerably and the surface phenomena predominate over the chemistry and physics in the bulk. Therefore, the sensor characteristics, such as sensitivity (Chu & Lo, 2009) and response time (Waich et al., 2008), can be dramatically improved.

Nanoparticles containing indicator dyes can either be used directly as nanosensors (NSs) or as the components of optical sensor materials. In the sensor matrix, more than one component can be encapsulated, thus allowing a synergistic approach to be employed (Aylott, 2003). Most of the NSs reported so far have used fluorophores as the sensitive and selective indicators. For making quantitative measurements in the intracellular environment, the so-called PEBBLE (Probes encapsulated by biologically localized embedding) NSs have been designed as they are small enough to be inserted into living cells with a minimum of physical perturbation (Buck et al., 2004). PEBBLES have many advantages over widely used fluorescence-dye-based methods, such as: a) the increased number of analytes that can be measured because NSs are not limited to using a single fluorophore and can utilize cooperative interactions between ionophores, enzymes, reporter dyes, etc. (e.g., pH-sensitive and oxygen-sensitive beads can be incorporated into one polymer), b) the matrix protects the intracellular environment from any potentially toxic effects of the sensing dye, c) the matrix protects the sensing dye from potential interferences in the cellular environment, e.g., non-specific binding proteins and organelles, d) no selective sequestration of the NSs into cellular compartments or leaking from, or being pumped out of, cells, e) enhanced ability to carry out ratiometric measurements, and f) the in-vitro calibration of NSs is valid for in-vivo measurements (Aylott, 2003).

NSs provide advantages, such as an improved sensitivity, response time and ability to perform in-vivo measurements. However, the down side of using “free” NSs for in-vivo measurements needs to be considered. The prime concern is the retention of these particles in the body and the harmful effect in the long run (Sounderya & Zhang, 2008) since NPs can be responsible for a number of material interactions that could lead to toxicological effects (Nel et al., 2006). In any case, the optical properties that can be controlled at the nanoscale are of great interest in the field of optical sensor designing (Borisov & Klimant, 2008). Some optical chemical NSs rely on quantum dots (Asefa et al. 2009), metal beads (Shtykov & Rusanova, 2008) and other materials; however, most of them make use of indicators embedded in polymer beads (Lapresta et al., 2009; Zenkl & Klimant, 2009) and sol-gels (Arduini et al., 2007; Hun & Zhang, 2007; Sun et al., 2006).

### 3. Selected applications

Optical chemical sensors provide the opportunity to continuously monitor chemical species and have thus found numerous applications in areas such as the chemical industry, biotechnology, medicine, environmental sciences, personal protection, etc. Books and reviews presenting various optical sensing schemes (fiber optics, capillary waveguides, microsystems and microstructures, refractive index-based, surface plasmon resonance-based, biosensing, etc.) and various applications (sensing gases, vapours, humidity, pH, ions, organic chemicals, certain bacteria, DNA, etc. in medical and chemical analyses, molecular biotechnology, marine

and environmental analysis, industrial production monitoring, bioprocess control, automotive industry) have been published in recent years. The most comprehensive studies include work by Baldini et al., 2006; Gauglitz, 2005; Gründler, 2007; McDonagh et al., 2008; Nagl & Wolfbeis, 2008; Wolfbeis, 2005; Wolfbeis, 2008.

The broad variety of applications of optical chemical sensors would deserve a special chapter devoted only to the applications. However, due to the limited space, we had to restrict our contribution to selected materials. Since the nano-world continues to rapidly enter our lives in many different ways, the following pages will survey the recently developed optical chemical nanosensors. The applications are selected for sensors or probes based on sol-gel and polymer NPs that have their dimensions  $\leq 100$  nm. Among the many optical methods employed in nanosensing, fluorescence has attracted particular attention because it is sensitive, offers several techniques to be used to explore various parameters that can serve as an analytical information; therefore, the luminescent approach is selected for the two types of nanoparticles mentioned.

### 3.1 Polymer-based nanoparticles

Polymer NPs are usually obtained by microemulsion polymerization. Microemulsions are clear, stable, isotropic liquid mixtures of oil, water and surfactant, sometimes in combination with a cosurfactant. The microemulsion polymerization of monomers may be achieved by incorporating a monomer in any of the water and oil phases of the system (Pavel, 2004). The two basic types of microemulsions, direct (oil dispersed in water, o/w) and reversed (water dispersed in oil, w/o) are frequently used. In w/o microemulsion nanodroplets of oil surrounded by the surfactant are dispersed in the continuous bulk water phase. The size of the synthesized particles is determined by the size of those droplets (Košak et al., 2004,2005).

NPs can also be prepared by the precipitation method, which is based on the use of two miscible solvents (Borisov et al., 2009; Higuchi et al., 2006). The nanobeads are formed by diluting the polymer solution with a poor solvent. Gradually, evaporation of the good solvent at room temperature causes precipitation of the polymer solute as fine particles. Using this method, NPs can be prepared from a variety of polymers (e.g., engineering plastics, biodegradable polymers and electro-conductive polymers, etc.). The diameter of the particles can be controlled by changing the concentration of the solution, and the mixing ratio of the good solvent and the poor solvent, respectively. It should be emphasized that this process does not require the addition of surfactants (and their subsequent removal) as in the case of NSs prepared via polymerization (Borisov et al., 2009).

An indicator can be added to the mixture of monomers to be entrapped in the bead during polymerization. Both physical (Borisov et al., 2009) entrapment and covalent (Sun et al., 2006) coupling are used. Physical entrapment of an indicator in NPs is preferred because of its simplicity and reproducibility. In contrast to bulk sensor films (typically several microns thick), in nanosensors many indicator molecules are located close to the surface so that leaching can become a serious problem. To avoid leaching, covalent binding can be used. However, in this case, both the dye and the beads require having a reactive group through which a covalent bond can be formed between the polymer and the indicator. This situation is often undesirable because excess reactive groups on the surface of the beads may compromise their properties and often make them more prone to aggregation (Borisov et al.,

2008b). Swelling is another widespread method for the encapsulation of indicators in NPs (Méallet-Renault, 2004; Frigoli et al., 2009). This method is only useful for hydrophobic materials that are not swellable in water. It is essential to use water-insoluble indicators for this method otherwise leaching can occur over time.

Nanosensors based on hydrophobic materials even allow the monitoring of hydrophilic species with acceptable response times (in contrast to monolithic films based on the identical composition), due to small diffusion distances. Polymers with polar properties (such as polyacrylonitrile) have a large surface-to-volume ratio and are therefore especially useful for ion sensing. Indicators of an amphiphilic nature are often located on the surface of the bead, allowing a response even to hydrophilic analytes.

### 3.2 Sol-gel based nanoparticles

Sol-gels (inorganic silica beads and organically modified silica - Ormosils) are very popular materials for designing optical nanosensors (Jain et al., 1998; Rossi et al., 2005; Shibata et al. 1997). This is due to the fact that the beads can easily be manufactured, are porous to allow an analyte to diffuse freely inside, are robust, and are biocompatible, making them suitable for intracellular measurements. Compared with polymer NPs, silica NPs possess several advantages. Silica NPs are easy to separate via centrifugation during particle preparation, surface modification, and other solution-treatment processes because of the higher density of silica (e.g., 1.96 g/cm<sup>3</sup> for silica vs. 1.05 g/cm<sup>3</sup> for polystyrene). Silica NPs are more hydrophilic and biocompatible, they are not subject to microbial attack, and no swelling or porosity change occurs with changes in the pH (Jain et al., 1998).

Nanoparticles based on sol-gel materials can be prepared by two general synthetic routes: the Stöber (Rossi et al., 2005; Shibata et al., 1997) and reverse microemulsion processes (Bagwe et al., 2004; Santra et al., 2005; Wang et al., 2005). In a typical Stöber-based protocol, a silica alkoxide precursor (such as tetraethyl orthosilicate, TEOS) is hydrolyzed in an ethanol and ammonium hydroxide mixture. The hydrolysis of TEOS produces silicic acid, which then undergoes a condensation process to form amorphous silica particles. In general, the lower the concentration of water and ammonia, the smaller are the particles. Indicators are typically entrapped inside the pores of the beads. However, that does not always prevent them from leaching into solution. Therefore, similar to the polymer beads, covalent coupling is often preferred.

Dye-doped silica NPs can also be synthesized by hydrolyzing TEOS in a reverse-micelle or water-in-oil (w/o) microemulsion system. In a typical w/o microemulsion system, water droplets are stabilized by surfactant molecules and remain dispersed in the bulk oil. The nucleation and growth kinetics of the silica are highly regulated in the water droplets of the microemulsion system, and the dye molecules are physically encapsulated in the silica network, resulting in the formation of highly monodispersed dye-doped silica NPs (Schmidt et al., 1999). Polar dye molecules are used in the w/o microemulsion system to increase the electrostatic attraction of the dye molecules to the negatively charged silica matrix, so that dye molecules are successfully entrapped inside the silica matrix. Water-soluble inorganic dyes, such as ruthenium complexes, can be readily encapsulated into nano-particles using this method (Brasola et al., 2003; Frasco & Chaniotakis, 2009; Méallet-Renault et al., 2004; Ramazzo et al., 2005). Various trapping methods can be used, such as introducing a

hydrophobic silica precursor (Tapeç et al., 2002), using water-soluble dextran-molecule-conjugated dyes, and synthesizing in acidic conditions (Frasco & Chaniotakis, 2009). The unique advantage of the w/o microemulsion method is that it produces highly spherical and monodisperse NPs of various sizes. It also permits the trapping of a wide variety of inorganic and organic dyes as well as other materials, such as luminescent quantum dots.

### 3.3 Core-shell systems for sensing chemistry

The core-shell nanostructures based on polymers and sol-gel materials are well known (Arduini et al., 2007; Burns et al., 2006; Frigoli et al., 2009; Sounderya & Zhang, 2008). The versatility matrix allows the sensing chemistry to be incorporated either into the core or into the shell of a bead, which for some NSs can slightly tune the sensitivity and helps to minimize interferences (Borisov et al., 2008a). Moreover, the encapsulation of two different fluorescent dyes in the core-shell structure, one analyte-sensitive dye and other analyte-insensitive incorporated into the core of the bead used as reference, allows ratiometric detection. This method overcomes the problems (fluctuations in light source intensity of the instrument, photobleaching of the analyte-sensitive dye, drifts in the optoelectronic setup and background fluorescence) associated with intensity-based measurements. Different approaches can be used to prepare ratiometric sensors, as shown in Fig. 3.

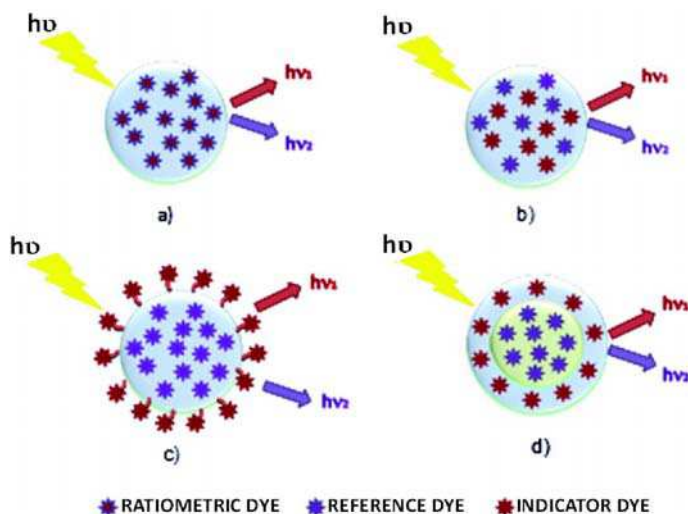


Fig. 3. Types of ratiometric approaches: a) ratiometric indicator dye is immobilized in the NP; b) indicator and reference dye are immobilized inside the NP; c) reference dye is immobilized (covalently attached or doped) in the NP, and the indicator dye is covalently bound to the NP surface; d) in the core-shell system, the reference dye is immobilized in the core and the indicator dye is immobilized in the shell.

### 3.4 Sensors based on polymer and sol-gel nanoparticles

In the following section the recently developed photoluminescence-based optical chemical NSs will be described, highlighting the most important sensor characteristics, such as the

indicator and matrix used, dynamic range, response time, limit of detection (LOD), indicator leaching, operational lifetime, interferences, etc.

### 3.4.1 Nanosensors for pH

The determination of pH has great importance for a wide range of applications, e.g., in the medical, environmental and biotechnological fields. The most common pH sensors are electrochemical devices (glass electrodes). Although they can be reliable analytical tools in many situations, their use for intracellular measurements is limited. In the field of biology and medicine, sensors able to monitor pH in real time are in great demand, as they can be used for the general understanding of biological processes and for biomedical diagnostics (Doussineau et al., 2009). Recently, a lot of work has been done on optical pH-sensitive micro- (Borisov et al., 2008a; Doussineau et al., 2009; Schulz et al., 2009; Hornig et al., 2008) and nano-sensors (Allard & Larpent, 2008; Burns et al., 2006; Gao et al., 2005; Gao et al., 2007; Kim et al., 2006; Peng et al., 2007; Sun et al., 2006). Here, the latter will be discussed, since they are less than 100 nm in size. Table 1 summarizes pH nanosensors.

Material	Indicator	pK <sub>a</sub> or dynamic range	Response time	Leaching	Operational lifetime	Effect of ionic strength	Ref.
Sol-gel (TEOS <sup>1</sup> )	RITC <sup>2</sup>	5.0-10.0	5 min	not given	not given	< 5% signal decrease	(Gao et al., 2005)
Sol-gel (TEOS)	Fluorescein	4-8	5 min	not given	5 weeks	< 4.5% signal decrease	(Gao et al., 2007)
Sol-gel (ICTES <sup>3</sup> )	NVP <sup>4</sup>	4-8	not given	not given	>6 months	not given	(Kim et al., 2006)
Sol-gel (TEOS, APTES <sup>5</sup> )	FITC <sup>6</sup>	4-7 0.05 pH units	1s	30% signal decrease	not given	not given	(Peng et al., 2007)
Sol-gel (TEOS, APTES)	FITC	6.4	not given	no leaching	not given	not given	(Burns et al., 2006)
Polystyren	FITC	5.6	few s	no leaching	>6 months	change in pK <sub>a</sub>	(Allard & Larpent, 2008)
Polyacrylamide	AF <sup>7</sup>	5.8-7.2	0.4 s	9% of the dye	not given	not given	(Sun et al., 2006)

<sup>1</sup>TEOS - Tetraethoxysilane

<sup>2</sup>RITC - Rhodamine- $\beta$ -Isothiocyanate

<sup>3</sup>ICTES - (3-isocyanatopropyl)triethoxysilane)

<sup>4</sup>NVP - Naphtalenylvinyl-pyridine

<sup>5</sup>APTES - Aminopropyltriethoxysilane

<sup>6</sup>FITC - Fluorescein isothiocyanate

<sup>7</sup>AF - Aminofluorescein

Table 1. Nanosensors/probes for pH.

Several sol-gel pH NSs were prepared using a microemulsion procedure (Allard & Larpent, 2008; Gao et al., 2005; Gao et al., 2007; Kim et al., 2006; Peng et al., 2007; Sun et al., 2006) and one by Stöber (Burns et al., 2006). Gao et al., 2007, designed pH sensors using the doping technique for the immobilization of indicators in sol-gel NPs. Although leaching can be a serious problem, in this case it was not tested. The pH dynamic range of sensing NPs ( $60 \pm 4$  nm) is between 5.0 and 10.0 (Gao et al., 2005) and between 4.0 and 8.0 for NSs ( $30 \pm 4$  nm) based on indicator Fluorescein (Gao et al., 2007). The response time (5 minutes) for both sensors is relatively long compared to other pH NSs (Table 1), even compared to macro-sized pH optical sensors (Jerónimo et al., 2007).

Kim et al., 2006, designed ormosil NPs ( $33 \pm 6$  nm) in which the ratiometric pH-responsive dye is covalently immobilized. Peng et al., 2007, and Burns et al., 2006, developed two-fluorophore-immobilized NPs sensors. The first author used fluorescein isothiocyanate as an indicator dye that was covalently crosslinked with the network formed by the hydrolysis of tetraethoxysilane and aminopropyltriethoxysilane, while tris(2,2'-bipyridyl) dichlororuthenium(II) hexahydrate (reference) was entrapped simultaneously inside the same NSs (42 nm) by electrostatic interaction. The second author synthesized a nanosensor (70 nm) via a modified Stöber method, incorporating a reference (tetramethylrhodamineisothiocyanate) and an indicator dye (fluorescein isothiocyanate) covalently bound to the matrix in the core-shell architecture. In this case the pH sensor is composed of a shell of covalently bound indicator-dye molecules surrounding a core of sequestered, covalently bound, reference-dye molecules. What is interesting is that although both authors used covalent immobilization, Peng et al., 2007, reported an extensive dye leakage.

Two different approaches have been used for the development of polymeric ratiometric pH nanosensors. In the first case a reference dye (Rhodamine B derivate) and a pH-sensitive dye (Aminofluorescein) were covalently embedded in polyacrylamide NPs (50 nm) (Sun et al., 2006). Allard & Larpent, 2008, presented a pH sensor based on polystyrene NPs, in the 20 nm range, with a hydrophobic reference dye (1,9-diphenylanthracene) embedded within the particle and the indicator dye (Fluorescein isothiocyanate) covalently attached to the surface. In this case the pH sensor may retain many of the drawbacks related to free fluorescent dyes because the indicator molecules are not protected from the cellular environment. It would be interesting to know, if the fotostability of the covalently attached indicator to the NP surface is improved compared to the free indicator.

### 3.4.2 Nanosensors for oxygen

Oxygen is undoubtedly one of the most important analytes. In particular, a determination of the dissolved oxygen is of utmost importance in many fields of science and technology (Papkovsky & O'Riordan, 2005), including biotechnology (Kostov et al., 2001), biology (Schmaelzlin et al., 2005), marine science (Schroeder et al., 2007), and in medicine (Kimura et al., 2007). Recent interest in methods for measuring dissolved oxygen has been focused mainly on optical sensors, due to their advantages over conventional amperometric electrodes in that they are faster and do not consume oxygen (McDonagh et al., 2002).

The principle behind the operation of these sensors is the reduction in the luminescent intensity as a consequence of the oxygen quenching of the emitting state. The sensor optode,

either in typical microparticles type (Borisov et al., 2008a; Waich et al., 2008) or in recent NP type (Borisov et al., 2009; Cywinski et al., 2009), consists of a dye entrapped in a matrix with a high permeability to oxygen. Borisov et al., 2009, showed that different polymer NPs (size 44–55 nm), depending on their gas permeability, embedded with iridium (III) coumarin, could be used as oxygen NSs. However, the characterisation of these sensors should be included. Cywinski et al., 2009, prepared ratiometric polystyrene-based oxygen NSs ( $20.9 \pm 7.1$  nm). Platinum(II)mesotetra(pentafluorophenyl)porphine was used as an indicator dye, whereas N,N-bis(1-hexylheptyl)perylene-3,4:9,10-bis-(dicarboximide) was used as a reference dye.

### 3.4.3 Nanosensors for ions

Table 2 summarizes the recently developed ion NSs. Lead ( $\text{Pb}^{2+}$ ) is one of the most toxic heavy metals, and it is particularly dangerous in terms of its effects on children. Therefore, the determination of lead in low concentrations is important. Arduini et al., 2007, developed a fluorescent nanosensor for the detection of  $\text{Pb}^{2+}$  ions. Silica core-shell NPs were produced from 50 nm diameter “pure” silica cores and a 5-nm-thick shell in which the indicator dansyl dye was covalently linked to a silica network. Then the surface of the shell was functionalized with (mercaptopropyl) triethoxysilane. Surface thiol groups play a key role in the recognition of the analyte. Selectivity tests show that  $\text{Cu}^{2+}$  is a serious interferent. On the other hand, no effect is observed after the addition of  $\text{Zn}^{2+}$ ,  $\text{Ca}^{2+}$ , and  $\text{Mg}^{2+}$ , while  $\text{Ni}^{2+}$  and  $\text{Co}^{2+}$  produce much less quenching than  $\text{Pb}^{2+}$ .

Copper ( $\text{Cu}^{2+}$ ) is an essential trace element that is required in various biological processes (hemopoiesis, metabolism, growth, and immune system (Uauy et al., 1998)). On the other hand, excess  $\text{Cu}^{2+}$  concentrations are extremely toxic. The detection of trace amounts of copper ions is of increasing importance in light of its environmental and biomedical implications. NSs for the detection of  $\text{Cu}^{2+}$  ions typically combine two components: a metal chelating molecule designed to bind the target ion selectively and a fluorophore as a readout system. The chelating molecules and the fluorophore are both covalently linked on to the surface of the NP (Brasola et al., 2003; Ramazzo et al., 2005) or the fluorophore is entrapped inside the NP (Méallet-Renault et al., 2004; Frigoli et al., 2009). The use of two different metal chelating ligands, picolinamide (Brasola et al., 2003) and (2-pyridinmethyl)-glycinamide (Ramazzo et al., 2005), and the same fluorescent dye (danslyamide) for the surface modification of silica NPs were reported. Méallet-Renault et al., 2004, described the concept of associating an efficient fluorescent reporter, a BODIPY derivative, and an excellent metal-chelating receptor, cyclam, in polymer NPs. The hydrophobic dye is entrapped within the particle core and the receptor, covalently linked to the polymer backbone, is mainly located near the surface. The detection is based on the quenching of fluorescence by energy transfer from the dye to the receptor-target complex.

Core-shell-type dual-fluorescent NPs (NPs) in the 16-nm-diameter range with a selective ligand (cyclam) attached to the surface and two fluorophores, 9,10-diphenyl-anthracene (donor, D) and pyromethene PM567 (acceptor, A), embedded within the polymer core were synthesized (Frigoli et al., 2009). Dual-dye-doped fluorescent NPs permit the design of cascade FRET-mediated sensing devices. The two sequential FRET processes, the energy transfer from D to A, and quenching of the resulting sensitized emission of A by copper complexes that are formed at the NP surface, provide an efficient means to sense

copper ions by monitoring the quenching of the acceptor dye upon irradiation at the donor excitation wavelength. This sensor is highly selective towards other divalent cations. Zheng et al., 2010, have developed a  $\text{Cu}^{2+}$  sensor based on a fluorescent ligand (N-(quinoline-8-yl)-2-(3-triethoxysilyl-propylamino)-acetamide) that acts as both a binding and readout system.

Zinc ( $\text{Zn}^{2+}$ ) is the second most abundant trace element in humans after iron. Most of the  $\text{Zn}^{2+}$  found in the body is bound to proteins such as carbonic anhydrase or zinc finger proteins. Zinc has been implicated in Alzheimer's and Parkinson's disease (Cuajungco & Lees, 1997; Frederickson et al., 2000) and as a neuromodulator (Choi & Koh, 1998). Since the full extent of zinc's purpose in the body remains unclear, the development of nanosensors is needed to further elucidate the role of zinc in vivo. Sumner et al., 2002, designed a polyacrylamide PEBBLE sensor, containing immobilized Newport Green as the indicator dye and Texas Red-dextran as the reference dye. The maximum response to zinc (percentage increase in the "intensity ratio") is 50%, which is less than observed with the Newport Green dye in solution (increase of approx. 250%). It is obvious that the matrix is affecting the indicator dye's sensitivity, but is on the other hand preventing the indicator dye from reacting to non-specific bindings of proteins (ex. bovine serum albumin). This is a prime advantage of the PEBBLES compared to free dyes, especially for cellular analysis. Teolato et al., 2007, selected the 6-methoxy-8-(p-toluensulfonamido)-quinoline (TSQ) as the active unit for the preparation of  $\text{Zn}^{2+}$  sensing silica NPs via the Stöber-Van Blaaderen procedure. The Coumarin 5 was used as a reference dye covalently linked to a silica network. The sensor suffers from the  $\text{Cu}^{2+}$  interferences and, to a minor extent, from  $\text{Cd}^{2+}$ .

Iron ( $\text{Fe}^{3+}$ ) is an integral metal ion in several physiological processes involving electron transfer and oxidation. Numerous enzymes use  $\text{Fe}^{3+}$  as a cofactor for hydroxylation, oxygen transport, DNA synthesis, etc. (Frausto da Silva & Williams, 1991). Because of iron's vital role in a number of proteins, deficiency during the developmental stages can lead to an irreversible loss of motor skills and has been linked to behavioral alterations in iron-deficient rats (Burdo & Connor, 2003). The accumulation of iron in the central nervous system has been implicated in a number of diseases. Therefore, the development of sensors that allow in-situ measurements would be beneficial. A PEBBLE sensor based on Alexa Fluor 448 (indicator dye) and Texas Red (reference) immobilized in polyacrylamide NPs for  $\text{Fe}^{3+}$  detection has been introduced (Sumner & Kopelman, 2005). What is surprising is that the reference dye is quenched by 20% in the presence of 1  $\mu\text{M}$  copper.

Changes in intracellular ion concentrations accompany many processes in living cells, including transport, signalling, and enzyme function (Nuccitelli, 1994). A magnesium-sensitive PEBBLE, which contains immobilized Coumarin 343 as the indicator dye, and Texas Red-dextran as a reference dye, has been reported (Park et al., 2003). The interference from calcium is a major complication of current strategies aimed at the measurement of measuring magnesium concentrations in biological environments (Gotoh et al., 1999). The results show that Coumarin 343 is insensitive to  $\text{Ca}^{2+}$ . A fluorescence-based calcium nanosensor was described (Hun & Zhang, 2007) that exploits silica NPs doped with calcein as an indicator dye for  $\text{Ca}^{2+}$  determination in blood serum. It is surprising that the effect of pH on the fluorescent intensity of the nanosensor was not tested in the clinically important pH range (6.6-7.8).



Analyte	Material	Indicator	LOD (M)	Response time	Leaching	Operational lifetime
Pb <sup>2+</sup>	Sol-gel (TEOS, MPS <sup>8</sup> )	Dansyl-amide	1.1×10 <sup>-6</sup>	not given	not given	>30 days
Cu <sup>2+</sup>	Sol-gel	Dansyl-amide	not given	not given	not given	not given
Cu <sup>2+</sup>	Sol-gel	Dansyl-amide	3.0×10 <sup>-8</sup>	not given	not given	not given
Cu <sup>2+</sup>	latex	BODIPY-ciklomat	5×10 <sup>-9</sup>	not given	no leaching	not given
Cu <sup>2+</sup>	Styren	DAP <sup>9</sup> -PM567 <sup>10</sup> -ciklomat	20×10 <sup>-9</sup>	not given	no	>6 months
Cu <sup>2+</sup>	Sol-gel	QIOEt <sup>11</sup>	3.8×10 <sup>-7</sup>	not given	not given	not given
Zn <sup>2+</sup>	Polyacrylamide	Newport Green	4×10 <sup>-6</sup>	<4 s	intensity signal drop for 3% aft. 2 days	not given
Zn <sup>2+</sup>	Sol-gel (TEOS)	TSQ <sup>12</sup>	2.6×10 <sup>-7</sup>	not given	not given	not given
Fe <sup>3+</sup>	Polyacrylamide	Alexa Fluor 448	1×10 <sup>-6</sup>	10 min	not given	not given
Mg <sup>2+</sup>	Polyacrylamide	Coumarin 343	340×10 <sup>-6</sup>	<4 s	intensity signal drop for less than 11.8 % after 24-h	not given
Ca <sup>2+</sup>	Sol-gel (TEOS)	calcein	7.48×10 <sup>-8</sup>		intensity signal drop for 17% after 12-h	not given

<sup>8</sup>MPS - (mercaptopropyl)triethoxysilane

<sup>9</sup>DAP - 9,10-diphenyl-anthracene

<sup>10</sup>PM567 - pyromethene

<sup>11</sup>QIOEt - N-(quinoline-8-yl)-2-(3-triethoxysilyl-propylamino)-acetamide

<sup>12</sup>TSQ - 6-methoxy-8-(p-toluensulfonamido)-quinoline

Table 2. Nanosensors/probes for ions.

Analyte	Material	Indicator	LOD (M)	Response time	Leaching	Operational lifetime	Interference
naproxen	Polyacryl-amide	mDMASP <sup>13</sup>	0.5×10 <sup>-3</sup>	not given	not given	not given	cAMP
glucose	Sol-gel (TEOS <sup>1</sup> , APTES <sup>9</sup> )	Eu complex	4.4×10 <sup>-6</sup>	20 min	not given	not given	no in t range o char
dipicoli-nic acid	Sol-gel (TEOS, APTES)	Eu-EDTA <sup>15</sup> complex	0.2×10 <sup>-9</sup>	30 s	not given	not given	n
dipicoli-nic acid	Sol-gel (TEOS, APTES)	Tb-EDTA complex	10.3×10 <sup>-9</sup>	not given	not given	not given	n

<sup>13</sup>mDMASP - (E)-4-[4-(dimethylamino)styryl]-1-[4-(methacryloyloxyethyl)benzyl]pyridinium chloride  
<sup>14</sup>cAMP - Adenosine 3:5-cyclic monophosphate  
<sup>15</sup>EDTA - Ethylenediamine tetracetic acid

Table 3. Nanosensors/ probes for other molecules

A nonenzymatic sensor for glucose based on amino-functionalized luminescent silica NPs (LSNPs) doped with the europium(III) mixed complex, Eu(TTA)<sub>3</sub>phen with 2-thenoyltrifluoroacetone (TTA) and 1,10-phenanthroline(phen) was reported (Gao et al., 2009). Lapresta et al., 2009, developed a fluorescent polyacrylamide nanosensor for the determination of non-steroidal, anti-inflammatory drug naproxen. The fluorescent monomer (E)-4-[4-(dimethylamino)styryl]-1-[4-(methacryloyloxymethyl)benzyl]-pyridinium chloride (mDMASP) was used as an indicator. Upon indicator immobilization in polymer NPs the sensitivity and LOD were reduced. The high LOD thus enables those NSs only to be used in wastewater or industrial routine tests. For the detection of dipicolinic acid, a chemical marker for bacterial spores, silica NSs have been developed based on Eu-complex (Ai et al., 2009) and Tb-complex (Taylor & Lin, 2009). In both cases the EDTA ligand is covalently attached to the surface of silica NPs doped with reference dyes, such as fluorescein isothiocyanate (Ai et al., 2009) or Ru-complex (Taylor & Lin, 2009). Interferences resulting from the nonselective binding of aromatic ligands (benzoic acid, m-phthalic acid, o-phthalic acid) to a Tb-complex should be tested. Moreover, it is surprising that a Ru-complex, a common indicator for oxygen sensors (Li et al., 2007; Wu et al., 2010; Zhang et al., 2008) has been used as a reference, but the possible effect of oxygen on its fluorescence properties has not been tested.

#### 4. Summary and trends

The design of an optical sensor is primarily governed by the application for which the sensor is to be developed. And because of the existence of many optical principles as well as of many sensor components that can be altered, optical chemical sensors (OCSs) can be applied to a huge number of applications. OCSs may either be very simple and cost-effective devices or enable advanced multisensor applications. In part by the sensitive layers, it is selectivity, sensitivity, stability, and reversibility that are the requirements for sensor systems that must be provided. Besides, the user normally expects the following sensor characteristics: a relatively high signal-to-noise ratio, short response times, low limits of detection, high sensitivity, low cost, a possibility for on-line, in-situ applications.

However, the most critical limitations of optical sensors result from unavailable or inadequate (unspecific) molecular probes. The detection limit that in certain cases is expected to lie in the  $10^{-13}$  to  $10^{-14}$  mol/L concentration range could also be improved. A preferred solution for improving the selectivity would be the use of sensor arrays (Paolesse et al., 2011), rather than a single sensor. It additionally turns out that most of the improvements that can be expected in optical detection methods are in the area of sensitive layers, which also have to provide reversibility and greater stability.

Another step in achieving improvements in sensor characteristics is the use of nanoscale materials for OCS, which has emerged as one of the most important research areas over the past decade. Nanomaterials exhibit highly tunable size- and shape-dependent chemical and physical properties show a unique surface chemistry, thermal and electrical properties, a high surface area and a large pore-volume per mass unit area. Because of their unique and advantageous features they can help to improve the sensitivity, response time and detection limit of sensors. Nevertheless, although zero-dimensional materials are applied in sensor design, the factors such as matrix, indicator and immobilization technique are still indispensable tools in achieving the desired sensor's characteristics.

However, as more and more types of smart nanomaterials with unique and tunable properties continue to be invented, increasing numbers of efficient and selective NSs are expected to emerge. Sensors capable of detecting very low analyte concentrations for non-invasive and non-degenerative analyses in a wealth of different promising applications will be produced. It is also believed that the cost of individual sensors will be radically reduced and sensors will be more easy to use for the end-users. Other important challenges, which are likely to move future trends in the research and development of OCS, such as the development of fully engineered monitoring systems requiring modules to collect the target molecules and bring them to the sensor, the nanosensor array to carry out the detection, a mechanism to refresh and regenerate the nanosensor as needed, and data-management capabilities to communicate and display the information as well as the sensors' long-term stability, wireless networks, optical materials and components, are expected to be fulfilled.

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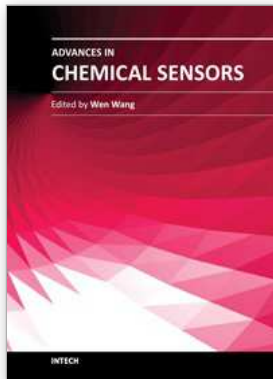
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The chemical sensor plays an essential role in the fields of environmental conservation and monitoring, disaster and disease prevention, and industrial analysis. A typical chemical sensor is a device that transforms chemical information in a selective and reversible way, ranging from the concentration of a specific sample component to total composition analysis, into an analytically useful signal. Much research work has been performed to achieve a chemical sensor with such excellent qualities as quick response, low cost, small size, superior sensitivity, good reversibility and selectivity, and excellent detection limit. This book introduces the latest advances on chemical sensors. It consists of 15 chapters composed by the researchers active in the field of chemical sensors, and is divided into 5 sections according to the classification following the principles of signal transducer. This collection of up-to-date information and the latest research progress on chemical sensor will provide valuable references and learning materials for all those working in the field of chemical sensors.

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