ELSEVIER

Sensors and Actuators B 54 (1999) 3–15

SENSORS AND ACTUATORS B CHEMICAL

Surface plasmon resonance sensors: review

Jiří Homola [a,*,1], Sinclair S. Yee [a], Günter Gauglitz [b]

[a] *Electrical Engineering Department, University of Washington, Box 352500, Seattle, WA 98195, USA*
[b] *University of Tübingen, Institute of Physical and Theoretical Chemistry, Auf der Morgenstelle 8, D-72076, Tübingen, Germany*

Abstract

Since the first application of the surface plasmon resonance (SPR) phenomenon for sensing almost two decades ago, this method has made great strides both in terms of instrumentation development and applications. SPR sensor technology has been commercialized and SPR biosensors have become a central tool for characterizing and quantifying biomolecular interactions. This paper attempts to review the major developments in SPR technology. Main application areas are outlined and examples of applications of SPR sensor technology are presented. Future prospects of SPR sensor technology are discussed. © 1999 Elsevier Science S.A. All rights reserved.

Keywords: Surface plasmon resonance; Optical sensor; Biosensor; Chemical sensor

1. Introduction

During the last two decades we have witnessed remarkable research and development activity aimed at the realization of optical sensors for the measurement of chemical and biological quantities. First optical chemical sensors were based on the measurement of changes in absorption spectrum and were developed for the measurement of CO_2 and O_2 concentration [1]. Since then a large variety of optical methods have been used in chemical sensors and biosensors including ellipsometry, spectroscopy (luminescence, phosphorescence, fluorescence, Raman), interferometry (white light interferometry, modal interferometry in optical waveguide structures), spectroscopy of guided modes in optical waveguide structures (grating coupler, resonant mirror), and surface plasmon resonance. In these sensors a desired quantity is determined by measuring the refractive index, absorbance and fluorescence properties of analyte molecules or a chemo-optical transducing medium [2–5].

The potential of surface plasmon resonance (SPR) for characterization of thin films [6] and monitoring processes at metal interfaces [7] was recognized in the late seventies. In 1982 the use of SPR for gas detection and biosensing was demonstrated by Nylander and Liedberg [8,9] [10]. Since then SPR sensing has been receiving continuously growing attention from scientific community. Development of new SPR-sensing configurations as well as applications of SPR-sensing devices for the measurement of physical, chemical and biological quantities have been described. A great deal of work has been done in the exploitation of SPR for optical biosensing—more than 75% of the research papers in Fig. 1 deal with applications of SPR to biomolecular interaction examination. In this area, SPR, as a surface-oriented method, has shown a great potential for affinity biosensors, allowing real-time analysis of biospecific interactions without the use of labeled molecules. The SPR sensor technology has been commercialized by several companies and has become a leading technology in the field of direct real-time observation of the biomolecular interactions.

2. Surface plasmon resonance

The phenomenon of anomalous diffraction on diffraction gratings due to the excitation of surface plasma waves was first described in the beginning of the twentieth century by Wood [11]. In the late sixties, optical excitation of surface plasmons by the method of attenuated total reflection was demonstrated by Kretschmann [12] and Otto [13]. Since then, surface plasmons have

* Corresponding author.
[1] On leave from Institute of Radio Engineering and Electronics, Chaberská 57, CZ-18251 Prague, Czech Republic.

PII: S0925-4005(98)00321-9

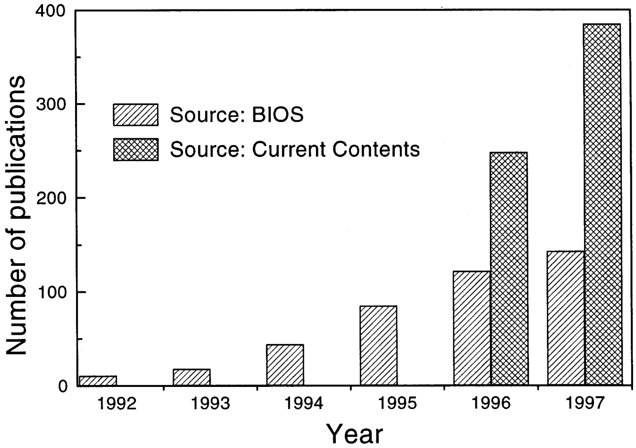

Fig. 1. Number of research papers on SPR sensors listed by scientific databases.

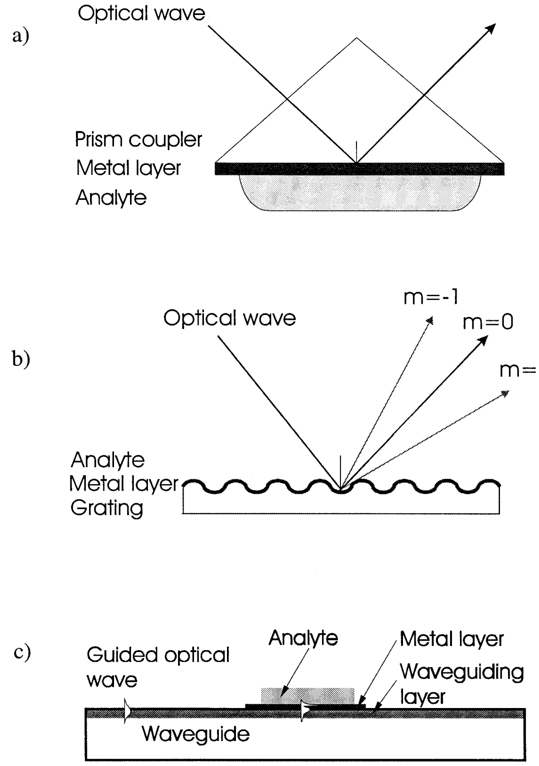

Fig. 2. Most widely used configurations of SPR sensors: (a) prism coupler-based SPR system (ATR method); (b) grating coupler-based SPR system; (c) optical waveguide-based SPR system.

been intensively studied and their major properties have been assessed [14,15].

Surface plasmon resonance is a charge-density oscillation that may exist at the interface of two media with dielectric constants of opposite signs, for instance, a metal and a dielectric. The charge density wave is associated with an electromagnetic wave, the field vectors of which reach their maxima at the interface and decay evanescently into both media. This surface plasma wave (SPW) is a TM-polarized wave (magnetic vector is perpendicular to the direction of propagation of the SPW and parallel to the plane of interface). The propagation constant of the surface plasma wave propagating at the interface between a semi-infinite dielectric and metal is given by the following expression:

$$\beta = k\sqrt{\frac{\varepsilon_m n_s^2}{\varepsilon_m + n_s^2}} \tag{1}$$

where k denotes the free space wave number, ε_m the dielectric constant of the metal ($\varepsilon_m = \varepsilon_{mr} + i\varepsilon_{mi}$), and n_s the refractive index of the dielectric [14]. As may be concluded from Eq. (1), the SPW may be supported by the structure providing that $\varepsilon_{mr} < -n_s^2$. At optical wavelengths, this condition is fulfilled by several metals [16] of which gold and silver are the most commonly used. For these metals a comparison of the main characteristics of SPW propagating along the interface between water and the surface plasmon active metal layer is given in Table 1.

Owing to high loss in the metal, the SPW propagates with high attenuation in the visible and near-infrared spectral regions. The electromagnetic field of an SPW is distributed in a highly asymmetric fashion and the vast majority of the field is concentrated in the dielectric. An SPW propagating along the surface of silver is less attenuated and exhibits higher localization of electromagnetic field in the dielectric than an SPW supported by gold.

Table 1
Major characteristics of surface plasma waves (SPW) at the metal–water interface[a]

Metal layer supporting SPW	Silver		Gold	
Wavelength	$\lambda = 630$ nm	$\lambda = 850$ nm	$\lambda = 630$ nm	$\lambda = 850$ nm
Propagation length (μm)	19	57	3	24
Penetration depth into metal (nm)	24	23	29	25
Penetration depth into dielectric (nm)	219	443	162	400
Concentration of field in dielectric (%)	90	95	85	94

[a] Optical constants of gold and silver were taken from [16].

3. Concept of surface plasmon resonance optical chemical sensors and biosensors

Generally, an SPR optical sensor comprises an optical system, a transducing medium which interrelates the optical and (bio)chemical domains, and an electronic system supporting the optoelectronic components of the sensor and allowing data processing. The transducing medium transformes changes in the quantity of interest into changes in the refractive index which may be determined by optically interrogating the SPR. The optical part of the SPR sensor contains a source of optical radiation and an optical structure in which SPW is excited and interrogated. In the process of interrogating the SPR, an electronic signal is generated and processed by the electronic system. Major properties of an SPR sensor are determined by properties of the sensor's subsystems. The sensor sensitivity, stability, and resolution depend upon properties of both the optical system and the transducing medium. The selectivity and response time of the sensor are primarily determined by the properties of the transducing medium.

4. Surface plasmon resonance-sensing configurations

As the propagation length of SPW is very limited (Table 1), the sensing action is performed directly in the area where the SPW is excited by an optical wave. The optical system used to excite the SPW is simultaneously used for the interrogation of SPR. Therefore, the sensitivity of SPR sensors cannot benefit from increasing the interaction length of the sensor as it is common in sensors employing guided modes of dielectric waveguides. As follows from Eq. (1), the propagation constant of SPW is always higher than that of optical wave propagation in the dielectric and thus the SPW cannot be excited directly by an incident optical wave at a planar metal–dielectric interface. Therefore the momentum of the incident optical wave has to be enhanced to match that of the SPW. This momentum change is commonly achieved using attenuated total reflection (ATR) in prism couplers and optical waveguides, and diffraction at the surface of diffraction gratings (Fig. 2).

As the excitation of SPW by optical wave results in resonant transfer of energy into the SPW, SPR manifests itself by resonant absorption of the energy of the optical wave. Owing to the strong concentration of the electromagnetic field in the dielectric (an order of magnitude higher than that in typical evanescent field sensors using dielectric waveguides) the propagation constant of the SPW, and consequently the SPR condition, is very sensitive to variations in the optical properties of the dielectric adjacent to the metal layer supporting SPW (transducing medium). Therefore, variations in the optical parameters of the transducing medium can be detected by monitoring the interaction between the SPW and the optical wave.

The following main detection approaches have been commonly used in SPR sensors:
1. measurement of the intensity of the optical wave near the resonance [9,8,17],
2. measurement of the resonant momentum of the optical wave including angular [18,19] and wavelength interrogation of SPR [20–22].

Recently attempts to exploit changes in polarization [23] and phase [24,25] associated with SPR have been also reported. Today, approaches based on the measurement of the resonant momentum of the optical wave are prevalent primarily owing to the inherent

Table 2
Theoretical sensitivity to variations in the refractive index of analyte and resolution of model SPR sensing structures: (a) prism-based system (BK7 glass—gold 50 nm thick—analyte with the refractive index of 1.32); (b) grating-based system (grating with the pitch and depth of 800 and 70 nm, respectively—gold—analyte with the refractive index of 1.32)[a]; optical constants of gold were taken from [16]

Detection approach	Angular interrogation		Wavelength interrogation		Intensity measurement	
Optical system used for excitation of SPW	Sensitivity (deg RIU^{-1})/ Resolution (RIU)[b]		Sensitivity (nm RIU^{-1})/ Resolution (RIU)[c]		Sensitivity (% RIU^{-1})/ Resolution (RIU)[d]	
	$\lambda = 630$ nm	$\lambda = 850$ nm	$\lambda = 630$ nm	$\lambda = 850$ nm	$\lambda = 630$ nm	$\lambda = 850$ nm
Prism coupler-based SPR sensor	191 5×10^{-7}	97 1×10^{-6}	970 2×10^{-5}	13 800 1×10^{-6}	3900 5×10^{-5}	15 000 1×10^{-5}
Grating coupler-based SPR sensor	43 2×10^{-6}	39 2×10^{-6}	309 6×10^{-5}	630 3×10^{-5}	1100 2×10^{-4}	4400 5×10^{-5}

[a] The following SPR instrumentation accuracies were assumed:
[b] 1×10^{-4} deg for angular resolution [10].
[c] For wavelength interrogation, 0.02 nm [32].
[d] For the intensity measurement, 0.2% of the optical power [33].

simultaneous multiple data measurement which offers better signal to noise figures than simple intensity measurements.

Sensitivity of SPR sensors is defined as the derivative of the monitored SPR parameter (e.g. resonant angle or wavelength) with respect to the parameter to be determined (refractive index, thickness of a thin overlayer, concentration, etc.). The sensitivity of SPR-sensing devices has been widely studied [26–30]. The sensitivity of SPR angular interrogation-based sensors to changes in the refractive index has been found to increase with decreasing operation wavelength [30], conversely, the sensitivity of SPR refractive index sensors using wavelength interrogation and intensity measurement increases with the wavelength [29]. In addition, SPR sensors based on wavelength interrogation and intensity measurement may benefit from using silver as an SPR active metal instead of gold [28,29]. The sensitivity of SPR sensors using ATR prism couplers is higher than that of SPR devices based on grating couplers [30]. The sensitivity of SPR sensors to changes in the thickness of a thin overlayer, which is relevant to most SPR biosensors has been shown to follow essentially the same trends [26,29]. Sensor *resolution* is the minimum change in the parameter to be determined which can be resolved by a sensing device. The sensor resolution depends upon the accuracy with which the monitored SPR parameter can be determined by the specific sensing device and as such is limited by sensor system noise. Recently, the noise in SPR-sensing devices has been systematically studied including an analysis of the influence of temperature, the light source, and photodetector noise on SPR sensor resolution [35,36]. Table 2 presents the sensor sensitivity for different detection approaches for model prism and grating-based SPR-sensing devices calculated using Fresnel equations for the prism-based system and the rigorous coupled-wave theory for the grating-based system [34]. To illustrate the relationship between the sensor resolution and the accuracy with which the measured SPR parameter has to be determined, the sensor resolution has been calculated by dividing the assumed accuracy of the SPR parameter (using values reported in the literature) by the sensitivity of a particular detection approach. It should be noted that the accuracy with which the measured SPR parameter can be determined is very dependent upon the experimental circumstances and the degree of optimization of the particular sensor and therefore the ultimate resolution of the particular SPR sensor may differ from that of the considered model systems. Another important parameter of an SPR sensor is its *operating range*, which is the range of values of the parameter to be determined, which can be measured by the sensor. While the operating range of intensity-measurement-based SPR sensors is naturally limited due to the limited width of the SPR dip, the operating range of angular and wavelength interrogation-based SPR sensors may be made much wider. In principle, the operating range of these sensors is determined by the detection system, more specifically by the angular or spectral range covered by the optical system-angular position detector array or spectrum analyzer, respectively. However, there is a trade-off between the dynamic range and resolution of these sensors. (If, for instance, SPR sensors based on angular and wavelength interrogation using 1000-element detector arrays are required to cover refractive index range of about 5×10^{-2} RIU and attain resolution of 1×10^{-5} RIU, the position of SPR must be determined with the accuracy better than 0.2 of a detector element).

Inherently, the SPR method detects 'integral' changes in the refractive index in the vicinity of the surface supporting SPW and generally does not allow quantifying spatial distribution of the refractive index. While the effects of background refractive index variations (e.g. due to temperature changes) can be effectively suppressed in multichannel SPR detection schemes, for the determination of the transducing medium refractive index spatial profile, the SPR method needs to be combined with another sensing technique which provides complementary information necessary for reconstructing the refractive index profile such as spectroscopy of guided modes in optical waveguides [37]. This method has been used for studying the process of diffusion of vapor molecules in a thin polymer layer [38]. The special problem of determining optical properties (refractive index and thickness) of homogeneous thin transparent films has been widely studied [6,39–42]. Theoretically, the desired parameters of thin films may be determined by fitting a single measurement of the angular reflectivity at a fixed wavelength. However, such a measurement requires very accurate data obtained on a well-characterized system to produce accurate results [40]. The uncertainty in the determined parameters may be reduced by combining two sets of measurements which were obtained for different refractive indices of the superstrate [42] or at different wavelengths [39].

4.1. Surface plasmon resonance sensors using attenuated total reflection optical prism couplers

Particularly the Kretschmann geometry of ATR method has been found to be very suitable for sensing and has become the most widely used geometry in SPR sensors. In this configuration a light wave is totally reflected at the interface between a prism coupler and a thin metal layer (of the thickness of about 50 nm) and excites an SPW at the outer boundary of the metal by evanescently tunneling through the thin metal layer. All the main detection approaches have been demonstrated in SPR prism-based sensors: measurement of the intensity of the reflected light wave [8,9], measurement of the resonant angle of incidence of the light wave [18,19], measurement of the resonant wavelength of the incident light wave [20]. Prism-based SPR sensors using angular interrogation have been extensively studied at Linköping University (Sweden) [19] and by BIAcore [31,43]. A refractive index resolution better than 3×10^{-7} RIU has been accomplished [44]. An earlier-developed wavelength interrogation-based SPR sensor attained a sensitivity of about 3200 nm RIU^{-1}, compensating for operation in the low sensitivity spectral region around 640 nm by using silver as SPR active medium. This approach has been further optimized leading to sensor sensitivity of about 8000 nm RIU^{-1} and noise of 0.02 nm [32]. Generally, the bulk prism-based SPR devices provide a great deal of flexibility in terms of the analyte refractive index covered. The use of high quality bulk optics allows for the development of SPR systems with limited optical noise making high resolution measurement possible. The bulk optical ATR configurations are attractive for development of multichannel SPR-sensing devices (e.g. 4-channel system based on angular interrogation by BIAcore [43], 16-channel system using intensity measurement [45]).

Miniaturized SPR sensors using the ATR method have been developed as an alternative to laboratory SPR systems to allow for the development of mobile, compact, and cost-effective sensing devices with potential for field applications. A miniaturized intensity SPR sensor has been reported by Vidal [17] which used the ATR method in a special design sensing element. An alternative to a prism-based SPR sensor with a convergent input light beam has been described by Foster [46] who proposed to replace a conventional prism coupler with a rectangular thin glass substrate with an SPR active metal layer. SPW is excited by a convergent beam of monochromatic light and the SPR angular position is determined using a CCD array. Another interesting concept is an SPR-sensing platform in which an SPW is excited on a thin glass lightguide by a white light at multiple angles, as proposed by Karlsen [47]. Recent study of this sensing geometry [48] has shown that this configuration is potentially capable of supporting multiple sensing channels. A resolution of about 4×10^{-5} RIU was achieved with this type of sensor [49]. Basically the same approach has been adopted for the development of a planar SPR probe [50] with about the same achieved sensor resolution. Another configuration of an SPR probe has been developed which utilizes a multireflection propagation of white light within a glass substrate coated with an SPR active metal layer [51]. Resolution as high as 4×10^{-5} RIU has been achieved with this type of SPR sensor [51]. Another setup for SPR sensing which integrates a light source, a detector and an optical system for excitation and interrogation of SPW into a single component has been developed by Texas Instruments [52]. This system relies on the detection of the angular position of SPR using a divergent light beam and a CCD array. With an incorporated temperature sensor a resolution of 1×10^{-5} RIU has been achieved [53].

4.2. Surface plasmon resonance sensors using grating couplers

If a metal–dielectric interface is periodically distorted, the incident optical wave is diffracted forming a series of beams directed away from the surface at a variety of angles [54]. The component of momentum of these diffracted beams along the interface differs from that of the incident wave by multiples of the grating wave vector. If the total component of momentum along the interface of a diffracted order is equal to that of the SPW, the optical wave may couple to the SPW [14]. The mathematics involved in modeling of grating SPR-sensing structures is more complex than that for planar prism-based systems [34,55]. Therefore modeling of the response of grating-based SPR structures and analysis of sensor data is more difficult. Grating-based optical SPR sensors have been demonstrated which use the measurement of the light intensity variations at SPR [56,57], and the wavelength interrogation [22,58]. A high-sensitivity SPR grating-based gas sensor using silver as an SPR active metal has attained sensitivity 1000 nm RIU^{-1} in wavelength interrogation mode [58], in angular interrogation mode, the system's sensitivity would be about 100 deg RIU^{-1}. Gold-based SPR grating sensors have been used for monitoring biomolecular interactions in aqueous environments [56,57], with estimated refractive index sensitivity of 30 deg RIU^{-1} and 900% RIU^{-1} in the angular interrogation and intensity measurement modes, respectively [56]. Recently an interesting modification of the resonant momentum detection approach has been demonstrated using an acousto-optical modulator and measurement of the modulation frequency [59]. This approach allows improving the accuracy with which the resonant wavelength in a wavelength interrogation-based SPR sensor is detected to about 5×10^{-4} nm, which led to a grating-based SPR sensor resolution below 1×10^{-6} RIU [59]. The grating coupler has been also used for the excitation of an SPW in an optoelectronic SPR-sensing device based on a Schottky-barier semiconductor structure, as demonstrated by Nikitin [60,61] with the resolution as high as 1×10^{-5} RIU. While the interrogation optical systems for SPR sensors using prism and grating coupler are essentially the same, accurate control of the thickness of the plasmon-active metal layer is not required in the grating-based SPR sensors. A drawback for certain applications is that in grating-based SPR systems, unlike prism-based systems, the light beam is incident through the sample solution and therefore the analyte and flow-cell need to be optically transparent.

4.3. Surface plasmon resonance sensors using optical waveguides

The use of optical waveguides in SPR sensors provides numerous attractive features such as a simple way to control the optical path in the sensor system (efficient control of properties of the light, suppression of the effect of stray light, etc.), small size and ruggedness. The process of exciting an SPW in an optical waveguide-based SPR-sensing structures is, in principle, similar to that in the Kretschmann ATR coupler. A light wave is guided by the waveguide and, entering the region with a thin metal overlayer, it evanescently penetrates through the metal layer. If the SPW and the guided mode are phase-matched, the light wave excites an SPW at the outer interface of the metal. Theoretically, the sensitivity of waveguide-based SPR devices is approximately the same as that of the corresponding ATR configurations. Despite increased design constraints compared to bulk prism-based SPR-sensing devices, all the main SPR detection approaches have been implemented in waveguide SPR sensors.

4.3.1. Surface plasmon resonance sensors based on optical fibers

Currently, optical fiber SPR probes present the highest level of miniaturization of SPR devices, allowing for chemical and biological sensing in inaccessible locations where the mechanical flexibility and the ability to transmit optical signals over a long distance make the use of optical fibers very attractive. The use of optical fibers for SPR sensing was first proposed by Jorgenson and Yee [21]. They used the wavelength interrogation technique and formed an SPR-sensing structure by using a conventional polymer clad silica fiber with partly removed cladding and an SPR active metal layer deposited symmetrically around the exposed section of fiber core. This approach allows construction of miniaturized optical fiber SPR probes with limited interaction area, with a length of about 10 mm. The fiber optic SPR sensor is capable of detecting variations in the refractive index within the operating range between 1.2 and 1.4 RIU with a resolution up to 5×10^{-5} RIU at higher refractive indices of analyte with a resonant wavelength resolution of 0.5 nm [21]. It has been demonstrated that the operating range of the sensor may be customized for sensor applications in the refractive index range 1–1.7 RIU by using a thin high-refractive index dielectric overlayer and high refractive index core fibers [62]. A similar structure in which the SPR-sensing area is formed not at the tip but in the middle of an optical fiber, has been reported to be used as an intensity measurement-based sensor [63,33]. In this configuration a collimated monochromatic light beam is launched into a fiber in such a fashion that only modes with propagation constants within a narrow range are efficiently excited. Variation in the refractive index of analyte are determined by measuring the transmitted optical power. The sensitivity of this SPR sensor is negatively influenced by exciting an SPW by fiber modes which are incident on the metal surface at slightly different angles. The reported resolution of 8×10^{-5} RIU for a gold-based sensor and of 5×10^{-5} RIU for a silver-based sensor is still fairly good and was achieved primarily because of relatively low system noise level which allowed resolving intensity changes as small as 0.2% [33,63]. Generally, both the types of multimode fiber optic SPR-sensing devices may suffer from rather low stability. The modal distribution of light in the fiber is very sensitive to mechanical disturbances and the disturbances occurring close to the sensing area of the fiber may cause intermodal coupling and modal noise. Because of the cylindrical shape of the sensing area, fabrication of homogeneous SPR coatings and functionalization of the sensors surface pose technological challenges. In order to overcome these drawbacks and to allow for further reduction of the sensing area, SPR sensors based on single-mode optical fiber have been proposed [64–66]. These SPR-sensing devices use a side-polished single-mode optical fiber with a thin metal layer supporting a surface plasma wave. The size of the sensing area is of the order of 1.5×0.01 mm. In the intensity mode, a maximum sensitivity as high as 4700 dB RIU^{-1} has been achieved [67] which corresponds to a resolution of 9×10^{-6} RIU for an output power resolution of 1%. In the wavelength interrogation mode a sensitivity of 6250 nm RIU^{-1} [67,68] has been measured. Naturally, the operating range of the single-mode fiber SPR sensors is very limited. The operating range of the sensor can be effectively tuned by a high refractive index dielectric overlayer, however, the presence of the dielectric overlayer may result in a drop in the sensitivity of the sensor [69]. A major drawback of optical fiber SPR sensors of this type is that they require reliable control of polarization state of the optical wave propagating in the fiber (e.g. by using polarization maintaining optical fibers). Recently, an alternative configuration of a wavelength interrogation –based SPR sensor using a single-mode optical fiber has been described [70]. In this configuration SPW is excited on a metal coated tapered single-mode optical fiber. It has been demonstrated that if the sensor is operated at wavelengths below 600 nm it may be used for monitoring variations in the refractive index of aqueous media. Sensor sensitivity as high as about 2200 nm RIU^{-1} has been reported [70].

4.3.2. Surface plasmon resonance sensors based on integrated optical waveguides

Integrated optical waveguide SPR sensors appear promising for the development of multichannel sensing devices on one chip with the potential for efficient referencing and multicomponent sensor analysis of complex samples. Research into integrated optical waveguide SPR sensors was pioneered by researchers at the University of Twente in the late eighties [71] and references therein. Since then, various groups have developed SPR-sensing devices using slab [72,73] and channel [74,75] single-mode integrated optical waveguides. An intensity-based integrated optical waveguide SPR-sensing device with a sensitivity of 2000 dB RIU^{-1} has been reported [72]. Similar to single-mode optical fiber SPR sensors, the integrated optical SPR-sensing devices exhibit rather limited operating range. Various possibilities for tuning the operating range of the sensor have been explored, such as using waveguides fabricated in low refractive index glass [74], a buffer layer [73], a high refractive index overlayer [76] and more complex multilayer structures [77,78]. However, all the approaches that introduced additional layers were found to yield less sensitive SPR-sensing devices because of a relatively lower concentration of electromagnetic field in the analyte. When optimized for operation in aqueous medium the sensitivity of the waveguide SPR-sensing devices in the wavelength interrogation mode was as follows: 150 nm RIU^{-1} for a device with a MgF_2 buffer [73]; 1700 nm RIU^{-1} for a device with a Ta_2O_5 overlayer [76]; and 830 nm RIU^{-1} for a device with a dielectric tuning multilayer [77].

5. Technologies and materials used in surface plasmon resonance-sensing devices

Because of the multidisciplinary nature of SPR chemical sensing and biosensing, numerous technologies are employed in the fabrication of SPR sensors. Particularly important are technologies for the fabrication of the optical part of the sensing element and technologies for the preparation of opto-chemical transducing medium.

5.1. Optical system—materials and technologies

In SPR-sensing devices based on prism couplers, the most commonly used materials are optical glasses. The material of the glass is chosen based on the analyte refractive index range to be covered by the sensor. Application of prism-based SPR sensors for monitoring optical parameters of high refractive index analytes requires the use of special and more expensive high refractive index glasses. Attempts to substitute glass couplers with their equivalents molded from plastic, leading to disposable cost-effective sensing elements, have been reported [52,79]. The grating couplers for the excitation of SPW are usually produced by a holographic technique in which the grating is formed by the interference of two laser beams whose standing pattern is exposed to a photoresist. Processing of the exposed resist results in a periodic pattern of lines. Very inexpensive gratings can be formed in plastic by replicating a 'master' grating [80].

Various technologies have been used to fabricate integrated optical waveguiding structures for SPR sensors. In particular, ion exchange and chemical vapor deposition (CVD) appear to be promising methods for the development of integrated optical waveguides for SPR sensing. SiO_xN_y waveguides produced by CVD technology on Si substrates exhibit low loss (below 0.5 dB cm^{-1} [81]) and their refractive index can be reproducibly adjusted within a wide range [81]. Inexpensive low-loss (< 0.3 dB cm^{-1}) integrated optical waveguides can be prepared by ion exchange in glass substrates in which ions in the glass—typically sodium—are locally replaced by potassium or silver ions resulting in locally increased refractive index [82]. The lateral confinement of the higher refractive index region is accomplished by using litographically produced diffusion masks.

Various metals have been examined for utilization in SPR sensors [83]. Today, the most commonly used surface plasmon active metals are gold and silver. While the use of silver leads to more sensitive SPR-sensing devices, in principle, the long-term stability of silver is poor. Recently methods for protecting thin silver films against oxidation have been reported which were shown to lead to substantially improved long-term stability [84]. Thin layers of SPR active metals are most often produced by vacuum evaporation and sputtering. Additional layers from dielectrics such as MgF_2, Ta_2O_5, SiO_2, TiO_2 [73,76], [78] used to optimize the performance of waveguide-based SPR devices are usually deposited using the same techniques.

5.2. Opto-chemical transducing medium—materials and technologies

In chemical SPR sensors the transducing layers are often formed from polymers (polysiloxanes, polyethylene, Teflon, etc.). Thin optically homogenous layers of the polymers can be produced using spin coating or dip coating techniques [85,86]. Thin films of organic materials such as phthalocyanines and polyaniline have been prepared using spin coating [87] and the Langmuir–Blodgett technique [88–90]. In contrast to spin coating, the Langmuir–Blodgett technique allows preparation of very thin (monomolecular) layers and provides good thickness control.

In SPR biosensors the transducing medium is usually formed as a matrix or layer of biomolecules which are capable of binding the analyte molecules. Various biomolecular interactions have been exploited in SPR biosensors including antigen–antibody, receptor–ligand, and hormone–receptor binding. In general, immobilization of biomolecules directly on the metal surface is not suitable for biosensors because it leads to low coverage of biomolecules with reduced activity and non-specific adsorption. Various surface chemistries which provide the desired chemical properties for stable and defined binding of ligands providing high functionality in conjunction with minimum non-specific binding to the surface have been developed. One approach is to use a streptavidine monolayer immobilized onto a gold film with biotin [91] which may be further functionalized with biotinylated biomolecules. The gold surface may also be functionalized by spreading out liposomes which is possible due to the hydrophobic character of the surface. Another approach is to form a self assembled monolayer (SAM) of thiol molecules (e.g. 16-thiohexadecanol, alkanethiols) [92,93] to introduce important biological substituents as tail groups on a gold surface. Then ligands may be bound to the tail groups forming a monolayer of ligand molecules. The SAM layer can also be used to allow the covalent binding of a dextran layer to the surface by using epichlorohydrin. After treating the dextran with iodoacetic acid, the resulting carboxylic groups are used to immobilize ligands in various ways. In most cases, the carboxylic groups are activated by means of *N*-hydroxy succinimide (NHS) and ethylmethyl-diaminopropyl-carbodiimide (EDC), in a second step it is then possible to couple a ligand with a functional group such as $-NH_2$. Another possibility is the immobilization of nitrilotriacetic acid (NTA) followed by Ni-chelation to capture histidine tagged ligands. The dextran layer may also contain streptavidine molecules allowing binding of biotinylated ligands [94] or to form different types of functionalized surfaces that can be used in a number of sensing schemes. A review of methods for controlled coupling to carboxymethyldextran surfaces in SPR sensing may be found in [95]. Alternatively, gold surfaces may be functionalized by using thin plasma polymerized films onto surface of which the ligands may by immobilized via amino groups [96].

6. Major areas of applications of surface plasmon resonance sensors

6.1. Surface plasmon resonance sensors for measurement of physical quantities

SPR sensors for the measurement of displacement [97] and angular position [98] have been described which rely on the sensitivity of SPR to the momentum of the incident light wave. Physical phenomena occurring in various optical transducing materials have been also exploited for the development of SPR-sensing devices including a humidity sensor utilizing humidity-induced refractive index changes of porous thin layers and polymers [78,99] and a temperature sensor based on the thermooptic effect in hydrogenated amorphous silicon [100].

6.2. Surface plasmon resonance chemical sensing

While in specific systems of limited complexity variations in the concentration of analyte may be determined by directly measuring refractive index using an SPR sensor (e.g. monitoring distillation processes [101]), most chemical SPR sensors are based on the measurement of SPR variations due to adsorption or a chemical reaction of an analyte with a transducing medium which results in changes in its optical properties. The applications relying primarily on changes in the refractive index of transducing layer induced by the adsorption of analyte molecules include monitoring of the concentration of vapors of hydrocarbons, aldehydes and alcoholes by adsorption in polyethylene glycol films [102], monitoring of vapors of chlorinated hydrocarbons by adsorption in polyfluoroalkylsiloxane [84], detection of vapors of tetrachlorethene [86] by adsorption in a polydimethylsiloxane film, and detection of vapors of aromatic hydrocarbons by their adsorption in Teflon films [85]. It has been also demonstrated that SPR-sensing devices using palladium as an SPR active metal can effectively detect molecular hydrogen because of intense sorption of hydrogen molecules in palladium [103,104]. Recently a sensitive sensor for NO_2 detection utilizing chemisorption of NO_2 molecules in a gold SPR active layer has been reported [105]. SPR structures have also been exploiting the interaction between the analyte molecules and the transducing layer allowing toluene detection via copper and nickel phthalocyanine [88], detection of NO_2 via copper [89] and cobalt [106] phthalocyanine films, and detection of NO_2 and H_2S via polyaniline film [90]. The use of SPR for detection of NH_3 vapors using the reaction of ammonia with a bromo-cresol purple film has been also reported [107]. Combined with anodic stripping voltammetry, SPR method has been utilized for detection of Cu and Pb ions [108,109].

6.3. Surface plasmon resonance biosensing

The first application of SPR to biosensing was demonstrated in 1983 [9]. Since then, the detection of biospecific interaction was developed by also some other groups [110,27]. In 1994 the first survey on real-time biospecific interaction analysis methods appeared [111] which have since been frequently used and constantly improved for examination of kinetic and thermodynamic constants of biomolecular interactions. Several assay formats for SPR sensors have been tested. In direct SPR biosensors, the analyte quantification is carried out by direct detection of the binding reaction, however, the increase in the refractive index produced by the adsorption of small molecules may not be sufficient to be detected directly, and sandwich [112] or competitive [113] assay methods may need to be used. Earlier works were focusing mainly on antigen-antibody interactions, the streptatividin–biotin reaction, and some IgG examinations, especially to test new algorithms in biospecific molecular interaction analysis, to characterize newly developed SPR set-ups, and to improve surface chemistry. Current research includes far more advanced systems. One of the new areas is the examination of protein–protein or protein–DNA interactions [114], even detecting conformational changes in an immobilized protein [115]. A domain within the tumor suppressor protein APC has been examined regarding its biochemical properties [116], as well as the binding kinetics of human glycoprotein with monoclonal antibodies [117]. Work has been done on the activator target in the RNA polymerase II holoenzyme [118]. In addition to the examination of structure-function relationship of antibacterial synthetic peptides [119], the binding conditions of the neuropeptide substance P to monoclonal antibodies have been examined, and equilibrium and kinetic studies reported [120]. Even libraries are now being tested in order to determine binding affinities of a T-4 monoclonal antibody Fab fragment for thyroxine analogs [121]. Epitope studies have been made in the case of characterization of recombinant hepatitis B surfaces with antigens [122]. Another important area are membrane examinations as in the case of plasma membrane Ca^{2+} ATPase being a pump important for intracellular Ca^{2+} homeostasis [123]. Another up-coming field are measurements to quantify T cell receptors in interaction with syngeneic or allogeneic ligands [124]. Phage peptide libraries constitute powerful tools for mapping epitopes where antibody-peptide interactions are monitored by SPR [125]. Extensive literature on SPR biosensor applications may be located by searching databases such as BIOSIS, Current Contents, Medline, and Chemical Abstract Service and [126].

7. Commercialization of surface plasmon resonance sensor technology

Systematic development of SPR biosensor technology by Swedish BIAcore AB (originally Pharmacia Biosensor AB) lead to launching of the first commercial SPR biosensor on the market in 1990. Since then the BIAcore sensor technology has been further refined in terms of speed, throughput and accuracy. Currently, BIAcore offers several models of SPR biosensors (BIACORE® 3000, BIACORE® 2000, BIACORE® X, BIACORE® 1000, BiacoreQuant™). Details may be found in [126]. Increasing interest in commercialization of optical biosensor systems has resulted in the development of another SPR biosensor system (TI-SPR-1 Experimenters Kit, Spreeta™ Evaluation Kit) by Texas Instruments (USA) [127]. Both BIAcore and Texas Instrument sensor systems utilize the angular interrogation of SPW excited using prism couplers. An SPR biosensor instrument relying on the wavelength interrogation of SPW in grating-based structures is offered by Quantech (USA) [128]. Another SPR biosensor system (called Kinetic Instrument 1) has been developed by BioTuL Bio Instruments GmbH (Germany) [129]. Most recently a new laboratory SPR system (called IBIS) by Intersens Instruments BV has been presented by Xantec Analysensysteme GbR (Germany). The only commercially available waveguide-based SPR-sensing device using wavelength interrogation in a multimode optical fiber has been developed by EBI Sensors (Washington, USA). Recently, EBI Sensors has been acquired by BIAcore and now the SPR fiber optic probe is marketed by BIAcore.

8. Future trends in development of surface plasmon resonance sensors

There is need for detection and analysis of chemical and biochemical substances in many important areas including medicine, environmental monitoring, biotechnology, drug and food monitoring. Surface plasmon resonance sensor technology holds potential for applications in these areas. Currently SPR biosensor devices compete with other types of biosensors [130], however, the major competitors of biosensors are immunoassays which are commonly and widely used for determination of numerous important substances and offer low-cost tests of high specificity and sensitivity. Today, the commercially available biosensors are covering a very limited area of (bio)chemical monitoring market aiming primarily at research and analytical laboratories. In order to reach out from specialized laboratories and centralized testing sites and gain a fair share of the (bio)chemical monitoring market, SPR sensors have to compete with existing technologies on the basis of factors such as low cost, ease of use, robustness, sensitivity, and stability. It is envisaged that this will drive research and development of SPR-sensing devices in the following directions:

1. Improvement of detection limits. Current direct SPR biosensors are limited to detection of about 1 pg mm^{-2} surface coverage of biomaterial which is not sufficient for detecting low concentrations of low molecular weight analytes. While further optimization of SPR optical instruments and development of efficient referencing concepts and sophisticated data processing methods may improve the resolution of SPR-sensing devices and lower the detection limits, at present no approach is available which can decrease this limit of detection by orders of magnitude.

2. Multichannel performance. The multichannel SPR sensors are required for direct detection in high throughput screening systems in the search of new pharmaceuticals. First steps in this direction include the system introduced by BIAcore and the approach proposed by Berger [45] which uses a 4-channel chip which can be rotated by 90 deg to provide 16 channels.
3. Development of advanced recognition elements. For applications of SPR sensors in complex realistic samples (e.g. blood) advanced stable receptor matrices which allow resolving sensor response from non-specific background effects will have to be developed.

Undoubtedly, in the future the SPR technology will benefit from the use of optical waveguide technology which offer the potential for the development of miniaturized, compact and rugged sensing elements with prospect of fabrication of multiple sensors on one chip.

9. Conclusions

During the last 10 years the surface plasmon resonance sensing technique has been developed into a very useful technology with numerous applications. This paper has reviewed this development and discussed emerging trends in SPR-sensing. In order to illustrate the potential of SPR-sensing devices, major application areas of SPR sensors have been outlined and examples of applications have been discussed. We envisage that progress in SPR sensor technology will further improve detection abilities of SPR sensors and allow sensitive, fast, and cost-effective (bio)chemical analysis both in laboratories and in the field. This development will further extend the potential of SPR-sensing technology and allow SPR sensors to be used far more widely.

Acknowledgements

The authors would like to acknowledge the support of the Defense Advanced Research Projects Agency (contract DAAL01-96-K-3614), the Center for Process Analytical Chemistry at the University of Washington (contract 66-9938) and the Grant Agency of the Czech Republic (contracts 102/96/1561 and 303/96/1358).

References

[1] D.W. Lubbers, N. Opitz, Eine neue pCO_2-bzw: pO_2-Messonde zur Messung des pCO_2 oder pO_2 von Gasen und Flüssigkeiten, Zeitschrift Für Naturforschung C 30 (1975) 532–533.
[2] O.S. Wolfbeis (Ed.), Fiber optic chemical sensors and biosensors, Boca Raton, CRC Press, 1991.
[3] A. Brecht, G. Gauglitz, Optical probes and transducers, Biosensors Bioelectron. 10 (1995) 923–936.
[4] G. Gauglitz, Opto-Chemical and Opto-Immuno Sensors, Sensor Update vol. 1, VCH Verlagsgesellschaft, Weinheim, 1996.
[5] G. Boisde, A. Harmer, Chemical and Biochemical Sensing with Optical Fibers and Waveguides, Artech House, Boston 1996.
[6] I. Pockrand, J.D. Swalen, J.G. Gordon, M.R. Philpott, Surface plasmon spectroscopy of organic monolayer assemblies, Surface Sci. 74 (1978) 237–244.
[7] J.G. Gordon II, S. Ernst, Surface plasmons as a probe of the electrochemical interface, Surface Sci. 101 (1980) 499–506.
[8] C. Nylander, B. Liedberg, T. Lind, Gas detection by means of surface plasmons resonance, Sensors and Actuators 3 (1982) 79–88.
[9] B. Liedberg, C. Nylander, I. Lundström, Surface plasmons resonance for gas detection and biosensing, Sensors and Actuators 4 (1983) 299–304.
[10] B. Liedberg, C. Nylander, I. Lundström, Biosensing with surface plasmon resonance—how it all started, Biosensors Bioelectron. 10 (1995) i–ix.
[11] R.W. Wood, On a remarkable case of uneven distribution of light in a diffraction grating spectrum, Phil. Magm. 4 (1902) 396–402.
[12] E. Kretschmann, H. Raether, Radiative decay of non-radiative surface plasmons excited by light, Z. Naturforsch. 23A (1968) 2135–2136.
[13] A. Otto, Excitation of surface plasma waves in silver by the method of frustrated total reflection, Z. Physik 216 (1968) 398–410.
[14] H. Raether, Surface plasmons on smooth and rough surfaces and on gratings, Springer-Verlag, Berlin, 1988.
[15] A.D. Boardman (Ed.), Electromagnetic surface modes, John Wiley and Sons, 1982.
[16] M.A. Ordal, L.L. Long, R.J. Bell, S.E. Bell, R.R. Bell, R.W. Alexander, J. Ward, C.A. Ward, optical properties of metals Al, Co, Cu, Au, Fe, Pb, Ni, Pd, Pt, Ag, Ti, and W in the infrared and far infrared, Appl. Opt. 11 (1983) 1099–1119.
[17] M.M.B. Vidal, R. Lopez, S. Aleggret, J. Alonso-Chamarro, I. Garces, J. Mateo, Determination of probable alcohol yield in musts by means of an SPR optical sensor, Sensors and Actuators B 11 (1993) 455–459.
[18] K. Matsubara, S. Kawata, S. Minami, Optical chemical sensor based on surface plasmon measurement, Appl. Opt. 27 (1988) 1160–1163.
[19] B. Liedberg, I. Lundstrom, E. Stenberg, Principles of biosensing with an extended coupling matrix and surface plasmon resonance, Sensors and Actuators B 11 (1993) 63–72.
[20] L.M. Zhang, D. Uttamchandani, Optical chemical sensing employing surface plasmon resonance, Electron. Lett. 23 (1988) 1469–1470.
[21] R.C. Jorgenson, S.S. Yee, A fiber-optic chemical sensor based on surface plasmon resonance, Sensors and Actuators B 12 (1993) 213–220.
[22] P.S. Vukusic, G.P. Bryan-Brown, J.R. Sambles, Surface plasmon resonance on grating as novel means for gas sensing, Sensors and Actuators B 8 (1992) 155–160.
[23] A.A. Kruchinin, Y.G. Vlasov, Surface plasmon resonance monitoring by means of polarization state measurement in reflected light as the basis of a DNA probe biosensor, Sensors and Actuators B 30 (1996) 77–80.
[24] S.G. Nelson, K.S. Johnston, S.S Yee, High sensitivity surface plasmon resonance sensor based on phase detection, Sensors and Actuators B 35–36 (1996) 187–191.
[25] P.I. Nikitin, A.A. Beloglazov, A.V. Kabashin, M.V. Valeiko, V.E. Kochergin, Surface plasmon resonance interferometry for sensor applications (published therein).
[26] H.E. de Bruijn, B.S.F. Altenburg, R.P.H. Kooyman, J. Greve, Choice of metal and wavelength for surface-plasmon resonance sensors: some considerations, Appl. Opt. 31 (1992) 440–442.

[27] R.P.H. Kooyman, H. Kolkman, J. van Gent, J. Greve, Surface plasmon resonance immunosensors: sensitivity considerations, Anal. Chim. Acta 213 (1988) 35–45.
[28] E.M. Yeatman, Resolution and sensitivity in surface plasmon microscopy and sensing, Biosensors Bioelectron. 11 (1996) 635–649.
[29] J. Homola, On the sensitivity of surface plasmon resonance sensors with spectral interrogation, Sensors and Actuators B 41 (1997) 207–211.
[30] J. Homola, I. Koudela, S. Yee, Surface plasmon resonance sensor based on diffraction gratings and prism couplers: sensitivity comparison (published therein).
[31] U. Jönsson, L. Fägerstam, B. Ivarsson, et al., Real-time biospecific interaction analysis using surface plasmon resonance and a sensor chip technology, Biotechniques 11 (1991) 620–627.
[32] P. Pfeifer, U. Aldinger, G. Schwotzer, S. Diekmann, P. Steinrücke, Real time sensing of specific molecular binding using surface plasmon resonance spectroscopy (published therein).
[33] C. Ronot-Trioli, A. Trouillet, C. Veillas, H. Gagnaire, Monochromatic excitation of surface plasmon resonance in an optical-fibre refractive-index sensor, Sensors and Actuators A 54 (1996) 589–593.
[34] M.G. Moharam, T.K. Gaylord, Rigorous coupled-wave analysis of metallic surface-relief gratings, J. Opt. Soc. Am. A 3 (1986) 1780–1787.
[35] A.A. Kolomenskii, P.D. Gershon, H.A. Schuessler, Sensitivity and detection limit of concentration and adsorption measurements by laser-induced surface-plasmon resonance, Appl. Opt. 36 (1997) 6539–6547.
[36] T. Chinowsky, L.S. Jung, S.S. Yee, Optimal linear data analysis for surface plasmon resonance biosensors (published therein).
[37] S. Herminghaus, P. Leiderer, Improved attenuated total reflectance technique for the investigation of dielectric surfaces, Appl. Phys. Lett. 54 (1989) 99–101.
[38] R.P. Podgorsek, U. Sandten, H. Franke, J. Woods, Monitoring of diffusion of vapor molecules in polymer films using SPR-leaky-mode spectroscopy, in: Fourth European Conference on Optical Chemical Sensors and Biosensors, March 1997, Munster, Germany, Book of Abstracts, 247–248.
[39] K.A. Peterlinz, R. Georgiadis, Two-color approach for determination of thickness and dielectric constant of thin films using surface plasmon resonance spectroscopy, Opt. Commun. 130 (1996) 260–266.
[40] J.M. Phelps, D.M. Taylor, Determining the relative permittivity and thickness of a lossless dielectric overlayer on a metal film using optically excited surface plasmon polaritons, J. Phys. D (Applied Physics) 29 (1996) 1080–1087.
[41] T.M. Chinowsky, S.S. Yee, Quantifying the information content of surface plasmon resonance reflection spectra, in: Fourth European Conference on Optical Chemical Sensors and Biosensors, March 1997, Munster, Germany, Book of Abstracts, 175, Sensors and Actuators (to be published).
[42] G.V. Beketov, Y.M. Shirshov, O.V. Shynkarenko, V.I. Chegel, Surface plasmon resonance spectroscopy: prospects of superstrate refractive index variation for separate extraction of molecular layer parameters, Sensors and Actuators B 48 (1998) 432–438.
[43] S. Löfås, M. Malmqvist, I. Rönnberg, E. Stenberg, B. Liedberg, I. Lundström, Bioanalysis with surface plasmon resonance, Sensors and Actuators B 5 (1991) 79–84.
[44] R. Karlsson, R. Ståhleberg, Surface plasmon resonance detection and multispot sensing for direct monitoring of interactions involving low-molecular-weight analytes and for determination of low affinities, Anal. Biochem. 228 (1995) 274–280.
[45] C.E.H. Berger, T.A.M. Baumer, R.P.H. Kooyman, J. Greve, Surface plasmon resonance multisensing, Anal. Chem. 70 (1998) 703–706.
[46] M.W. Foster, D.J. Ferrel, R.A. Lieberman, Surface plasmon resonance biosensor miniaturization, Proc. SPIE 2293 (1994) 122–131.
[47] S.R. Karlsen, K.S. Johnston, S.S. Yee, C.C. Jung, First-order surface plasmon resonance sensor system based on a planar light pipe, Sensors and Actuators B 32 (1996) 137–141.
[48] J. Homola, S. Yee, Surface plasmon resonance sensor based on planar light pipe, theoretical optimization analysis, Sensors and Actuators B 37 (1996) 145–150.
[49] S. Shen, K.S. Johnston, S.S. Yee, Optical lightpipe sensor based on surface plasmon resonance, Pacific Northwest Fiber Optic Sensor Workshop, Portland, USA, May 8–9, 1996, Proc. SPIE 2872 (1996) 10–16.
[50] K.S. Johnston, T.M. Chinavsky, S.S. Yee, Planar substrate surface plasmon resonance probe, Denver, August 4–9, 1996, Proc. SPIE 2836 (1996) 178–185.
[51] C.P. Cahill, K.S. Johnston, S.S. Yee, A Surface plasmon resonance sensor probe based on retro-reflection, Sensors and Actuators B 45 (1997) 161–166.
[52] J. Melendez, R. Carr, Bartholomew, et al., A commercial solution for surface plasmon sensing, Sensors and Actuators B 35–36 (1996) 212–216.
[53] J. Melendez, R. Carr, D. Bartholomew, H. Taneja, S. Yee, C. Jung, C. Furlong, Development of a surface plasmon resonance sensor for commercial applications, Sensors and Actuators B 39 (1997) 375–379.
[54] M.C. Hutley, Diffration gratings, Academic Press, London, 1982.
[55] J. Chandezon, M.T. Dupuis, G. Cornet, D. Maystre, Multicoated gratings: a differential formalism applicable an the entire optical region, J. Opt. Soc. Am. 72 (1982) 839–846.
[56] D.C. Cullen, R.G. Brown, C.R. Lowe, Detection of immunocomplex formation via surface plasmon resonance on gold-coated diffraction gratings, Biosensors 3 (1987) 211–225.
[57] D.C. Cullen, C.R. Lowe, A direct surface plasmon-polariton immunosensor: preliminary investigation of the non-specific adsorption of serum components to the sensor interface, Sensors and Actuators B 1 (1990) 576–579.
[58] M.J. Jory, P.S. Vukusic, J.R. Sambles, Development of a prototype gas sensor using surface plasmon resonance on gratings, Sensors and Actuators B 17 (1994) 1203–1209.
[59] M.J. Jory, G.W. Bradberry, P.S. Cann, J.R. Sambles, A surface-plasmon-based optical sensor using acousto-optics, Meas. Sci. Technol. 6 (1995) 1193–1200.
[60] P.I. Nikitin, A.A. Beloglazov, A multi-purpose sensor based on surface plasmon polariton resonance in a Schottky structure, Sensors and Actuators A 41–42 (1994) 547–552.
[61] P.I. Nikitin, A.A. Beloglazov, M.V. Valeiko, J.A. Creighton, A.M. Smith, N.A. Sommerdijk, J.D. Wright, Silicon-based surface plasmon resonance chemical sensors, Sensors and Actuators B 38 (1997) 53–57.
[62] R.C. Jorgenson, S.S. Yee, Control of the dynamic range and sensitivity of a surface plasmon resonance based fiber optic sensor, Sensors and Actuators A 43 (1994) 44–48.
[63] A. Trouillet, C. Ronot-Trioli, C. Veillas, H. Gagnaire, Chemical sensing by surface plasmon resonance in a multimode optical fibre, Pure Appl. Opt. 5 (1996) 227–237.
[64] R.E. Dessy, W.J. Bender, Feasibility of a chemical microsensor based on surface plasmon resonance on fiber optics modified by multilayer vapor deposition, Anal. Chem. 66 (1994) 963–970.
[65] J. Homola, Optical fiber sensor based on surface plasmon excitation, Second European Conference on Optical Chemical Sensors and Biosensors, Florence, Italy, April 1994, Sensors and Actuators B 29 (1995) 401–405.
[66] J. Homola, R. Slavík, Fibre-optic sensor based on surface plasmon resonance, Electron. Lett. 32 (1996) 480–482.

[67] R. Slavík, J. Homola, J. Čtyroký, Novel surface plasmon resonance sensor based on single-mode optical fiber, Chemical, Biochemical and Environmental Fiber Sensors IX, Munich, Germany, June 1997, Proc. SPIE 3105 (1997) 325–331.
[68] J. Homola, R. Slavík, J. Čtyroký, Interaction between fiber modes and surface plasmon waves: spectral properties, Opt. Lett. 22 (1997) 1403–1405.
[69] R. Slavík, J. Homola, J. Čtyroký, Optical fiber surface plasmon resonance sensor for an aqueous environment, Twelfth International Conference on Optical Fiber Sensors, Williamsburg, USA, October 1997, Tech. Digest Series 16 (1997) 436–439.
[70] A.J.C. Tubb, F.P. Payne, R.B. Millington, C.R. Lowe, Single-mode optical fiber surface plasma wave chemical sensor, Sensors and Actuators B 41 (1997) 71–79.
[71] P.V. Lambeck, Integrated opto-chemical sensors, Sensors and Actuators B 8 (1992) 103–116.
[72] J. Homola, J. Čtyroký, M. Skalský, J. Hradilová P. Kolářová, A surface plasmon resonance based integrated optical sensor, Sensors and Actuators B 38–39 (1997) 286–290.
[73] C.R. Lavers, J.S. Wilkinson, A waveguide-coupled surface-plasmon sensor for an aqueous environment, Sensors and Actuators B 22 (1994) 75–81.
[74] R.D. Harris, J.S. Wilkinson, Waveguide surface plasmon resonance sensors, Sensors and Actuators B 29 (1995) 261–267.
[75] C. Mouvet, R.D. Harris, C. Maciag, et al., Determination of simazine in water samples by waveguide surface plasmon resonance, Anal. Chim. Acta 338 (1997) 109–117.
[76] J. Čtyroký, J. Homola, M. Skalský, Tuning of spectral operation range of a waveguide surface plasmon resonance sensor, Electron. Lett. 33 (1997) 1246–1248.
[77] M.N. Weiss, R. Srivastava, H. Groger, P. Lo, S.F. Luo, A theoretical investigation of environmental monitoring using surface plasmon resonance waveguide sensors, Sensors and Actuators A 51 (1996) 211–217.
[78] M.N. Weiss, R. Srivastava, H. Groger, Experimental investigation of a surface plasmon-based integrated-optic humidity sensor, Electron. Lett. 32 (1996) 842–843.
[79] I. Stemmler, A. Brecht, G. Gauglitz, Compact SPR-transducers with spectral readout for biosensing applications (published therein).
[80] C.R. Lawrence, N.J. Geddes, D.N. Furlong, J.R. Sambles, Surface plasmon resonance studies of immunoreactions utilizing disposable diffraction gratings, Biosensors Bioelectron. 11 (1996) 389–400.
[81] W. Gleine, J. Müller, Low-pressure chemical vapor deposition silicon-oxynitride films for integrated optics, Appl. Opt. 31 (1992) 2036–2040.
[82] A. Miliou, H. Zhenguang, H.C. Cheng, R. Srivastava, R.V. Ramaswamy, Fiber-compatible K^+-Na^+ ion-exchanged channel waveguides: fabrication and characterization, IEEE J. Quantum Electron. 25 (1989) 1889–1897.
[83] J.W. Sadowski, J. Lekkala, I. Vikholm, Biosensors based on surface plasmons excited in non-noble metals, Biosensors Bioelectron. 6 (1991) 439–444.
[84] A. Abdelghani, J. M. Chovelon, N. Jaffrezic-Renault, C. Ronot-Trioli, C. Veillas, H. Gagnaire, Surface plasmon resonance fiber-optic sensor for gas detection, Sensors and Actuators B 38–39 (1997) 407–410.
[85] R.P. Podgorsek, T. Sterkenburgh, J. Wolters, T. Ehrenreich, S. Nischwitz, H. Franke, Optical gas sensing by evaluating ATR leaky mode spectra, Sensors and Actuators B 39 (1997) 349–352.
[86] M. Niggemann, A. Katerkamp, M. Pellmann, P. Bolsmann, J. Reinbold, K. Cammann, Remote sensing of tetrachlorethene with a micro-fiber optical gas sensor based on surface plasmon resonance, Sensors and Actuators B 34 (1996) 328–333.
[87] P.S. Vukusic, J.R. Sambles, J.D. Wright, Surface plasmon resonance characterization of spin-deposited phthalocyanine films, J. Mater. Chem. 2 (1992) 1105–1106.
[88] C. Granito, J.N. Wilde, M.C. Petty, S. Houston, P.J. Iradale, Toluene vapor sensing using copper and nickel phthalocyanine Langmuir-Blodgett films, Thin Solid Films 284–285 (1996) 98–101.
[89] D.G. Zhu, M.C. Petty, M. Harris, An optical sensor for nitrogen dioxide based on a copper phthalocyanine Langmuir-Blodgett film, Sensors and Actuators B 2 (1990) 265–269.
[90] N.E. Agbor, J.P. Cresswell, M.C. Petty, A.P. Monkman, An optical gas sensor based on polyaniline Langmuir-Blodgett films, Sensors and Actuators B 41 (1997) 137–141.
[91] H. Morgan, D.M. Taylor, A surface plasmon resonance immunosensor based on the streptavidin biotin complex, Biosensors Bioelectron. 7 (1992) 405–410.
[92] C.D. Bain, E.B. Troughton, Y.Y. Tao, J. Evall, G.M. Whitesides, R.G. Nuzzo, Formation of monolayer films by spontaneous assembly of organic thiols from solution onto gold, J. Am. Chem. Soc. 111 (1989) 321.
[93] L. Bertilsson, B. Liedberg, Infrared study of thiol assemblies on gold: preparation, characterization, and functionalization of mixed monolayers, Langmuir 9 (1993) 141–149.
[94] J. Spinke, M. Liley, H.J. Guder, L. Angermaier, W. Knoll, Molecular recognition at self-assembled monolayers: the construction of multicomponent layers, Langmuir 9 (1993) 1821–1825.
[95] S. Löfås, B. Johnsson, A. Edstrom, A. Hansson, G. Lindquist, R.M.M. Hillgren, L. Stigh, Methods for site controlled coupling to carboxymethyldextran surfaces in surface plasmon resonance sensors, Biosensors Bioelectron. 10 (1995) 813–822.
[96] R. Nakamura, H. Muguruma, K. Ikebukuro, S. Sasaki, R. Nagata, I. Karube, H. Pedersen, A plasma polymerized film for surface plasmon resonance immunosensing, Anal. Chem. 69 (1997) 4649–4652.
[97] G. Margheri, A. Mannoni, F. Quercioli, A new high-resolution displacement sensor based on surface plasmon resonance, Proc. SPIE 2783 (1996) 211–220.
[98] J.K. Schaller, R. Czepluch, C.G. Stojanoff, Plasmon spectroscopy for high resolution angular measurements, Proc. SPIE 3098 (1997) 476–486.
[99] J. Homola, G. Schwotzer, H. Lehmann, R. Willsch, W. Ecke, H. Bartelt, A new optical fiber sensor for humidity measurement, Photonics' 95, Prague, Czech Republic, August 1995, EOS Annual Meeting Digest Series, 2A 245–248.
[100] B. Chadwick, M. Gal, An optical temperature sensor using surface plasmons, Japn. J. Appl. Phys. 32 (1993) 2716–2717.
[101] E.G. Ruiz, I. Garcez, C. Aldea, M.A. Lopez, J. Mateo, J. Alonso-Chamarro, S. Alegret, Industrial process sensor based on surface plasmon resonance (SPR): distillation process monitoring, Sensors and Actuators A 37–38 (1993) 221–225.
[102] S. Miwa, T. Arakawa, Selective gas detection by means of surface plasmon resonance sensors, Thin Solid Films 281–282 (1996) 466–468.
[103] B. Chadwick, M. Gal, Enhanced optical detection of hydrogen using the excitation of surface plasmons in palladium, Appl. Surface Sci. 68 (1993) 135–138.
[104] B. Chadwick, M. Gal, A hydrogen sensor based on the optical generation of surface plasmons in a palladium alloy, Sensors Actuators B 17 (1994) 215–220.
[105] G.J. Ashwell, M.P.S. Roberts, Highly selective surface plasmon resonance sensor for NO_2, Electron. Lett. 32 (1996) 2089–2091.
[106] P.S. Vukusic, J.R. Sambles, Cobalt phthalocyanine as a basis for the optical sensing of nitrogen dioxide using surface plasmon resonance, Thin Solid Films 221 (1992) 311–317.

[107] J. van Gent, P.V. Lambeck, R.J. Bakker, T.J. Popma, E.J.R. Sudholter, D.N. Reinhoudt, Design and realization of a surface plasmon resonance-based chemo-optical sensor, Sensors and Actuators A 26 (1991) 449–452.
[108] C.C. Jung, S.B. Saban, S.S. Yee, R.B. Darling, Chemical electrode surface plasmon resonance sensor, Sensors and Actuators B 32 (1996) 143–147.
[109] T.M. Chinowsky, S.B. Saban, S.S. Yee, Experimental data from a trace metal sensor combining surface plasmon resonance with anodic stripping voltammetry, Sensors and Actuators B 35 (1996) 37–43.
[110] M.T. Flanagan, R.H. Pantell, Surface plasmon resonance and immunosensors, Electron. Lett. 20 (1984) 968–970.
[111] I. Lundström, Real-time biospecific interaction analysis, Biosensors Bioelectron. 9 (1994) 725–736.
[112] A.H. Severs, R.B.M. Schasfoort, M.H.L. Salden, An immunosensor for syphilis screening based on surface plasmon resonance, Biosensors Bioelectron. 8 (1993) 185–189.
[113] A. Brecht, G. Gauglitz, Label free immunoprobes for pesticide detection, Anal. Chim. Acta 347 (1997) 219–233.
[114] D.R. Mernagh, P. Janscak, K. Firman, G.G. Kneale, Protein–protein and protein–DNA interactions in the Type I restriction endonuclease R.EcoR124I, Biol. Chem. 379 (1998) 497–503.
[115] H. Sota, Y. Hasegawa, M. Iwakura, Detection of conformational changes in an immobilized protein using surface plasmon resonance, Anal. Chem. 70 (1998) 2019–2024.
[116] J. Deka, J. Kuhlmann, O. Muller, A domain within the tumor suppressor protein APC shows very similar biochemical properties as the microtubule-associated protein Tau, Eur. J. Biochem. 253 (1998) 591–597.
[117] V. Regnault, J. Arvieux, L. Vallar, T. Lecompte, Immunopurification of human Beta(2)-glycoprotein I with a monoclonal antibody selected for its binding kinetics using surface plasmon resonance biosensor, J. Immun. Methods 211 (1998) 191–197.
[118] S.S. Koh, A.Z. Ansari, M. Ptashne, R.A. Young, An activator target in the RNA polymerase II holoenzyme, Mol. Cell 1 (1998) 895–904.
[119] D.S. Chapple, D.J. Mason, C.L. Joannou, E.W. Odell, V. Gant, R.W. Evans, Structure–function relationship of antibacterial synthetic peptides homologous to a helical surface region on human lactoferrin against *Escherichia coli* serotype 0111, Infect. Immunol. 66 (1998) 2434–2440.
[120] V. Hanin, O. Dery, D. Boquet, M.A. Sagot, C. Creminon, J.Y. Couraud, J. Grassi, Importance of hydropathic complementarity for the binding of the neuropeptide substance P to A monoclonal antibody: equilibrium and kinetic studies, Mol. Immunol. 34 (1997) 829–838.
[121] M. Adamczyk, D.D. Johnson, P.G. Mattingly, J.A. Moore, Y. Pan, Immunoassay reagents for thyroid testing, 3: determination of the solution binding affinities of a T-4 monoclonal antibody Fab fragment for a library of thyroxine analogs using surface plasmon resonance, Biocon. Chem. 9 (1998) 23–32.
[122] J.S. Tung, J. Gimenez, C.T. Przysiecki, G. Mark, Characterization of recombinant hepatitis B surface antigen using surface plasmon resonance, J. Pharm. Sci. 87 (1998) 76–80.
[123] E. Kim, S.J. DeMarco, S.M. Marfatia, A.H. Chishti, M. Sheng, E.E. Strehler, Plasma membrane Ca^{2+} ATPase Isoform 4b binds to membrane-associated guanylate kinase (MAGUK) proteins via their PDZ (PSD-95/Dlg/ZO-1) domains, J. Biol. Chem. 273 (1998) 1591–1595.
[124] K. Christoper Garcia, M.D. Tallquist, L.R. Pease, et al., Alpha-beta T cell receptor interactions with syngeneic and allogeneic ligands: affinity measurements and crystallization, Proc. Natl. Acad. Sci. USA 94 (1997) 13838–13843.
[125] P. Sibille, A.D. Strosberg, A FIV epitope defined by a phage peptide library screened with a monoclonal anti-FIV antibody, Immunol. Lett. 59 (1997) 133–137.
[126] http://www.biacore.com/
[127] http://www.ti.com/spr/
[128] http://www.biosensor.com/
[129] http://www.biotul.com/
[130] V. Owen, Real-time optical immunosensors—a commercial reality, Biosensors Bioelectron. 12 (1997) i–ii.

Biographies

Jiří Homola received his diploma in physical electronics from the Czech Technical University, Prague, Czech Republic in 1988, and a Ph.D. degree in the field of guided-wave optics from the Academy of Sciences of the Czech Republic in 1993. In 1993 he joined the Institute of Radio Engineering and Electronics of the Academy of Sciences of the Czech Republic, Prague, as a research scientist, working on fiber optic sensors and surface plasmon resonance-based sensing devices. Currently he is a visiting scientist at the University of Washington, Seattle. His research interests are in guided-wave optics, and optical sensors and biosensors.

Sinclair S. Yee received B.S., M.S., and Ph.D. degrees in electrical engineering from the University of California, Berkeley, in 1959, 1961, and 1965, respectively. In 1964, he joined the Lawrence Livermore Laboratory as a research engineer working on semiconductor devices. Since 1966 he has been on the faculty of the Department of Electrical Engineering at the University of Washington, where in 1974, he became a full professor. In 1972–1974, he was a NIH Special Research Fellow, and since 1979, he has been an IEEE Fellow. His main research interests are concerned with silicon-based and GaAs quantum well optical modulator devices, surface plasmon resonance, as well as microsensor arrays.

Günter Gauglitz received his M.S. degree at the University of Iowa, Iowa City, in 1965, a diploma at the University of Tübingen 1968, and a Ph.D. in 1972 for research activities in Philadelphia on rapid detection systems in pharmacology. He received his habilitation in physical chemistry in 1979. He became a professor of physical chemistry and professor of analytics and informatics at the University of Tübingen in 1982 and 1988, respectively. His research interests include photokinetics, UV/Vis spectroscopy, chemical and biochemical sensors, theoretical and mechanistic considerations on kinetics, new optical approaches in sensing, interferometry, ellipsometry, laser dyes, and oxygen plasma research.