Anal. Chem. **2004,** *76,* 3269−3284

Fiber-Optic Chemical Sensors and Biosensors

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Review Contents

This biannual review covers the time period from January 2002 to January 2004 and is written in continuation of previous reviews (*A1*, *A2*). An electronic search in SciFinder and MedLine resulted in 532 hits. Since the number of citations in this review is limited, a stringent selection had to be made. Priority was given to fiber-optic sensors (FOS) for defined chemical, environmental, and biochemical significance and to new schemes and materials. The review does not include (a) FOS that obviously have been rediscovered; (b) FOS for nonchemical species such as temperature, current and voltage, stress, strain, and displacement, for structural integrity (e.g., of constructions), liquid level, and radiation; and (c) FOS for monitoring purely technical processes such as injection molding, extrusion, or oil drilling, even though these are important applications of optical fiber technology.

Fiber optics serve analytical sciences in several ways. First, they enable optical spectroscopy to be performed on sites inaccessible to conventional spectroscopy, over large distances, or even on several spots along the fiber. Second, fiber optics, in being waveguides, enable less common methods of interrogation, in particular evanescent wave spectroscopy. Fibers are available now with transmissions over a wide spectral range. Major fields of applications are in medical and chemical analysis, molecular biotechnology, marine and environmental analysis, industrial production monitoring and bioprocess control, and the automotive industry. *Note:* In this article, sensing refers to a continuous process, while probing refers to single-shot testing.

FOS are based on either direct or indirect (indicator-based) sensing schemes. In the first, the intrinsic optical properties of the analyte are measured, for example its refractive index, absorption, or emission. In the second, the color or fluorescence of an immobilized indicator, label, or any other optically detectable bioprobe is monitored. Active current areas of research include advanced methods of interrogation such as time-resolved or spatially resolved spectroscopy, evanescent wave and laser-assisted spectroscopy, surface plasmon resonance, and multidimensional data acquisition. In recent years, fiber bundles also have been employed for purposes of imaging, for biosensor arrays (along with encoding), or as arrays of nonspecific sensors whose individual signals may be processed via artificial neural networks.

This review is divided into sections on books and reviews (A), specific sensors for gases and vapors (B), ions and salinity (C), miscellaneous inorganic and organic chemical species (D), and biosensors (E), followed by sections on application-oriented sensor types (F), new sensing schemes (G), and new sensor materials (H), respectively.

BOOKS AND REVIEWS

A remarkable review focuses on aspects of sensor sensitivity and sensor performance ("quality") (*A3*). In the author's opinion, remarkable progress has been made in terms of designing and improving sensing schemes, but the comparability of trace analytical data produced (especially in different laboratories) has not been improved to the same degree. It is stated that it is mandatory to validate the performance of (bio)sensors by the same scrutiny as are more traditional analytical instruments, e.g., by applying established reference methods.

The size of certain FOCs is approaching the nanometer dimension. Following early approaches on ion nanosensors based on measurement of luminescence decay time (*A4*), fiber-optic nanosensors (in fact nanoprobes) have been introduced using antibodies (*A5*). The article covers general information on biosensors, a description of the fabrication methods and detection systems, and applications in single-cell analysis. The fundamentals of optical chemical sensors and biosensors are covered in a respective chapter in a textbook (*A6*). Narayanaswamy and Wolfbeis have edited a book on optical sensors for industrial, environmental, and clinical applications (*A7*).

Fluorescence-based fiber-optic arrays represent a universal platform for sensing as they are easily integrated into a multitude of different sensing schemes (*A8*, *A9*). The arrays are made up from a multitude of single sensors, from relatively straightforward pH sensors to more complex ones including artificial olfaction sensors, high-density oligonucleotide arrays, and high-throughput cell-based arrays. Imaging fiber bundles composed of thousands of fused optical fibers are the basis for an optically connected, individually addressable parallel sensing platform.

Ligler and Rowe-Taitt have edited a book on optical biosensors (*A10*). As far as fiber optics are concerned, the chapters on fiber-optic biosensors (written by Rowe-Taitt and Ligler), on biosensors based on measurement of fluorescence decay time (by Thompson), on evanescent wave fiber-optic biosensors (by Rowe-Taitt, Ligler, and Phil), and on optrode-based fiber-optic biosensors (by Biran and Walt) are most relevant.

Reviews have appeared on analytical methods (including sensors) for aflatoxins (*A11*); on biosensors for DNA sequencing (*A12*); on fluorometric DNA biosensors (*A13*); on DNA aptamers as new recognition elements for biosensors (*A14*); on optical biosensors for food pathogen detection (*A15*) using fiber-optic

10.1021/ac040049d CCC: $27.50
Published on Web 05/20/2004

tips, optical biosensors with particles, surface plasmon resonance (SPR), and optical sensor membranes; on fluorescence-based fiber optic arrays that—in the authors' opinion—represent a universal platform for sensing (*A16*); on in situ fluorescence-based probes being considered as useful tools for noninvasive bioprocess monitoring (*A17*), on applications and new developments in fiber-optic fluorescence spectroscopic techniques for the analysis of polycyclic aromatic hydrocarbons (*A18*); on multiparametric fluorescence techniques based on spectral change, intensity, lifetime, and polarization; this versatility is said to pave the way for analyzing multicomponent mixtures without separation procedures; on nanobiosensors that can "probe the sanctuary of individual living cells" (*A19*); and on mid-IR fiber-optic sensors in general (*A20*).

Lopez-Higuera has edited a handbook on optical fiber sensors (*A21*) that contains chapters on fiber-optic biosensors (written by Rowe-Taitt and Ligler); on fiber-optic sensors for environmental applications (written by Holst and Mizaikoff); on biomedical fiber-optic sensors (written by Baldini and Mignani); on gas spectroscopy techniques for optical fiber sensors (written by Culshaw), on broadband superfluorescent fiber-optic sources (written by the editor); and on optical noses that can mimic a vertebrate's olfaction capability via sensor arrays giving typical signal pattern (written by Walt and Stitzel); among others. The progress made during the past five years in the field of optical fiber biosensors was reviewed (*A22*), as was the use of advanced luminescent labels, probes, and beads in (fiber-optic) luminescence bioassay and imaging (*A23*).

Fiber-optic gas sensing using absorption spectroscopy is a kind of evergreen and the present state has been reviewed (*A24*). Spectroscopic methods include open-path fiber-coupled microoptic cells, evanescent wave sensors using D-shaped optical fibers and holey fibers, systems using broadband sources and laser sources, techniques for sensitivity enhancement and noise reduction, and various multipoint gas detection systems.

Medical applications of Raman spectroscopy and the principles to clinical implementations such as early detection of cancers, monitoring of the effect of various agents on the skin, determination of atherosclerotic plaque, and rapid identification of pathogenic microorganisms also were reviewed (*A25*). Finally, the potential of fiber-optic (mainly Bragg grating) sensors was discussed by Rao (*A26*).

SENSORS FOR GASES, VAPORS, AND HUMIDITY

This section covers all gaseous species including their solutions. Hydrogen remains to be a target gas in fiber-optic sensing simply because of the intrinsic safety of FOS. A scheme for distributed hydrogen sensing using evanescent wave spectroscopy along with platinum-supported tungsten trioxide thin films that change color on exposure to hydrogen has been described (*B1*). The sensor shows fast response to 1 vol % H_2 and can be operated in the optical time domain reflectometer (OTDR) mode to enable the localization of hydrogen leakage points. In closely related work, the sensor was shown to work even at very low temperature and to be useful for detection of hydrogen in fuel cell cars (*B2*). Low-cost fiber sensors, also intended for use in H-fueled passenger vehicles, were reported (*B3*). An optical fiber SPR sensor was developed for the detection of hydrogen leakages (*B4*). A thin layer of palladium metal deposited on the bare core of a multimode fiber was used as the transducer whose resonance angle changes on exposure to hydrogen. The sensor has good detection limits (0.8%) and is acceptably fast (3−5 min)

Gaseous hydrocarbons can be sensed via sapphire fiber sensors coated with a thin layer of poly(dimethylsiloxane) (*B5*). A range of hydrocarbons, from hexane to pentadecane, was analyzed at 2930 cm^{-1} using both fiber-coupled FT-IR spectroscopy and a modular prototype system. A 64-point fiber-optic methane sensor installed on a landfill site was described that works under harsh conditions but is reported to perform satisfactorily, detecting methane in the range of 50 ppm to 100% (*B6*). Hydrocarbon leaks also may be located by an OTDR fiber-optic chemical sensor (*B7*). The distributed sensing system is built from a polymer-clad silica fiber adapted to an OTDR setup. OTDR measurements allow locating and detecting chemicals by measuring the time delay between short light pulses entering the fiber and discrete changes in the backscatter signals that are caused by local extraction of hydrocarbons into the fiber cladding. Distributed sensing of pure liquid hydrocarbons (HC) and aqueous HC solutions with a mini-OTDR (operated at 850 nm) and adapted to sensing fibers of up to 1-km length could be demonstrated.

A simple gas cell was designed for determination of methane (*B8*). The length of the light beam interacting with methane is 4 times the physical length of the optical cell, thus resulting in much better limits of detection. An in situ multiplexing long-path fiber-optic remote sensing system for methane that uses a single laser source was described (*B9*). It can measure the spatial distribution of methane via frequency modulation spectroscopy and harmonic detection. Using a fiber-optic splitter, the remote monitoring system can employ a single laser source to obtain multicenter measurements in the near-IR region.

Optical sensors for oxygen based on dynamic quenching of luminescence have had particular success in the past years, and they are now being improved (albeit not in principle) and adapted to specific problems. A plastic fiber-based optical sensor array has been introduced for the in situ measurement of ground air oxygen concentrations in a lignite mine tailing affected by acid mine drainage formation (*B10*). The instrument evaluates the oxygen-dependent change of the luminescence lifetime of an oxygen indicator using a phase modulation technique. Multiposition sensing of dissolved oxygen has been reported that is based on room-temperature phosphorescence quenching (*B11*). Both triplet lifetimes and phosphorescence intensities were measured and applied to multiposition analysis of water-dissolved oxygen in four different locations. Water-dissolved oxygen in shake flasks was continuously monitored via a sensor patch placed inside the flask (*B12*). The sensor signal remained unaffected during 80 autoclaving cycles, which suggests its multiusage. Specifically, cultivation of *Corynebacterium glutamicum* was studied and optimized.

An interesting new scheme for remote determination of oxygen operates at millimeter wave frequencies (*B13*). A 9.5−10.5-GHz signal from a yttrium iron garnet is carried via an IR laser down a 1-km fiber-optic cable. The sixth harmonic of the transmitted microwave signal is generated directly with an active sextrupler, which permits working in the 57−66-GHz band. Absorption measurements are undertaken using a Fabry−Perot cavity absorption cell. Oxygen can be quantified using the 57−66- and 114−

128-GHz bands. Water vapor in air also can be quantified between 5×10^{-5} and 0.025 volume fraction in air.

A highly sensitive device for probing ozone has been introduced that is based on an glass optical waveguide (*B14*). The waveguide is coated with a starch film incorporating potassium iodide that (irreversibly) turns blue on exposure to ozone. Ando et al. have shown that thin films of poly(*N*-methylaniline) undergo a reversible color change if contacted with gaseous ozone (*B15*). The films showed changes of optical absorbance at 500−800 nm in the presence of 50−100 ppm ozone in air at room temperature. The effect is partially reversible.

A multipoint fiber-optic detection system for carbon monoxide and oxygen based on intracavity spectroscopy was reported that uses fiber Bragg gratings as wavelength-selective cavity mirrors and a tunable filter to tune the operating wavelength to the wavelength of a selected Bragg grating (*B16*). The Bragg wavelengths of the gratings are chosen to be aligned to different absorption lines of a gas or gases, allowing gas concentrations at multiple locations to be determined. Several gases have been determined simultaneously in combustion gases by using a tunable diode laser IR sensor (*B17*). In addition to carbon monoxide and oxygen, water vapor and gas temperature were sensed in industrial furnaces.

Water-dissolved carbon dioxide was quantified with a reservoir-type capillary microsensor (*B18*). A pH indicator in the form of its ion pair with a quaternary ammonium base and a buffer in an ethyl cellulose matrix, all placed at the tip of an optical fiber, served as the sensing chemistry. The dynamic range is between 1 and 20 hPa pCO_2. The response time is 15 s, and the detection limit is 1 hPa pCO_2. The sensitivity of fiber-optic CO_2 sensors utilizing indicator dyes was studied once more (*B19*). Gastric CO_2 can be monitored with optical fibers of similar design (*B20*), and the results compare favorably with those obtained with a commercial (non-fiber-optic) instrument. A sol−gel-based optical carbon dioxide sensor that employs dual luminophore internal referencing and is intended for application in food packaging technology was described **(***B21*). A fluorescent pH indicator was immobilized in a hydrophobic organically modified silica matrix, along with cetyltrimethylammonium hydroxide as an internal buffer. Fluorescence is measured in the phase domain by means of the dual luminophore referencing scheme. The resolution is <1%, and the limit of detection is 0.08% CO_2. Oxygen cross-sensitivity is minimized by immobilizing the reference luminophore in polymer nanobeads.

Ammonia can be determined in the ppt concentration range with a composite optical waveguide pH sensor (*B22*). The sensitive element is based on a TiO_2 film that was deposited onto the surface of an ion-exchanged glass waveguide and whose surface was coated with a thin film of the pH indicator dye bromothymol blue by spin coating. Gas sensors for ammonia, carbon dioxide, and water were reported that operate near 2 μm (*B23*). The ammonia transition at a frequency of 5016.977 cm^{-1} is isolated from water and carbon dioxide interference, while the carbon dioxide transition at 5017.030 cm^{-1} is isolated from both ammonia and water interference, and the transition at 5017.100 cm^{-1} is specific for water.

The spectra of polyaniline are known to be pH dependent in the 300−1500-nm range. This has been expolited in a sensor for remote detection of gaseous ammonia (*B24*). Gaseous ammonia is monitored at 1300 nm (but may as well at shorter wavelengths) since this corresponds to a region of high optical transmission for optical fibers and is also compatible with telecom devices and technology. Typically, the transmission of the polyaniline films at 1300 nm increases by about 1% in response to gaseous ammonia levels of 6 ppm at 50% relative humidity. It takes several hours for the output to reach the equilibrium, so calibration curves were obtained using two readings 15 s apart.

Fiber-optic evanescent sensing of gaseous ammonia with two forms of a new pH-sensitive near-infrared dye was reported by the same group (*B25*). The dye was compared to phenol red whose absorption changes maximally at 565 nm, while the new copper complexes used change color at 735 and 744 nm if exposed to gaseous ammonia. Again, response times were rather slow.

A new scheme for probing nitric oxide is based on the reaction between the Cu(II) complex of eriochrome cyanine R and nitric oxide in phosphate buffer of pH 7.4 (*B26*). The range for NO was from 0 to 60 μmol L^{-1}, with a detection limit of 1.2 μmol L^{-1}. This reaction was then used as the basis in the development of a fiber-optic probe for NO gas.

Hydrofluoric acid and ammonia have been monitored in stack gases with a portable tunable diode laser analyzer (*B27*). The device incorporates a fiber-optic port to which a variety of measurement heads can be connected. It can be inserted into a single stack sampling port and is capable of providing instantaneous in situ stack gas measurements. The system is self-calibrating and works under practical HF and NH_3 sensing conditions where stack temperatures can reach 300 °C and moisture levels vary between 10 and 25%.

A vapor-sensing system has been reported that is based on a hydrophobic alumina thin film formed by the electrostatic self-assembly monolayer process (*B28*). Thin films of Al_2O_3 and polymer were deposited on the ends of optical fibers, and the resulting sensors respond to organic vapors of acetone, CH_2Cl_2, ethanol, and the like. Another vapor sensor utilizes the lutetium bisphthalocyanine complex and can be operated at standard telecommunication wavelengths (*B29*). If contacted with vapors of ethanol, hexanal, butyl acetate, acetic acid, etc., the refractive index changes and this can be detected at an analytical wavelength of 1310 nm. The capability of discriminating vapors can be improved by mimicking a canine nasal cavity flow environment (*B30*). Nasal cavities play an important role in vertebrate olfaction but have not previously been incorporated into gas-phase sensor technology. By exposing identical sensors to different flow environments, measurements of the combined sensor responses provided increased discrimination of alcohols as compared to measurements obtained from a single sensor. This method may improve the discriminatory power of sensors employed in artificial noses.

A relative humidity (RH) sensor with Bragg gratings that uses polyimide-recoated optical fibers is reported to have a linear, reversible, and accurate response at 10−90% RH between 13 and 60 °C (*B31*). Conventional fiber-optic sensors may as well be applied for sensing RH and chemical warfare agents (*B32*). The sensor described is based on monitoring the refractive index changes exhibited by the reactive coating applied to the surface of the optical fiber in response to analytes. The coating for the

RH sensor is made of carboxymethyl cellulose, while the coating for chemical warfare agents employs metal nanoclusters embedded in polyethylenimine.

ION SENSORS

This section covers sensors for all kinds of inorganic ions including the proton ("pH"), cations and anions, and salinity. Optical sensing of pH remains of greatest interest even though all optical sensors suffer from cross-sensitivity to ionic strength. A major recent application is in sensing pH inside cavities such as microtiter plates and microbioreactors, which has the advantage of a noncontact measurement, which can help to avoid microbial contamination. Quantitive binding constants of proton-selective chromoionophores and anion ionophores in solvent polymeric sensing membranes were determined (*C1*) by the so-called sandwich membrane method. The pK_a values of eight chromoionophores in plasticized PVC are given, as are the complex formation constants of the Co(III)cobyrinate nitrite ionophore and an organomercury chloride ionophore.

pH was monitored continuously in a perfused bioreactor system using an optical pH "sensor". In fact, however, the indicator phenol red was dissolved in the medium (*C2*). The system initially was calibrated and then used for 124 days during which it showed adequate performance. A pH optical fiber sensor without a pH-sensitive dye was described (*C3*) in which a porous SiO_2 film made by the sol−gel method was cladded onto a fiber core. It exploits the changes in refractive index that occur as the pH of a solution changes the charge of the sol−gel surface and, thus, its loading with alkali cations. The sensitivity to pH is up to 0.66 dB per pH unit for the pH range from 7 to 10.5. Another microbent fiber-optic pH sensor was reported (*C4*) where a permanently microbent portion of a plastic fiber was coated with a thin film of the pH-sensitive dye impregnated into a sol−gel material. The pH of highly acidic solutions was assessed via a heterocore structured fiber-optic "sensor", with a pH sensitive dye placed in the solution to be studied (*C5*). The heterocore sensing elements have been fabricated only by cleaving and fusion splicing, and the color of the dye is measured via evanescent wave interaction.

Plasticizers are widely used in ion-selective electrodes based on PVC membranes. In optical sensors, their tendency to leach can cause substantial problems, for example, because the apparent pK_a and binding constants of optical indicators strongly depend on the fraction of plasticizer being present in a sensor membrane. Thus, leaching of a pasticizer results in temporal drifts and in shifts of the response curve. A sensor polymer containing a covalently immobilized Ca^{2+}-selective ionophore but no plasticizer was reported (*C6*) and used in potentiometric and optical sensors. Diffusion was greatly diminished for the immobilized ionophore. The copolymer matrix, unblended and blended with plasticized PVC, confirmed that covalently bound ionophores are fully functional for maintaining selective ion extraction and binding.

Three nanoparticle fabrication technologies were applied to produce fluorescent nanosensors for potassium, calcium, oxygen, and pH imaging inside living cells (*C7*). Each nanosensor was provided with specific ionophores, or enzymes, to impart selective response for the component to be sensed. The inhibitory effect of heavy metals on urease was exploited to detect heavy metal ions using an optical fiber biosensor (*C8*). Immobilized urease is inhibited by Hg(II), Ag(I), Cu(II), Ni(II), Zn(II), Co(II), and Pb(II), and the pH change resulting from the hydrolysis of urea was monitored using a commercial pH indicator strip. The linear response is between 1×10^{-9} and 1×10^{-5} mol L^{-1}, and the limit of detection is 1×10^{-9} mol L^{-1} (= 0.2 μg L^{-1}) for Hg(II). The immobilized urease was regenerated by L-cysteine. A similar test was reported before for a cuvette-based scheme and has now been extended to fiber optics.

Other sensors for heavy metals include those for Cu(II). In one sensor, Fast Sulfon Black F was immobilized onto a cation exchanger (*C9*). In another scheme (*C10*), the ion was detected at trace levels in seawater using a copper-binding protein labeled with a fluorophore that undergoes a change in decay time when copper ion binds to the protein. The subpicomolar detection limit reported is quite remarkable. In a third type of sensor, the metal ion indicator Pyrocatechol Violet (PV) was immobilized in plasticized PVC (*C11*). PV appears to bind Cu^{2+} in the sensor membrane with high selectivity. Cu(II) can be quantified in the range between 1 and 100 μmol L^{-1} range.

Cobalt can be sensed via the reaction of Co^{3+} with 1-(2-pyridylazo)-2-naphthol in the presence of peroxodisulfate (*C12*). An interesting and novel scheme was introduced for determination of lead ion. The so-called photonic crystal optrode sensor (*C13*) utilizes a polymerized colloidal array photonic crystal material that diffracts light in the visible spectral region. Changes in diffraction wavelength due to binding of Pb^{2+} to an 18-crown-6 ether are detected with a diode array spectrometer and a fiber-optic reflectance probe. Environmental nickel can be sensed via a fluorescence-based system using the nickel-binding protein from *Escherichia coli* (*C14*). When the protein binds nickel, it undergoes a conformational change that is detected fluorometrically using a protein label. The detection limit for Ni^{2+} is 8×10^{-8} mol L^{-1}. The assay also was adapted to microtiter plate and fiber-optic bundle formats.

An engineered bacteria based biosensor was reported for monitoring bioavailable heavy metal ions such as Cu^{2+} (*C15*). A strain of *Alcaligenes eutrophus* was genetically engineered by inserting a luxCDABE operon from *Vibrio fischeri* under the control of a copper-induced promoter. As a result, copper ions induce bioluminescence that is proportional to the concentration of the triggering ion (Cu^{2+}). The detection limit was 1 μmol L^{-1}. A sensing system for metal ions based on the combination of separation/preconcentration by a permeation liquid membrane and fiber-optic detection (*C16*) uses a wall of a polypropylene hollow fiber that serves as support for the permeable liquid membrane. The lumen of the fiber contains the strip solution in which Cu^{2+} is accumulated. Calcein, a fluorochromic dye, acts as stripping agent and at the same time as metal indicator. The quenching of the calcein fluorescence upon metal accumulation in the strip phase is monitored with a multimode optical fiber.

Two types of evanescent wave fiber-optic sensors for trace analysis of Fe^{3+} in water (*C17*) were reported in which the unclad portion of a multimode silica fiber or the microbent portion of a multimode plastic fiber acts as the sensing regions. "Sensing" (which in this case is more a kind of remote spectroscopy) is performed by measuring the absorption of the evanescent wave in the reagent medium surrounding the fibers. In two rather closely related articles, flow-through optical fiber reflectance

sensors for lead ion and based on immobilized gallocyanine were described (*C18, C19*).

The problem of limited selectivity of indicators for metal ions was addressed by creating a cross-reactive metal ion sensor array (*C20*). Unspecific probes for metal ions (having almost identical fluorescence spectra, thus enabling (a) interrogation at identical analytical wavelengths and (b) imaging of the probes contained in the wells of the MTP using a CCD camera and an array of blue-light-emitting diodes as a light source) were deposited in the wells of a microtiter plate. The unselective response of the indicators in the presence of mixtures of five divalent cations generates a characteristic pattern that was analyzed by chemometric tools.

Water, soil extracts, and pastes analyzed were for nitrate with a common ATR ZnSe crystal and with silver halide fibers. Mid-IR spectra of nitrate, phosphate, carbonate, sulfate, ammonium, and organic constituents in samples were collected to study cross-interferences. By applying the simple mode of the cross-correlation method, direct monitoring of soil and water nitrate becomes possible by FT-IR using silver halide sensors or membrane systems (*C21*). Direct transmission of mid-IR radiation through ion-exchange membranes, partially loaded with nitrate or carbonate, was found to represent an effective alternative. Simultaneous monitoring of nitrate and nitrite in surface water by sequential injection analysis also was described (*C22*). In the fully automated procedure, nitrite is determined directly by means of the Griess diazo-coupling reaction (detected at 540 nm) in the flow cell of the fiber-optic spectrophotometer, while nitrate was first reduced by passing it through a reducing minicolumn. Following this reduction step, the nitrite formed is analyzed in the same way. A total of 0.05−1.0 (nitrite) and 0.5−50 mg of nitrogen L^{-1} (nitrate) are detectable. Another type of nitrate optical sensor employs a lipophilic fluorescent potential-sensitive dye (*C23*). The sensor material consists of a polymer-stabilized emulsion composed of a hydrogel with entrapped plasticizer droplets which, in turn, contain a cationic potential-sensitive fluorescent dye (PSD) located near its surface. The PSD also acts as an anion-exchange catalyst that extracts nitrate into the plasticizer droplet. This process causes a decrease of micropolarity near the dye, resulting in a strong increase in the fluorescence intensity of the PSD. Both intensity and fluorescence phase shift can be masured. Nitrate can be sensed in the 0.1−50 mM range, with response times in the order of 3 min.

Mechanistic insights were presented regarding the mechanism and function of optical chloride sensors based on a mercuracarborand ionophore (*C24*). Fluorescent microspheres containing a highly chloride selective ionophore were prepared for clinical measurements. The stoichiometries were optimized to result in chloride sensors that display reduced sodium interference. The optimized composition shifted the analytical range to physiological conditions, making them useful for the assessment of chloride in undiluted and diluted blood at pH 7.4. An optical serum and blood chloride sensor commercialized in the late 1990s in the form of a clinical electrolyte analyzer was published (*C25*). It is based on dynamic quenching of the fluorescence of lucigenin photoimmobilized on a thin film of an acrylamide−acrylonitrile copolymer. The decrease in fluorescence intensity on exposure of the sensor to 100 mM chloride typically is −60%. Chloride can be assayed in the 1−200 mM concentration range. Bromide, iodide, and salicylate interfere.

SENSORS FOR SPECIFIC CHEMICAL COMPOUNDS

This chapter covers sensors for (a) pollutants, agrochemicals, and nerve agents; (b) explosives; (c) drugs and pharmaceuticals; and (d) miscellaneous organics. Chlorinated hydrocarbons and nitroaromatic compounds form hardly biodegradable classes of compounds, and respective sensors are of substantial interest. Fiber-optic biosensors were reported (*D1*) for halogenated organics in groundwater that make use of plasmid-encoded haloalkane dehalogenases expressed from *E. coli*. Detection limits are less than 0.1 ppb, and linear responses range over at least 2−4 orders of magnitude of, for example, dichloroethane. The biosensors did not respond to naturally occurring nonchlorinated chemicals such as acetate and amino acids or to structurally different chlorinated hydrocarbons.

Fiber waveguide sensors were reported for explosive-related vapors (*D2*). The mid-IR sensors can detect and quantify explosive-related chemicals associated with land mines. Thin polymer films were coated onto a mid-IR transmissive chalcogenide fiber. The chemicals partition into the polymer film, where they absorb IR radiation at characteristic wavelengths in the evanescent wave region near the fiber−polymer interface. Reversible detection of dinitrobenzene and dinitrotoluene at low concentrations in air is demonstrated. Nitroaromatics in water may be determined in situ with a sol−gel-coated mid-infrared fiber-optic sensor (*D3*). Sol−gels were deposited on silver halide fibers by dip coating. Nitrobenzene and parathion diffuse into this layer and can be detected by evanescent wave IR spectroscopy in the low-ppm concentration range.

Water can be analyzed for polycyclic aromatic hydrocarbons by laser-excited time-resolved Shpol'skii spectrometry with fiber-optic probes (*D4*). The assay includes a rapid solid−liquid extraction procedure, a cryogenic fiber-optic probe for fluorescence measurements in frozen matrixes at 4.2 K, and an instrumental system for laser-excited time-resolved Shpol'skii spectrometry. Fifteen U.S. EPA priority pollutants were quantified in less than 5 min. Volatile organic compounds in groundwater can be sensed online using mid-infrared fiber-optic evanescent wave spectroscopy (*D5*). A prototype was tested at a pilot-scale plant. A 10-cm-long core-only section at the center of the fiber was mounted on a sensor head and coated with a hydrophobic polymer layer. The sensing zone was immersed into the sample under circumstances close to field conditions. The evolution of the concentration of analytes injected into the system was monitored over time. Surface-enhanced Raman spectroscopy (SERS) has been applied to monitor water for warfare agents (*D6*). It was demonstrated that SERS is a viable method for detecting traces of agents directly in an aqueous environment. Specifically, cyanide, 2-chloroethyl ethyl sulfide, phosphonates, and Gram-positive and Gram-negative bacteria were determined.

The seemingly ubiquitous herbicide atrazine remains to be a target analyte in research on chemical sensors. A novel fiber-optic biosensor based on immobilized glutathione S-transferase and sol−gel-entrapped bromcresol green was reported to be suitable for determination of atrazine (*D7*). The enzyme was immobilized on a layer of a hydrophilic poly(vinylidene fluoride) membrane.

This membrane was supported on an inner glass disk by means of an intermediate binder sol−gel layer that incorporated bromcresol green. The rate of the enzymic reaction (more specifically the decrease in pH) served as an analytical signal. The calibration curve covers the 2.5−125 μM range, the detection limit being 0.8 μM. The immobilized enzyme retained about 75% of its original activity after 1 month of use. A portable fiber-optic pesticide biosensor was also reported by this group. It is based on immobilized cholinesterase and sol−gel-entrapped bromcresol purple (*D8*). As in rather similar previous sensors of that kind, the rate of the inhibited reaction served as the analytical information.

Assays and sensor platforms for the detection of aflatoxins were compared (*A11*, *D9*). The dissolution rate of solid pharmaceutical preparations can be continuously monitored in situ by using a multiple-channel fiber-optic sensor (*D10*). The sensing scheme is based on the capability of certain drugs to quench the fluorescene of certain immobilized fluorophores. The dissolution rates of tablets containing ofloxacin, metronidazole, and nitrofurantoin were monitored.

A reversibly responding optical sensor was reported for hydrogen peroxide (HP). A fluorescent probe (the Eu^{3+}−tetracycline complex) was immobilized on a hydrogel, and its fluorescence at 616 nm (which increases 3-fold on contact with HP) served as the analytical signal (*D11*). The largest signal changes with HP are observed at pHs between 6.5 and 7.5, and the response is between 10 and 300 ppm of HP, equal to 0.3−10 mmol L^{-1}). Phosphate, Cu^{2+}, and citrate interfere. Also, the spatial distribution of HP concentrations in the wells of a microtiter plate was imaged using a battery of blue LEDs as the excitation light sources and measurement of luminescence decay time by two methods, which were compared (*D12*).

BIOSENSORS

Biosensors make use of biological components in order to sense a species of interest (which by itself need not be a "biospecies"). On the other side, chemical sensors not using a biological component but placed in a biological matrix *are not biosensors* by definition. It should be noted that some of the biosensors can be found in other chapters where they are placed more properly.

Enzymes are still indispensable tools in biosensing. An algal biosensor using alkaline phosphatase for determination of heavy metals was reported (*E1*). It exploits the inhibitory action of heavy metals on the alkaline phosphatase present in the membrane of *Chlorella vulgaris* microalgae. The microalgal cells were immobilized on removable membranes placed in front of the tip of an optical fiber bundle.

If alcohol oxidase is immobilized on the surface of an oxygen sensor, a biosniffer for ethanol vapor is obtained (*E2*). Ethanol solutions (0.5−9 mmol L^{-1}) were analyzed. Ethanol vapor (containing 0.7−51.5 ppm ethanol) was also assayed with good selectivity. A prototype for measurement of the activity of the enzyme lipoxygenase was developed (*E3*). Activity was determined by measurement of the rate of oxygen consumption using oxygen sensors. A flow injection optical fiber biosensor for glucose based on the electrochemiluminescence (ECL) of luminol was presented (*E4*), where glucose oxidase (GOx) was immobilized on the surface of a glassy carbon electrode, and glucose was quantitated by ECL between 50 μmol L^{-1} and 10 mmol L^{-1}, with a detection limit of around 26 μmol L^{-1}. The GOx showed excellent operational stability. A glucose biosensor based on the optical measurement of hydrogen peroxide HP formed during the glucose oxidase-catalyzed oxidation of glucose uses an immobilized optical probe for HP (*D11*). It is considered to be the first reversible glucose biosensor based on the measurement of the formation of HP. It is capable of sensing glucose in concentrations between 0.1 and 5 mmol L^{-1}.

One more biosensor for urea makes use of the sol−gel technology (*E5*). The decomposition of urea by the enzyme causes an increase in pH, which causes changes in the absorption of a pH indicator. Sepharose-immobilized firefly luciferase was employed for determination of lucigenin and ATP (*E6*). The peak intensity of bioluminescence was linear with respect to ATP concentration in the range of 10^{-9}−10^{-5} mol L^{-1}. In a fiber-optic biosensor for glutamate (*E7*), the enzyme glutamate dehydrogenase (GDH) was encapsulated in a silica sol−gel film on the tip of an optical fiber. GDH catalyzes the oxidative deamination of glutamate to α-ketoglutarate and the simultaneous reduction of NAD^+ to NADH. To quantify glutamate, the rate of formation of the NADH fluorescence is measured as a function of time. NADH was photochemically recycled with thionine.

The activity of the enzyme telomerase in tumor cells can be measured using fiber-optic biosensors (*E8*). Enzymic inclusion of fluorescein-labeled dUTP enabled real-time indication of the elongation of a phosphothioate telomeric substrate-modified primer. The elongated strand was detected by hybridization with a fluorescein-labeled complementary linear DNA probe. A comparison of the telomerase activity using labeled and unlabeled nucleotides indicated the inhibition effect of the FITC-labeled nucleotides by slowing down the rate of enzyme formation.

A second large group of biosensors is based on the use of antibodies or antigens. A study of antibody immobilization techniques on quartz and fiber-optic surfaces for immunosensors has been carried out (*E9*). Methods of covalent antibody immobilization that have not previously been applied to optical fibers were investigated and compared with classical methods found in the literature. A thin-film composite optical waveguide was applied in a sensitive immunosensor (*E10*).The sensing element consisted of a TiO_2 film deposited onto the surface of a K^+ ion-exchanged waveguide. Protein A was coated onto the composite surface to give an immunosensor with a short response time and a detection limit of 70 pg mL^{-1} immunoglobulin. The RAPTOR biosensor has been described again in several papers. For example, an improved fluoroimmunoassay is reported by using the dye Alexa Fluor 647 (*E11*), and the advantages of this diode laser-compatible label were demonstrated in both direct binding assays and in a sandwich immunoassay for staphylococcal enterotoxin B. The redesign of the RAPTOR instrument (including recent upgrades) has been reported (*E12*). Microorganisms and toxins have been detected with evanescent wave fiber-optic immunosensors (*E13*), which can significantly improving sensitivity, selectivity, and in particular speed.

Fiber-optic immunosensors also have been developed (*E14*) for the detection of protein C (PC), factor V Leiden (FVL), and cardiac troponin T (cTnT). They are capable of detecting PC

deficiency (0.5−2.5 μg mL^{-1}). Monoclonal antibodies were developed as the reagents for a FVL biosensor. In a feasibility study, the cTnT sensor was shown to be capable of quantifying the cTnT level (1−3 ng mL^{-1}) in plasma, discriminating the abnormal from the normal. The sensing performance of another immunosensor for PC) was reported (*E15*). A deficiency in the anticoagulant PC can result in clotting complications that interfere with oxygen and nutrient transport. The fiber-optic biosensor developed can provide real-time diagnosis of PC deficiency and was tested to quantify PC level in human plasma. The effects of blocking buffers and plasma proteins on the performance of the protein C biosensor were also studied (*E16*). Blocking buffers can reduce the noise caused by nonspecific adsorption. The effect of various PC homologues (factors II, VII, IX, and X) on the biosensor performance was investigated.

Fluorescent qantum dots were studied with respect to their ability to act as reporters in immunoassay (*E17*). The fiber-optic detector utilizes fluorescent semiconductor quantum dots (QDs) as the reporter labels for different antibodies with the aim to detect multiple pathogens within a single fiber. CdSe/ZnS core−shell QDs of differing size were synthesized, functionalized, and covalently attached to rabbit anti-ovalbumin antibody. These labeled antibodies exhibit selective binding to ovalbumin antigen. The decay time of QDs depends on their size, the intensity of their optical excitation, and whether they are functionalized and conjugated to antibody.

Optical DNA sensors are difficult to control in terms of selectivity and relative surface affinities. Short single-stranded DNA oligonucleotides were grown on the surface of fused silica by nucleic acid synthesis and then submitted to hybridization (*E18*). The characteristic melt temperature of a 20-mer shifts by up to 10 °C when a single base pair mismatch is present in the center of a target oligonucleotide. Results based on fiber-optic biosensors that are used to study binding of fluorescein-labeled complementary DNA demonstrate that it is possible to achieve a selectivity coefficient of fully matched to single base pair mismatch of ∼ 85:1, while maintaining >55% of the maximally possible signal that can be obtained from the fully matched target duplex. Design guidelines for optimizing the collection of free propagating fluorescence for capillary waveguide sensors for the detection of nucleic acids were discussed (*E19*). Evanescent wave excitation of the coating layer containing a DNA probe is achieved by using a fiber-optic ring arrangement for coupling light directly into the capillary wall. The central part of the connector is used for injecting a DNA or RNA target into the capillary channel. In situ hybridization has been used to detect target molecules at a concentration of 30 pg mL^{-1}.

Another DNA hybridization assay has been reported that is based on evanescent fluorescence excitation and collection (*E20*). A tapered fiber-optic probe is used onto which is immobilized a single-stranded, synthetic oligonucleotide. Hybridization is detected with a fluorescently labeled signaling probe. In another type of DNA sensor, the intercalating dye thiazole orange is used for detection of hybridization (*E21*). Substantial fluorescence enhancement of thiazole orange occurs when the dye intercalates into double-stranded DNA. Direct selective detection of genomic DNA from coliform is possible by using a fiber-optic biosensor (*E22*). Several oligomers were covalently immobilized on fibers, and hybridization was detected. Nonselective adsorption of noncomplementary oligonucleotides was found to occur at a significantly faster rate than hybridization of complementary oligomers in all cases, but this did not inhibit selective interactions between immobilized DNA and cDNA.

A gas-phase multiple sensor array and a method for monitoring a PCR reaction for detection of DNA in real time were described in a patent (*E23*). A sensitive and specific assay for parallel analysis of mRNA isoforms on a fiber-optic microarray platform was introduced (*E24*). The method permits analysis of mRNA transcripts without prior RNA purification or cDNA synthesis. Using an endogenously expressed viral transcript as a model, the authors demonstrate that the assay readily detects mRNA isoforms from as little as 10−100 pg of total cellular RNA or directly from a few cells. Zeptomole detection limits were achieved with a high-density fiber-optic genosensor microsphere array (*E25*). A random array composed of oligonucleotide-functionalized 3.1-μm-diameter microspheres on the distal face of a 500-μm etched imaging fiber was monitored for binding to fluorescently labeled complementary DNA sequences. Specific hybridization was observed for each of three sequences in an array yielding a detection limit of 10^{-21} mol (equivalent to about 600 DNA molecules).

A fiber-optic biosensor has been designed for the detection of *E. coli O157:H7*. Following PCR, the presence of at least 103 cfu mL^{-1} *E. coli O157:H7* can be detected in a sample in less than 10 h (*E26*). The same strain can be analyzed in ground beef, chicken carcass, and lettuce samples with an immunomagnetic chemiluminescence fiber-optic biosensor (*E27*). Samples inoculated with *E. coli O157:H7* were first centrifuged and suspended in buffered peptone water and then incubated with anti-*E. coli O157* antibody-coated magnetic beads and peroxidase-labeled anti-*E. coli O157* antibodies to form sandwich complexes. The number of *E. coli O157:H7* cells was determined by collecting the peroxidase-catalyzed chemiluminescence signal from the bead surface through a fiber-optic light guide. The detection limits are between 300 and 500 cfu mL^{-1}. Genomic target sequences from *E. coli* can be detected via fluorescent intercalating agents such as SYBR 101 that can report hybridization events with target strands (*E28*). The biosensors were able to detect genomic targets at a picomole level in a time of a few minutes, and dozens of cycles of use have been demonstrated.

A fiber-optic biosensor reported to be capable of monitoring streptococci in human saliva (*E29*) utilizes evanescent wave spectroscopy to monitor a bacterial-mediated biochemical reaction. A short length of the fiber cladding is removed, the core surface is coated with a thin film of porous sol−gel, and the streptococci-mediated reaction with sucrose is monitored using a photosensitive indicator immobilized within the porous sol−gel. A rather related paper also appeared (*E30*).

Bacterial biosensors have been designed for determination of environmental pollutants. Thus, a biosensor was developed for the detection of tributyltin using a bioluminescent recombinant *E. coli::luxAB* strain (*E31*), and a strain of microorganisms from *A. eutrophus* was genetically engineered by inserting a luxCDABE operon from *V. fischeri* that is triggered by copper ion (*E32*). The sensitivity of a gas biosensor was improved by improved immobilization of a recombinant bioluminescent bacterium (*E33*). The genetically engineered bioluminescent bacterium (lac::lux-

CDABE) was immobilized to develop a whole cell biosensor for the detection of toxic gases. The toxicity of chemicals can be evaluated through the bioluminescent reaction as it reduces in intensity when the cells experience toxic or lethal conditions. The biosensor was fabricated by immobilization in a solid agar medium, and the vapors tested include those of benzene, toluene, ethylbenzene, and xylene. A cell array biosensor was developed (*E34*) that is composed of thousands of individual bacteria cells expressing a reporter gene that responds to the presence of environmental pollutants. The array was produced by immobilizing the cells in wells on an imaging fiber bundle. Each microwell was used to accommodate a single living bacterium, allowing simultaneous monitoring of the genetic responses of all the cells in the array. This platform appears to provide a powerful tool for various environmental and industrial applications.

Using a chemiluminescent fiber-optic biosensor and magnetic particles, a simple, sensitive, and rapid method to determine *Staphylococcus aureus* enterotoxin A in military rations was developed (*E35*). The assay was compared to the Analyte 2000, a commercial fluorescent fiber-optic biosensor. The "sensitivities" (= limits of detection) of chemiluminescent and fluorescent immunoassays were 1 ng, significantly lower than the levels needed to cause illness. Alternatively, staphylococcal enterotoxin B (SEB) may be detected with a miniature fiber-optic surface plasmon resonance sensor (*E36*). The sensor is based on spectral interrogation of surface plasmons in a miniature sensing element based on a side-polished single-mode optical fiber with a thin metal overlayer. The surface of the sensor is functionalized with a covalently cross-linked double layer of antibodies against SEB. Nanogram quantitities of SEB per milliliter of sample can be detected in less than 10 min.

Volatile products of the metabolism of (toxic) bacteria on food and other biological samples can be recognized by gas sensors and spectral footprints (*E37*). The sensor yields a gas "signature" or "spectral footprint " of the volatile products, which can be compared to the data of a library. The method can be used to detect spoilage of food and to identify microorganisms, in particular pathogens.

An optical fiber biosensor based on anomalous reflection of a gold surface was demonstrated for the system streptavidin−biotin (*E38*). The presence of a transparent surface layer on gold produces a large decrease in the reflectivity of the gold surface due to multiple reflections in the surface layer. This anomalous reflection has been exploited to monitor the adsorption of octadecanethiol to the gold surface and the binding of streptavidin onto a biotin-labeled monomolecular layer on gold. Furthermore, gold in the form of colloidal particles was used to modify the surface of an optical fiber to make them amenable to chemical and biochemical sensing (*E39*). The unclad portion of an optical fiber was modified with self-assembled gold colloids (SAGC). The optical properties and, hence, the attenuated total reflection spectrum of SAGC changes with the refractive index of its environment. The SAGC was functionalized with biotin in order to study the binding of streptavidin, which can be detected in concentrations as low as $\sim 10^{-10}$ mol L^{-1}. Hence, is appears to be suitable for label-free detection of affinity events.

Colorimetric resonant reflection can be applied as a direct biochemical assay technique (*E40*). A colorimetric resonant diffractive grating surface is used as a surface binding platform. An optical structure is used that, if illuminated with white light, is designed to reflect only a single wavelength. When biomolecules are attached to the surface, the reflected wavelength (color) is shifted due to the change of the optical path of light that is coupled into the grating. By linking receptor molecules to the grating surface, complementary binding molecules can be detected. The readout system consists of a white light lamp that illuminates a small spot of the grating at normal incidence through a fiber-optic probe and a spectrometer that collects the reflected light through a second fiber, also at normal incidence.

APPLICATIONS

This section comprises sensors for biotechnological, industrial, environmental, food, pharmaceutical, medical, and related applications. Optical sensors for oxygen have been used for noninvasive analysis of dissolved oxygen in shake flasks for cell cultures. The oxygen-sensitive element is a thin, luminescent patch affixed to the inside bottom of the flask. Both intensity (*F1*) and decay time (*B12*) may be measured, the latter said to be more reliable, particularly with respect to repeated sterilization. Mass-transfer coefficients are reported as well. The sensors are fast, do not consume oxygen, and are affordable. Oxygen gradients have been determined in engineered tissue using a fluorescent sensor spot (*F2*). Optical sensor patches containing a luminescent O_2-sensitive indicator were placed on the bottom of a Petri dish, and oxygen supply in a tissue of chondrocytes was monitored over a 3-week culture period. Two-dimensional pO_2 images across the tissue section were acquired over the duration of the experiment. Oxygen supply seemed to depend on cell density and cell function. pO_2 values below 11 Torr impair proper tissue development. The results illustrate that the method is ideally suited to assess the oxygen demand of cartilage cultures. pH can be continuously monitored in-line in perfused bioreactors using an optical pH sensor (*C2*). The pH indicator phenol red was added to the medium, and its spectra were recorded over time. The design of a prototype miniature bioreactor for high-throughput automated bioprocessing was described (*F3*). A miniature bioreactor with a diameter equal to that of a single well of a 24-well plate was provided with parameter-sensitive fluorophores (such as for oxygen) whose fluorescence was read with fiber-optic probes. Mass-transfer coefficients are reported as well.

Proteins in the eluate of a preparative continuous annular chromatograph were detected with a quartz fiber-optic system that measures the intrinsic absorption of two aromatic amino acids (Tyr, Trp) in proteins (*F4*). Two types of optical multichannel detectors were developed. The first is a multichannel detector, and the second is a circular optic device. UV absorption is recorded at 280 nm. Calibration plots were established for a series of stock solutons of known concentrations of proteins. The 16-channel detector has a limit of detection that corresponds to absorbance changes of 10^{-4} unit.

Near-IR (NIR) spectroscopy has been developed as a noninvasive tool for the direct, real-time monitoring of glucose, lactic acid, acetic acid, and biomass in liquid cultures of microorganisms of the genera *Lactobacillus* and *Staphylococcus* (*F5*). This was achieved by employing a steam-sterilizable optical fiber probe immersed in the culture. Second-derivative spectra were subjected

to partial least-squares regression, and the results were used to build predictive models for each analyte of interest. Interfacing of the NIR system to the bioreactor control system allowed the implementation of completely automated monitoring of different cultivation strategies (continuous, repeated batch).

Novel infrared optical probes have been introduced for process monitoring and analysis based on silver halide fibers (*F6*). Compared to near-IR spectroscopy, for which quartz fiber probes can be applied, the application of previously used mid-IR fiber materials was restricted due to deficiencies with regard to their optical transmission and mechanical properties. Several flexible probes of different geometries were constructed that are suitable for process monitoring. Oil aerosols from natural pipelines can be detected with an optical sensor assembly (*F7*). Sensors for moisture and pH value in reinforced concrete were reported (ref *F8*; also see sections B and C). The dye pyridinium-*N*-phenolate shows a moisture-dependent absorption. It was embedded in a polymer matrix. Increasing moisture causes a shortwave shift of the absorption. pH in concrete was measured with a fiber-optic sensor consisting of a pH indicator dye immobilized in a hydrophilic polymer matrix. The sensor system is reported to display long-term stability even in media of pH 12−13. Rugged, low-cost diode laser sensors for water and temperature were described (*F9*). These provide fast, accurate, and nonintrusive methods for monitoring species and temperature in combustors. A two-channel system was developed that combines lasers at 1343 and 1392 nm into a fiber that transmits the beam to the probe location. Modulation of each laser at a different frequency enables both channels to be detected by a single detector, simplifying the system.

In situ gas diagnostics can be performed in harsh environments such as volcano fumaroles or industrial combustion of glass furnaces using a compact, rugged, and portable fiber-optic evanescent field laser sensor (*F10*). The beam of a single-mode diode laser operated at around 1570 nm is coupled into the fiber. At the other end of the fiber, an IR detector is used to record the transmitted light intensity. Due to frustrated total reflection (FTR) and attenuated total reflection (ATR), the intensity is attenuated when passing the fiber. The FTR is related to a change of the index of refraction while the ATR is related to a change of the absorption coefficient. By tuning the laser wavelength across the absorption lines of analytes surrounding the fiber, a spectral intensity profile is obtained. Results from first field measurements at a volcano site were reported. H_2S, CO_2, and H_2O were directly detected in the gas stream.

Laser-based gas analysis for process control in waste incineration applications was reported (*F11*). A commercial gas analyzer based on tunable diode laser spectroscopy has successfully been applied to control and monitoring applications in the waste incineration industry. The analyzer was optimized for process control in the industrial environment and provides real-time signals for water vapor, oxygen, and temperature. A fiber-optic sensor was described that can detect fault gas dissolved in transformer oil (*F12*). Outlet pipes of petroleum wells can be continuously monitored for petroleum, water, and gases (*F13*). The sensor signals were transmitted to a microprocessing unit for pattern recognition analysis. An alarm can be given if the percentages of components (i.e., crude petroleum, water, and gases) exceed certain levels at predetermined times. An OTDR-based fiber-optic chemical sensor was applied to the localization of hydrocarbon leakage (*F14*). The time delay was measured between short light pulses entering the fiber and discrete changes in the backscatter signals caused by local extraction of hydrocarbons into the fiber cladding. Distributed sensing of pure liquid hydrocarbons and their aqueous solutions was demonstrated with a mini-OTDR adapted to sensing fibers of up to 1-km length.

Fibers are increasingly being used in spectroscopy during polymer melt processing (*F15*). New software allowed real-time acquisition and manipulation of spectra during melting. Chemometric techniques can be applied to produce robust calibration models for analysis of polymer melt compositions and to control melting (and molding) processes. A method and apparatus for in situ determination of molten polymer compositions using electronic absorption spectroscopy has been patented (*F16*). The application of various multivariate methods to determine the composition of a flowing, molten, immiscible, polyethylene−polypropylene blend from near-IR spectra was examined (*F17*). On the basis of previous approaches, several methods were investigated, namely, second-derivative absorptiometry, multiplicative scatter correction, and a combination of the two methods. The latter method was found to be most suitable. The continuum regression approach, a method that encompasses ordinary least-squares, partial least-squares, and principal component regression models, was then implemented and provided the best prediction model.

A new sensor head was developed for mid-infrared fiber-optic underwater sensors (*F18*). It was found that a U-shaped sensor head was the most suitable sensor geometry. A prototype was attached to an underwater FT-IR spectrometer and subjected to simulated real-world flume tank tests under controlled conditions. The sensor head allowed qualitative and quantitative analysis of a range of environmentally relevant analytes down to ppb concentrations. Real-time in situ determination of free Cu(II) at picomolar levels in seawater is possible with a fluorescence lifetime-based fiber-optic biosensor (*F19*).

Direct and chemically mediated absorption spectroscopy using optical fiber instrumentation can be used to monitor chromium in sewage, but also for determination of gasoline (*F20*). In all these sensors, a combination of broadband and multiband spectral measurements is collected using the same custom instrumentation unit consisting of LED light sources and an optical fiber microspectrometer. The custom instrumentation implemented to address these sensors is their key feature. It opens the possibility of addressing other sensors making use of absorption-based optrodes.

Metal ions in soil are detectable with a “direct push” sensor (*F21*) that enables real-time, in situ measurement in soils. The response is affected by the soil matrix conditions of grain size, composition, and water content. Calibration standards were used to generate a site-specific calibration curve. To compensate for moisture content, extra laser pulses are used to volatilize the water. When multiple spectra are taken of a single, homogenized soil sample, there is a significant amount of variability in the peak intensities. There is no internal standard available to correct for this variability. An optical algal biosensor for heavy metals expolits the inhibitory effect of heavy metals on alkaline phosphatase

(*F22*). The enzyme is present in the external membrane of *C. vulgaris* microalgae. Oxygen in underground air can be analyzed with a plastic fiber sensor array (*B10*). Oxygen, consumed in a lignite mine tailing affected by acid mine drainage formation, displays a strong concentration gradient to a depth of ~6 m.

Fiber optics can be used to monitor the dissolution of drugs such as rifampicin (*F23*) and the concentration of adriamycin in rabbit blood (*F24*). The excitement about the possibility of monitoring glucose noininvasively via near-IR spectroscopy appears to have ceased since the number of respective articles has fallen dramatically. A novel glucose fiber probe was reported (*F25*) that consists of one central optical fiber around which several others were arranged in circle. Light was shone onto the skin surface through the circle fibers, and scattered light reaching the central detecting fiber was collected and transmitted to the detection system. Glucose intake experiments showed that there is good correlation between the optically determined glucose levels and the values determined with blood samples, particularly if measured at around 1600 nm.

Breath ammonia, resulting from *Helicobacter pylori* infection, can be analyzed with an ammonia sensor (*F26*). Before urea ingestion, pylori-positive subjects had significantly lower breath ammonia levels than negative subjects, but had a significantly larger increase in breath ammonia after urea ingestion. Molecularly self-assembled thin-film materials may be incorporated in optical fiber waveguides to form humidity and other gas sensors of use in biomedical diagnostic systems. Distal end sensors based on this concept may be fabricated by molecularly self-assembling selected polymers and functionalized inorganic nanoclustesr into multilayered thin films on the cleaved and polished flat ends of single-mode optical fibers (*F27*).

The gastroesophageal system can be monitored with optical fiber sensors (*F28*). Specifically, foregut diseases can be diagnosed using sensors for the bile, carbon dioxide, and pH. The clinically relevant parameter is the exposure time of the stomach/oesophagus mucosa to the bile. A combined imaging and detection sensor for localized L-glutamate release at the insect neuromuscular junction was presented (*F29*). The sensor gel, spin-coated onto the tip of an optical imaging fiber, is composed of L-glutamate oxidase (GlOx), a pH-sensitive fluorescent dye, and poly(acrylamide-*co*-*N*-acryloxysuccinimide). Ammonia is liberated from the interaction of L-glutamate with GlOx, which reversibly reduces the fluorescence of the pH probe. The sensor has a spatial resolution of 3−4 μm and a detection limit of between 10 and 100 μM for L-glutamate.

Mid-infrared attenuated total reflection spectroscopy was applied to the human epidermis (stratum corneum) using a silver halide fiber probe of square cross section and adhesive tape stripping. (*F30*). Evanescent wave spectroscopy using a flexible fiber-optic probe from silver halide fibers of square cross section was employed for characterization and keratinocyte quantification on adhesive tapes.

SENSING SCHEMES

This section reports on improved or novel sensing schemes based on the use of fiber optics and related waveguides. Aside from their use as plain waveguides, fibers have been used for evanescent wave excitation of fluorescence or Raman scatter, for imaging and sensor array purposes, in microsensors and nanosensors, in surface plasmon resonance, and for distributed sensing, to mention only the more important ones.

The use of a plain fiber-optic coupler as a platform for bioassays and biosensing was described (*G1*). The coupler fabrication and design elements crucial to the sensor performance are described, and protein detection was demonstrated. Porous silicon can act as a transducer for immunosensors (*G2*) because it possesses visible photoluminescence and electroluminescence. A laboratory prototype of an immunosensor based on the photoluminescence of porous silicon is described for the determination of myoglobin in serum. Two-photon fluorescence spectroscopy through optical fibers leads to new sensing schemes (*G3*). In a typical experiment, the uptake of a targeted drug delivery agent into cultured cancer cells was studied.

A hybrid sensor was applied to simultaneously sense temperature and oxygen, and the temperature information was used to compensate for the temperature effect on the oxygen signal (*G4*). A fast and low-cost digital signal processor enables simultaneous multifrequency measurement to resolve different analytes in the luminescence signal of a sensor foil. Enhanced two-photon biosensing is possible with double-clad photonic crystal fibers (*G5*). A double-clad photonic crystal fiber was used to improve detection efficiency over a standard single-mode fiber in a two-photon fluorescence detection scheme in which a dye was excited and its backscattered fluorescence was detected through the same fiber.

An improved refractive index microsensor based on SPR for fine-scale measurements in aquatic environments was introduced (*G6*). Refractive index measurements in marine environments were performed to characterize light conditions around photosynthetically active organisms. The sensor achieves a spatial resolution of better than 1 mm, covering the range of 1.30−1.38 refractive index units with an accuracy of 5×10^{-4}. Swellable polymer microspheres also have been studied. A scheme for multiwavelength optical fiber liquid refractometry based on intensity modulation uses two fibers and a mirror as thed reflector (*G7*). The sensing scheme is based on reflective intensity modulation. A novel sensing probe was designed with the outer ring of fibers acting as illuminating fibers and a center fiber acting as the read fiber.

A sensing device has been introduced that utilizes a polymerized colloidal array photonic crystal material that diffracts light in the visible spectral region due to the periodic spacing of colloidal particles. On binding a chemical species through molecular recognition, the polymer swells, and this can be detected (*G8*). The "dual closed-loop optoelectronic autooscillatory detection circuit" was introduced as a new technique for fluorescence lifetime-based chemical/biological sensor arrays (*G9*). The instrument comprises a primary, closed loop and a secondary loop controlling a variable-phase delay within the primary loop. This system is said to be simple, inexpensive, and scalable for sensor array purposes. Its capabilities were demonstrated with a pH-sensitive fluorescent probe and an immunosensor based on fluorescence resonance energy transfer.

The finding of an anomalous reflection of light on thin gold films has led to a new sensing scheme that was demonstrated for the system biotin−streptavidin (*E38*). Colloidal gold-modified

optical fibers were shown to enable chemical and biochemical sensing (*E39*). Colorimetric resonant reflection has been introduced as a new direct assay technique (*E40*). A guided mode resonant phenomenon is used to produce an optical structure that, when illuminated with white light, is designed to reflect only a single wavelength. When (bio)molecules are attached to the surface, the reflected wavelength is shifted due to the change of the optical path of light that is coupled into the grating. By linking a molecular receptor to the grating surface, complementary molecules can be detected without the use of any kind of fluorescent probe or label.

Recent advances in long-period gratings, including (1) widely tunable single resonant band long-period gratings, (2) long-period gratings fabricated in single crystal sapphire fibers, and (3) long-period gratings fabricated in photonic crystal fibers, may result in highly sensitive biosensors (among other applications) (*G10*). A fiber-optic amplifier loop was used to improve gas sensing by cavity ringdown absorption (*G11*). The ring-down cavity consists of an optical fiber loop containing a microoptic cell and an erbium-doped fiber amplifier. The amplifier introduces gain into the cavity to increase the ringdown times and therefore the overall sensitivity of the system.

A gas-permeable liquid core waveguide was used as a long-path length spectrophotometric cell for sensing CO_2 (*G12*). The partial pressure of CO_2 in natural waters and the atmosphere was quantified. A liquid core (capillary) waveguide filled with an indicator and bicarbonate buffer) undergoes spectral changes if exposed to CO_2. Using an 18-cm cell with low indicator concentrations (10 μM), this system displays adequate precision and an accuracy in the pCO_2 range of 200−500 μatm. The response time is 2 min even for low-level pCO_2. A reservoir-type capillary microsensor was employed for pCO_2 analysis in seawater (*B18*).

A theoretical study of tapered, porous clad optical fibers for detection of gases revealed that the sensor response time and the minimum detectable concentrations depend on the taper ratio and geometry of the taper profiles, the absorptivity of gas, and the diffusion coefficients in the porous cladding (*G13*). U-Shaped fiber-optic pH probes were characterized in terms of effects of bending radius of the probe and the numerical aperture of the fiber on the sensitivity of the sensor (*G14*). U-Shaped probes also enable the determination of the critical micelle concentration of detergents (*G15*). A decrease in the bending radius of the U-shape is found to increase sensitivity. Heat-drawn biconical tapers were used for fluorescent sensing of solutions of fluorescein (*G16*). A capillary biosensor was demonstrated that uses the waveguiding properties of the capillary to integrate the signal over an increased surface area without simultaneously increasing the background noise from the detector. This biosensor achieves limits of detection of 30−50 pg mL^{-1} in immunoassays. Two different approaches to using the capillaries as immunosensors are described, either of which could be adapted for multianalyte sensing (*G17*). A microbend fiber-optic chemical sensor was described in a patent (*G18*). Light guided through the microbend section scatters out of the fiber core and interacts, either directly or indirectly, with the chemical in the sample, inducing fluorescence radiation that is scattered back into the microbend section and returned to an optical detector.

Sensor arrays are en vogue. A randomly ordered high-density fiber-optic microsensor array enables organic vapor discrimination, thus mimicking vertebrate olfaction (*G19*). Sensor arrays may also detect explosives and result in high-throughput genomic interrogation techniques. High-density microarray platforms also have applications in live cell, protein, and enzymic assays. A fiber-optic apparatus and its use in combinatorial material science was patented (*G20*). A cross-reactive metal ion sensor array in a microtiter plate format and making use of rather unspecific metal ion probes having almost identical fluorescence spectra was presented (*C19*). The unselective responses of the indicators in the presence of mixtures of cations generate a characteristic pattern that was imaged and analyzed by chemometric tools. Fiber-optic techniques also have been applied in time-resolved imaging of hydrogen peroxide using sensor membranes in a microwell format (*D12*). An optical imaging fiber-based recombinant bacterial biosensor (*G21*) was presented that is composed of thousands of individual bacteria cells expressing a reporter gene that responds to the presence of environmental pollutants. Each microwell at the tip of a fiber was used to accommodate a single living bacterium, allowing simultaneous monitoring of the genetic responses of all the cells in the array.

Microspheres have served as useful materials in new sensing schemes. Thus, a high-density fiber-optic genosensor microsphere array was introduced that enables zeptomole detection limits (*E26*). Fluorescent oligonucleotide-functionalized microspheres positioned on the distal face of an etched imaging fiber served to study the binding of oligomers to fluorescently labeled complementary DNA sequences. Microspheres also were used in ionophore-based ion sensors and in ion extraction (*G22*). The microspheres do not contain a plasticizer, but sensing components including H^+-selective (or K^+-selective) chromoionophores, and anionic sites. One type of particle responded to an anion−proton coextraction mechanism, while the other functioned by ion exchange. It is said that with the advent of plasticizer-free sensor microspheres a wide variety of ions may be assessed using bead-based sensing strategies, such as lab-on-a-chip technologies, bundled optical fiber arrays, and flow cytometry, without experiencing the deleterious effects resulting from plasticizer leaching. The ionophores may be covalently immobilized (*G23*). In a scheme for automatic decoding of sensor types within randomly ordered, high-density optical sensor arrays (*G24*), use is made of vapor-sensitive microbeads containing the dye Nile Red. On exposure to vapors, these undergo reproducible spectral changes, which allow the beads to be grouped into categogies by optical decoding.

The production, properties, and applications of fluorescent nanosensors for potassium, oxygen, calcium, and pH imaging inside live cells were reported as well (*G25*). The novel platform for intracellular monitoring uses three different nanoparticle fabrication technologies. These nanosensors, based on polyacrylamide, cross-linked decyl methacrylate, or silica-based sol−gel, were tested in intracellular surroundings. Each bead matrix can be combined with specific indicators, ionophores, or enzymes to produce sensors selective for the component of interest.

Chemical vapor-deposited diamond films can improve the self-referencing of fiber-optic Raman probes (*G26*). Diamond films grown by a microwave plasma deposition process exhibit es-

sentially no Raman spectral background while exhibiting a strong Raman peak at 1332 cm^{-1}. Internal referencing is accomplished by normalizing all spectral intensities of the chemical species to the integrated area of the diamond reference peak and verified using ethanol/water mixtures. Fiber-optic Raman probes have been used for analysis of gas mixtures in enclosures (*G27*). It was found that unfiltered, nonimaging probes have lower detection thresholds than a filtered, imaging, fiber-optic probe. Achievable thresholds for hydrogen, oxygen, nitrogen, carbon monoxide, and methane in gas mixtures were demonstrated to be <1 kPa with 10-s signal acquisition. Ambient carbon dioxide in air (0.03 kPa) was detectable in a 20-min acquisition process while ambient water vapor was well above the detection threshold.

MATERIALS

This section summarizes recent work in material sciences as related to FOS. Specifically, it covers aspects such as new polymers (including polymers for molecular imprints), sol−gels and porous glasses, and organic conductive polymers. Numerous organic polymers have been used as coatings on waveguides to specifically extract gaseous or organic chemicals into the coating, which then may be sensed, e.g., via refractometry or (mid-)IR absorption. A study has been presented (*H1*) on the factors affecting the diffusion of chlorinated hydrocarbons into polyisobutylene and polyethylene-*co*-propylene for evanescent wave sensing. Polyisobutylene and polyethylene-*co*-propylene were considered as preconcentration media for chlorinated compounds using mid-IR evanescent wave spectroscopy. A silver halide sensing fiber coupled to a FT-IR spectrometer served as the waveguide. Other polymer coatings serving the same purpose have been treated above in section D.

Sol−gels are widely used for encapsulation of chemicals, reagents, indicators, or enzymes and also as coatings on waveguides for extraction of specific chemicals that then may be sensed by direct spectroscopy, often via evanescent waves. The application of organically modified sol−gels as recognition membranes for mid-IR fiber-optic sensors was demonstrated (*H2*). The sol−gels were applied onto the surface of silver halide fibers by dip coating. The coating process was monitored in situ using FT-IR spectroscopy. Homogeneity of the layers was analyzed by SEM. The sensors were studied with respect to their capacity to suppress interfering water background absorptions, repeatability of dissolved analyte enrichment, and sensor response time. Nitrobenzene and parathion were studied in detail. Sol−gels were also employed in an optical sensor for carbon dioxide in modified atmospheric packaging applications (*B2*), once again for oxygen-sensing membranes (*H3*), and in photopatternable optical oxygen sensors based on hybrid sol−gel materials (*H4*).

Diamond films were deposited on quartz substrates and shown to be useful for self-referencing fiber-optic Raman probes (*G25*). Polyaniline, so far used in planar sensors only, was deposited on the cladding of fibers to result in sensors for chemical vapors (*H5*). Both the light absorption and the refractive index of the polymer change on exposure to vapors. In an indium tin oxide-coated immunosensor (*H6*), a thin film of polypyrrole was electropolymerized onto a fiber core to create a surface-conductive polymer, If the surface is avidinylated, biotin-conjugated cholera toxin B binds to the surface, and this can be detected.

The so-called hydrogels (in essence hydrophilic polymers) come in a wide variety of compositions and are being used for making sensing films and coatings for use in sensors forions and water soluble organic species including the saccharides. Recent polymers include the polyurethanes with a water uptake capacity of up to 100% of their own weight (*A23, H7*) and a copolymer between acrylamide and acrylonitrile (*C25*). Another hydrogel was employed in a sensor for humidity (*H7*). Organic polymers other than hydrogels have been used in microbead-based sensing schemes. This work has been treated above in sections C and G. Polyacrylonitrile is a hardly gas-permeable polymer that is not permeated by molecular oxygen (*H8*). The fluorescence of dyed nanobeads therefore is not quenched. A new antibiofouling coating for optical fiber sensors was introduced (*H9*). It is composed of a cross-linkable phosphocholine polymer with silane functionality that improves adhesion on glasses and other silicates. The formation of biofilm in a brewery water pipeline system was followed with an optical fiber device (*H10*) and allowed for detection of biofilms up to 10^{10} cells cm^{-2}. A pseudofouling detector and its application to control an industrial water process was patented (*H11*).

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AC040049D