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Polymers in sensor applications

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Abstract

Because their chemical and physical properties may be tailored over a wide range of characteristics, the use of polymers is finding a permanent place in sophisticated electronic measuring devices such as sensors. During the last 5 years, polymers have gained tremendous recognition in the field of artificial sensor in the goal of mimicking natural sense organs. Better selectivity and rapid measurements have been achieved by replacing classical sensor materials with polymers involving nano technology and exploiting either the intrinsic or extrinsic functions of polymers. Semiconductors, semiconducting metal oxides, solid electrolytes, ionic membranes, and organic semiconductors have been the classical materials for sensor devices. The developing role of polymers as gas sensors, pH sensors, ion-selective sensors, humidity sensors, biosensor devices, etc., are reviewed and discussed in this paper. Both intrinsically conducting polymers and non-conducting polymers are used in sensor devices. Polymers used in sensor devices either participate in sensing mechanisms or immobilize the component responsible for sensing the analyte. Finally, current trends in sensor research and also challenges in future sensor research are discussed.

Keywords: Polymer; Sensor devices; Biosensor; Gas sensor; Humidity sensor; Chemical sensor; Immobilization

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Contents

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1. Introduction

During the last 20 years, global research and development (R&D) on the field of sensors has expanded exponentially in terms of financial investment, the published literature, and the number of active researchers. It is well known that the function of a sensor is to provide information on our physical, chemical and biological environment. Legislation has fostered a huge demand for the sensors necessary in environmental monitoring, e.g. monitoring toxic gases and vapors in the workplace or contaminants in natural waters by industrial effluents and runoff from agriculture fields. Thus, a near revolution is apparent in sensor research, giving birth to a large number of sensor devices for medical and environmental technology. A chemical sensor furnishes information about its environment and consists of a physical transducer and a chemically selective layer [1]. A biosensor contains a biological entity such as enzyme, antibody, bacteria, tissue, etc. as recognition agent, whereas a chemical sensor does not contain these agents. Sensor devices have been made from classical semiconductors, solid electrolytes, insulators, metals and catalytic materials. Since the chemical and physical properties of polymers may be tailored by the chemist for particular needs, they gained importance in the construction of sensor devices. Although a majority of polymers are unable to conduct electricity, their insulating properties are utilized in the electronic industry. A survey of the literature reveals that polymers also acquired a major position as materials in various sensor devices among other materials. Either an intrinsically conducting polymer is being used as a coating or encapsulating material on an electrode surface, or non-conducting a polymer is being used for immobilization of specific receptor agents on the sensor device.

2. Classical materials for sensor application

The principle of solid-state sensor devices is based on their electrical response to the chemical environment, i.e. their electrical properties are influenced by the presence of gas phase or liquid phase species. Such a change in electrical properties is used to detect the chemical species. Although silicon based chemical sensors, such as field effect transistors (FETs), have been developed, they are not currently produced commercially because of technological and fundamental problems of reproducibility, stability, sensitivity and selectivity. Semiconducting metal oxide sensors, such as pressed powders and thin films of SnO_2, are themselves catalytically active, or are made active by adding catalysts [2]. Table 1 provides a list of materials used for the construction of various sensor devices.

‘Solid-state sensors’ have been made not only from classical semiconductors, solid electrolytes,

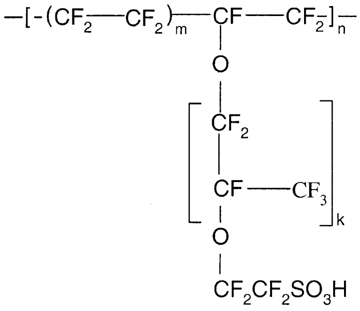
Table 1
Materials for various types of classical sensors

Type of sensor	Materials	Analyte	Ref.
Semiconductor based solid-state sensors	Si, GaAs	H^+, O_2, CO_2, H_2S, propane etc.	[3]
Semiconducting metal oxide sensors	SnO_2, ZnO, TiO_2, CoO, NiO, WO_3	H_2, CO, O_2, H_2S, AsH_3, NO_2, N_2H_4, NH_3, CH_4, alcohol	[4–15]
Solid electrolyte sensors	Y_2O_3 stabilized ZrO_2	O_2 in exhaust gases of automobiles, boilers etc.	[16]
	LaF_3	F^-, O_2, CO_2, SO_2, NO, NO_2	[17,18]
	$SrCl_2$–KCl–AgCl, $PbCl_2$–KCl	Chlorine	[19,20]
	Ba $(NO_3)_2$–AgCl, $(AlPcF)_n$	NO_2	[21,22]
	ZrO_2–Y_2O_3	Dissolved oxygen in molten metals	[23]
	Na_2SO_4–$Y_2(SO_4)_3$–SiO_2	SO_2	[24]
	ZrO_2–Y_2O_3	N_2O	[25]
	Antimonic acid, HUP (hydrogen-uranylphosphate), Zr $(HPO_4)_2.nH_2O$, PVA/H_3PO_4, Nafion	H_2	[26–30]
	$Zr(HPO_4)_2.nH_2O$, Nafion	CO	[28]
	$SrCe_{0.95}Yb_{0.05}O_3$	H_2O	[29]
Membranes	Ion-exchange membranes	Cations and anions	[31–37]
	Neutral-carrier membranes	Cations and anions	[38–41]
	Charged carrier membrane	Anions	[42,43]
Organic semiconductors	Polyphenyl acetylene, phthalocyanine, polypyrrole, polyamide, polyimide	CO, CO_2, CH_4, H_2O, NO_x, NO_2, NH_3, chlorinated hydrocarbons	[44–48]

insulators, metals and catalytic materials, but also from different types of organic membranes. Most solid-state sensors are based on catalytic reactions. This is especially true for sensors based on semi conducting oxides. The oxides themselves can be catalytically active, or catalysts can be added to provide sensitivity, selectivity and rapid response to changes in composition of the ambient gas.

Silicon is used in field-effect transistors (FETs), consisting of a thin conductance channel at the surface of the silicon, controlled by the voltage applied to a metal film (a gate) separated from the channel of conductance by a thin insulator layer (e.g. silicon dioxide). The electrical properties of semiconductors are sensitive to the gases with which they are in contact. Taguchi [49] first made a commercial device using the sensitivity of semiconductors to adsorbing gases, with SnO_2 as the semiconductor, to avoid oxidation in air and other reactions. The use of compressed SnO_2 powder rather than a single crystal resulted in a practical device for the detection of reducing gases in air. The semiconductor sensor is based on a reaction between the semiconductor and contact gases, which produces a change in semiconductor conductance. Possible reactions include either the conversion of the semiconductor to another compound, or a change in stoichiometry. Another possible reaction might be the extraction of an electron by oxygen absorbed from the atmosphere, thereby decreasing the conductivity of the semiconductor. Organic vapor, if present in the atmosphere, may produce a regain in the conductivity by reacting with the negatively charged oxygen, becoming oxidized, perhaps to H_2O and CO_2, and the electrons are returned to the semiconductor solid. As a result the conductivity is higher in the presence of organic vapor than in pure air. This concept provides interesting future guidance towards developing novel sensor materials and devices. Ion exchange between the semiconductor and the gas near the surface might be another possibility for change in the semiconductor property.

In solid electrolytes, the conductivity depends on ionic mobility rather than electron mobility, where the conductivity is dominated by one type of ion only. Therefore, solid electrolytes play an important role in commercial gas and ion sensors. In such sensors solid electrolytes are present as nonporous membranes, which separate two compartments containing chemical species at different concentrations on either side. By measuring the potential across such a membrane, one can determine the concentration of the chemical species on one side if the concentration on the other side (i.e. the reference side) is known. Solid electrolytes were used in commercial gas and ion sensors, e.g. yttria (Y_2O_3) stabilized zirconia (ZrO_2), an O^{2-}conductor at high temperature (>300 °C), for determination of oxygen in exhaust gases of automobiles, boilers or steel melts and LaF_3 for the determination of F^- even at room temperature. Solid polymer electrolytes (SPEs) are another membrane of interest for detection of ions in solution as the electrolyte in electrochemical gas sensors. With this membrane, water must penetrate the solid before the solid becomes an ionic conductor. Nafion (**I**), a perfluorinated hydrophobic ionomer with ionic clusters, has been employed as a SPE for a variety of room temperature electrochemical sensors [50].



Nafion (**I**)

3. Polymers in sensor devices

3.1. Gas sensor

The emission of gaseous pollutants such as sulfur oxide, nitrogen oxide and toxic gases from related industries has become a serious environmental concern. Sensors are needed to detect and measure the concentration of such gaseous pollutants. In fact analytical gas sensors offer a promising and inexpensive solution to problems related to hazardous gases in the environment. Some applications of gas sensors are included in Table 2. Amperometric sensors consisting of an electrochemical cell in a gas flow, which respond to electrochemically active gases and vapors, have been used to detect hazardous gases and vapors [51, 52]. Variation in the electrodes and the electrode potentials can be utilized to identify the gases present. There have been improvements using a catalytic micro-reactor in the gas flow leading to the amperometric sensors [53]. Such a reactor with a heated filament of platinum causes the analyte to undergo oxidation so that previously electrochemically unreactive species can be detected. Table 3 gives a picture of the sensor characteristics of different polymers used in gas sensors based on different working principles. Conducting polymers showed promising applications for sensing gases having acid–base or oxidizing characteristics. Conducting polymer composites with other polymers such as PVC, PMMA, etc. polymers with active functional groups and SPEs are also used to detect such gases.

Hydrogen chloride (HCl) is not only the source of dioxin produced in the incineration of plants and acid rain, but it also has been identified as a workplace hazard with a short-term exposure limit of 5 ppm. To detect HCl in sub-ppm levels, composites of alkoxy substituted tetraphenylporphyrin–polymer composite films were developed by Nakagawa et al. [54]. The sensor response and recovery behavior is improved if the matrix has a glass transition temperature below the sensing temperature. The alkoxy group imparts basicity to the material, and hence increases sensitivity to HCl. The changes in the Soret-and Q-bands with HCl gas in ppm levels have been examined. It has been found that high selectivity to sub ppm levels of HCl gas was achieved using a 5,10,15,20-tetra (4′-butoxyphenyl)porphyrin-butylmethacrylate [TP (OC_4 H_9)PH_2-BuMA] composite film. Supriyatno et al. [55] showed optochemical detection of HCl gas using a mono-substituted tetraphenylporphin–polymer composite films. They achieved a higher and preferable sensitivity to sub-ppm levels of HCl using a polyhexylmethacrylate matrix in the composite.

Amperometric sensors have been fabricated by Mizutani et al. [56] for the determination of dissolved oxygen and nitric oxide using a perm selective

Table 2
Various sensors and their applications

Sensor type	Polymer used	Fields of applications	Special features	Ref.
Biosensor	Cellulose membrane of bacterial origin	Glucose sensor	Improvement in the long-term stability of the amperometric sensor	[437]
Biosensor	PVC	Analysis of creatinine in urine	Polymer membrane with natural electrically neutral lipids as plasticizer	[438]
Biosensor	Polyaniline	Estimation of glucose, urea, triglycerides	Polymer deposition and enzyme immobilization done electrochemically	[280]
Biosensor	Poly (*o*-aminophenol)	Glucose biosensors	Immobilization on platinized GCE	[278]
Biosensor	Polypyrrole	Estimation of glucose	Electrode immobilization of an enzyme by electropolymerisation of pyrrole	[289]
Biosensor	Polytyramine	Estimation of L-amino acids	Enzyme immobilization by electropolymerisation	[330]
Biosensor	Poly (*o*-aminophenol)	Detection of uric acid	Polymer modified bienzyme carbon paste electrode used for detection	[439]
Biosensor	Nafion	Estimation of glucose	Sensor based on polymer modified electrodes optimized by chemometrics method	[440]
Biosensor	Cross-linkable redox polymer	Enzyme biosensors	Cross-linkable polymers used in construction of enzyme biosensors	[441]
Biosensor	Polysiloxane	Blood glucose determination	Composite membrane was formed by condensation polymerisation of dimethyldichlorosilane at the surface of a host porous alumina membrane	[286]
Biosensor	Polypyrrole, Poly (2-hydroxy ethyl methacrylate)	Estimation of glucose	Polypyrrole and enzyme is entrapped in poly(2-hydroxy ethylmethacrylate)	[442]
Biosensor	Poly [3-(1-pyrrolyl) propionic acid, Poly (*o*-phenylene diamine)PPD, Nafion	Estimation of glucose	PPD and Nafion forms inner films Carbodiimide forms covalent linkage between GOD and polypyrrole derivatives	[443]
Biosensor	Polypyrrole derivative containing phosphatidyl choline, Nafion or poly (*o*-phenylenediamine)	Estimation of glucose	Hemocompatible glucose sensor	[444]
Biosensor	Poly (1,2-diaminobenzene) Polyaniline	Sensing glucose	Insulating poly (1,2-diaminobenzene) was grown on polyaniline film to vary sensitivity	[445]
Biosensor	Polyaniline	Sensing glucose	Sensor was constructed in bread/butter/jam configuration	[446]
Biosensor	PVC-NH_2 membrane	Glucose and urea detection	Enzyme immobilized on solid-state contact PVC-NH_2 membrane	[447]
Biosensor	Polypyrrole	Can sense fructose	Enzyme entrapped in membrane shows sharp increase in catalytic activity	[448]
Biosensor	Polypyrrole	Can sense H_2O_2	Pyrrole oligomers can act as mediator	[449]
Biosensor	Ferrocene modified pyrrole polymer	Estimation of glucose.	Ferrocene–pyrrole conjugate efficient oxidant of reduced GOD	[450]
Biosensor	Polymerized phenols and its derivatives	Estimation of glucose	Electrochemical immobilization of enzymes	[329]
Biosensor	Polypyrrole	Estimation of glucose	GOD was covalently attached to polypyrrole at *N*-(2-carboxyethyl) group	[451]
Biosensor	Redox polymer	Detection of glucose, lactate, pyruvate	Glucose, lactate, pyruvate biosensor array based on enzyme –polymer nanocomposite film	[295]

(*continued on next page*)

Table 2 (*continued*)

Sensor type	Polymer used	Fields of applications	Special features	Ref.
Chemical sensor	Poly (vinyl chloride)	Estimation of pethidine hydrochloride in injections and tablets	Pethidine–phosphate tungstate ion association as electroactive material	[192]
Chemical sensor	Divinyl styrene polymer and isoprene polymer	Environmental control of trace organic contaminants	Piezoelectric	[385]
Chemical sensor	Methyl and butyl acrylate copolymer	Measurement of Cu ion concentrations	Polymer paste used to produce ion-sensitive membranes	[143]
Chemical sensor	Hydrophobic polymers	To detect organic pollutants in drinking water	Polymer and macrocyclic calixarene forms the sensitive layer	[452]
Chemical sensor	Nafion	Detection of dissolved O_2 in water	Gold-solid polymer-electrolyte sensor	[57]
Chemical sensor	PVC	Determine phentermine	PVC with tris(2-ethylhexyl)phosphate as solvent mediator and NaHFPB as ion-exchanger	[202]
Chemical sensor	Polyaniline (emeraldine base)	Can sense humidity, NH_3, NO_2. Can be used to fabricate other molecular devices	Nanocomposite ultra-thin films of polyaniline and isopolymolybdic acid	[74]
Chemical sensor	Polyester	Determination of H_2O_2	Glassy carbon and graphite/polyester composite electrode modified by vanadium-doped -zirconia	[453]
Chemical sensor	Polyaniline and its derivatives	Sensing aliphatic alcohols	Extent of change governed by chain length of alcohol and its chemical	[183]
Chemical sensor	Cross-linked PVA	Sensing chemicals	Polymer used for immobilizing indicators	[454]
Chemical sensor	Epoxy resin	Lithium ion detection	Λ-MnO_2-based graphite-epoxy electrode	[150]
Chemical sensor	PVC	Used for detection of phosphate ions	Plasticised PVC membrane containing uranyl salophene derivative	[158]
Chemical sensor	Carbon black poly(ethylene-*co*-vinyl acetate) and poly (caprolactone) composite	Vapor detector	Composite gives reversible change in resistance on sorption of vapor	[455]
Chemical sensor	Poly (dimethyl siloxane)	Sensing chemicals	Support membrane is coated with polymer	[456]
Chemical sensor	Polyaniline	Measure pH of body fluids and low ionic strength water	Polymer thin film electrodeposited onto ion-beam etched carbon fiber	[457]
Chemical sensor	Polyaniline	pH sensing	Optical method	[132]
Odor sensor	Poly (4-vinyl phenol), poly (*N*-vinyl pyrrolidone), poly (sulfone), poly (methyl methacrylate), poly (caprolactone), poly (ethylene-*co*-vinyl acetate), poly (ethylene oxide) polyethylene, poly (vinylidene fluoride), poly (ethylene glycol)	Odor detection	Array of conducting polymer composites	[377]

(*continued on next page*)

Table 2 (*continued*)

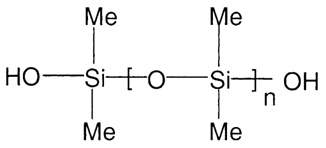
Sensor type	Polymer used	Fields of applications	Special features	Ref.
Odor sensor	Polyisobutylene, poly [di(ethyleneglycol) adipate], poly[bis(cyanoallyl) polysiloxane], polydimethylsiloxane, polydiphenoxyphospha-zene, polychloroprene, poly [dimethylsiloxane-*co*-methyl (3-hydroxypropyl) siloxane]-g-poly(ethylene glycol)3-aminopropyl ether, hydroxy-terminated polydimethyl-siloxane, polystyrene beads	Identification of volatile organic compounds	Sensor array	[458]
Odor sensor	Poly (3-methylthiophene), polypyrrole, polyaniline	Discriminate among different virgin olive oils	Doping agents used	[378]
Gas sensor	Copolymers of poly (EDMA-*co*-MAA)	Detection of terpene in atmosphere	Piezoelectric sensor coated with molecular imprinted polymer	[384]
Gas sensor	Polyethylmethacrylate, chlorinated polyisoprene, polypropylene (isotactic, chlorinated), styrene/butadiene, aba block copolymer, styrene/ethylene/butylene aba block copolymer, polyepichlorohydrin	Identify gases and gas mixtures	Polymer -carbon black composite films used	[382]
Gas sensor	Nafion	Detection of ethanol gas concentration	Fuel cell with polymer electrolyte membrane were used	[119]
Gas sensor	Polyaniline (PANI), polyaniline and acetic acid mixed film PANI-polystyrenesulfonic acid composite film	NO_2 was detected	Layers of polymer films formed by Langmuir-Blodgett and self-assembly techniques	[108]
Gas sensor	Poly [3-(butylthio)thiophene]	Gas Sensor	Films of polymer prepared via LB deposition and casting technique	[110]
Gas sensor	PVC	Detection of gaseous NO_2 in air	A solid polymer electrode of 10% PVC is present in the sensor	[109]
Gas sensor	Polypyrrole nanocomposite	Sensing CO_2, N_2, CH_4 gases at varying pressures	Nanocomposite of iron oxide polypyrrole were prepared by simultaneous gelation and polymerisation process	[247]
Gas sensor	Propylene–butyl copolymer	Detection of toluene, xylene gas	Polymer film coated quartz resonator balance	[118]
Humidity sensor	PVA	Optical humidity sensing	Crystal violet and Methylene blue are incorporated in PVA/H_3PO_4	[244]

(*continued on next page*)

Table 2 (*continued*)

Sensor type	Polymer used	Fields of applications	Special features	Ref.
Humidity sensor	Poly (*o*-phenylene diamine), poly (*o*-amino phenol), poly (*m*-phenylene diamine) or poly (*o*-toluidine) and PVA	Sensing change in humidity	In this sensor various polymer composites used	[459]
Humidity sensor	Poly (ethylene oxide)	Humidity sensing	Alkali salt doped poly (ethylene oxide) hybrid films used	[212]
Humidity sensor	Perfluorosulfonate ionomer (PFSI)	Humidity sensing	Incorporation of H_3PO_4 improves sensitivity of the film	[214]
Optical sensor	PVA	Optical sensing of nitro-aromatic compounds	Fluorescence quenching of benzo[K] fluoranthene in PVA film	[203]
Immuno sensor	Poly (methylmethacrylate)	Can detect RDX	Capillary-based immuno sensors	[394]
Thin film sensor	Poly (HEMA)	–	Electrodes coated with poly (HEMA)	[460]

polydimethylsiloxane (PDMS) (**II**) membrane. A hydrophobic polymer layer with a porous structure is useful for the selective permeation of gases. A very low concentration of nitric oxide (20 nM–50 μM) could be measured with these sensors at 0.85 V versus Ag/AgCl without serious interference from oxidizable species, such as L-ascorbic acid, uric acid and acetaminophen. They prepared the electrode by dip coating from an emulsion of PDMS. Being perm selective, the polymer coating is capable of discriminating between gases and hydrophobic species, which co-exist in the samples to be measured. Gases permeate easily through the pores to reach the electrode surface, whereas the transport of the hydrophilic compounds is strongly restricted.

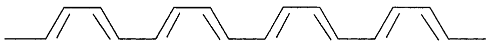


$$\mathrm{HO{-}Si(Me)_2{-}[O{-}Si(Me)_2]_n{-}OH}$$

Polydimethylsiloxane (PDMS) (**II**)

Chou, Ng and Wang [57] prepared a Au-SPE sensor for detecting dissolved oxygen (DO) in water, with Nafion as the SPE. It is a very good sensor for detecting DO in water, with a lower limit of 3.8 ppm. The authors also claimed excellent stability for this sensor.

Polyacetylene (III) is known to be the first organic conducting polymer (OCP). Exposure of this normally resistive polymer to iodine vapor altered the conductivity by up to 11 orders of magnitude [58,59]. Polyacetylene is doped with iodine on exposure to iodine vapor. Then, charge transfer occurs from polyacetylene chain (donor) to the iodine (acceptor) leads to the formation of charge carriers. Above approximately 2% doping, the carriers are free to move along the polymer chains resulting in metallic behavior.



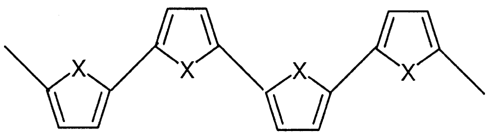
cis-Polyacetylene (**III**)

Later heterocyclic polymers, which retain the π-system of polyacetylene but include heteroatom bonded to the chain in a five membered ring were developed [60]. Such heterocyclic OCPs (IV) include polyfuran (X = O), polythiophene (X = S) [61], and polypyrrole (X = N–H). The intrinsically conducting polymers are π-conjugated macromolecules that show electrical and optical property changes, when they are doped/dedoped by some chemical agent. These physical property changes can be observed at

Table 3
Polymers used in various gas sensors

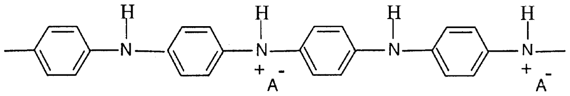
Gas	Device/techniques/principles	Polymer	Sensor characteristics	Ref.
NH_3	Change in optical-transmittance using a 2 nm laser (He–Ne) source	PANI–PMMA	Sensitivity of PANI–PMMA coatings are ~10–4000 ppm, reversible response	[75]
	Electrical property measurement	Polypyrrole	Response time <20 s, recovery time ~60 s	[77]
	Electronic property of the film played the part in NH_3 sensing	PPY–PVA Composite	Resistance increases with NH_3 concentration but becomes irreversible beyond 10% NH_3	[78]
	Electrical property measurement	PANI–isopolymolybdic acid nanocomposite	Resistance increases with NH_3 concentration and is reversible up to 100 ppm NH_3	[74]
	Electrical property measurement	Acrylic acid doped polyaniline	Highly sensitive to even 1 ppm of NH_3 at room temperature and shows stable responses upto 120 days	[76]
NO_2	Electrical property measurement	PANI–isopolymolybdic acid nanocomposite	Resistance increases with NO_2 concentration	[74]
	An amperometric gas sensor based on Pt/Nafion electrode	Nafion	Electrode shows sensitivity of 0.16 μA/ppm at room temperature, response time of 45 s and recovery time of 54 s, a long-term stability >27 days	[107]
	Amperometric gas sensor	SPE (10% PVC, 3% tetra butyl ammonium hexafluoro-phosphate, 87% 2-nitorphenyl octyl ether)	Sensitivity is 277 nA/ppm, recovery time is 19 s	[109]
NO	Amperometric gas sensor	Polydimethylsiloxane (PDMS)	Shows sensitivity to 20 nM gas, high performance characteristics in terms of response time and selectivity	[56]
O_2	Amperometric gas transducer	PDMS	Analyte can be measured up to 1.2 mM	[56]
	Optical sensing method	Tris(4,7′-diphenyl-1,10′-phenanthroline)Ru(II) perchlorate-a luminescent dye dissolved in polystyrene layer	–	[99]
	Electrical property measurement	Nafion	Sensitivity 38.4 μA/ppm, lowest limit 3.8 ppm, stability excellent (30 h)	[57]
SO_2	QCM-type gas sensor	Amino-functional poly (styrene-*co*-chloromethyl styrene) derivatives	DPEDA functional copolymer with 5 wt% of siloxane oligomer shows 11 min response time and good reversibility even near room temperature (50 °C)	[96]
HCl	Optochemical sensor	5,10,15,20-tetra (4′-alkoxyphenyl) porphyrin [TP (OR) PH_2] embedded in poly (hexyl acrylate), poly (hexylmethacrylate), poly (butyl methacrylate)	Reversibly sensitive to sub-ppm levels of HCl	[54]
	Optochemical detection	Ethylcellulose, poly(hexylmethacrylate)	Sensitivity smaller but faster recovery time compared to that of tetra-hydroxy substituted tetraphenylporphin	[55]
H_2S	Electrochemical detection	Nafion	High sensitivity (45 ppb v/v), good reproducibility, short response time (0.5 s)	[94]

room temperature, when they are exposed to lower concentrations of the chemicals, which make them attractive candidates for gas sensing elements.



Heterocyclic organic conducting polymer (**IV**)

Nylander et al. [47] investigated the gas sensing properties of polypyrrole by exposing polypyrrole-impregnated filter paper to ammonia vapor. The performance of the sensor was linear at room temperature with higher concentrations (0.5–5%), responding within a matter of minutes. Persaud and Pelosi reported conducting polymer sensor arrays for gas and odor sensing based on substituted polymers of pyrrole, thiophene, aniline, indole and others in 1984 at the European Chemoreception Congress (ECRO), Lyon, followed by a detailed paper in 1985 [62,63]. It was observed that nucleophilic gases (ammonia and methanol, ethanol vapors) cause a decrease in conductivity, with electrophilic gases (NO_x, PCl_3, SO_2) having the opposite effect [64]. Most of the widely studied conducting polymers in gas sensing applications are polythiophene and its derivatives [65,66], polypyrroles [67,68], polyaniline and their composites [65,69–71]. Electrically conducting polyacrylonitrile (PAN)/polypyrrole (PPY) [72], polythiophene/polystyrene, polythiophene/polycarbonate, polypyrrole/polystyrene, polypyrrole/polycarbonate [73] composites were prepared by electropolymerization of the conducting polymers into the matrix of the insulating polymers PAN, polystyrene and polycarbonates, respectively. These polymers have characteristics of low power consumption, optimum performance at low to ambient temperature, low poisoning effects, sensor response proportional to analyte concentration and rapid adsorption/desorption kinetics.



Polyaniline (emeraldine salt) (**V**)

Electroactive nanocomposite ultrathin films of polyaniline (PAN) and isopolymolybdic acid (PMA) for detection of NH_3 and NO_2 gases were fabricated by alternate deposition of PAN and PMA following Langmuir–Blodgett (LB) and self-assembly techniques [74]. The process was based on doping-induced deposition effect of emeraldine base. The NH_3-sensing mechanism was based on dedoping of PAN by basic ammonia, since the conductivity is strongly dependent on the doping level. In NO_2 sensing, NO_2 played the role of an oxidative dopant, causing an increase in the conductivity when emeraldine base is exposed to NO_2.

Nicho et al. [75] found that the optical and electrical properties of π-conjugated polyaniline change due to interaction of the emeraldine salt (ES) (**V**) with NH_3 gas. The interaction of this polymer with gas molecules decreases the polaron density in the band-gap of the polymer. It was observed that PANI–PMMA composite coatings are sensitive to very low concentrations of NH_3 gas (< 10 ppm). Chabukswar et al. [76] synthesized acrylic acid doped polyaniline for use as an ammonia vapor sensor over a broad range of concentrations, viz. 1–600 ppm. They observed the sensor response in terms of the dc electric resistance on exposure to ammonia. The change in resistance was found to increase linearly with NH_3 concentration up to 58 ppm and saturates thereafter. They explained the decrease in resistance on the basis of removal of a proton from the acrylic acid dopant by the ammonia molecules, thereby rendering free conduction sites in the polymer matrix. A plot of the variation of relative response of the ammonia gas sensor with increase in the concentration of ammonia gas is shown in Fig. 1. Acrylic acid doped polyaniline showed a sharp increase in relative response for around 10 ppm ammonia and subsequently remained constant beyond 500 ppm, whereas the nanocomposite of polyaniline and isopolymolybdic acid (PMA) showed a decrease of relative response with the increase in ammonia concentration. Yadong et al. [77] reported that submicrometer polypyrrole film exhibits a useful sensitivity to NH_3. The NH_3 sensitivity was detected by the change in resistance of the polypyrrole film. They interpreted the resistance change of the film in terms of the formation of a positively charged electric barrier of NH_4^+-ion in the submicrometer

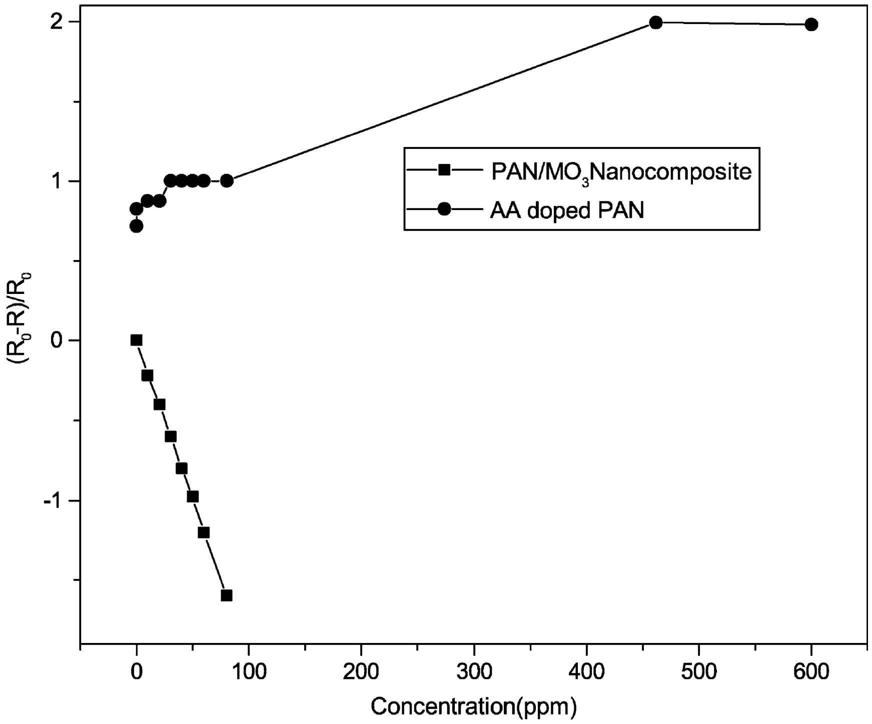


Fig. 1. Variation of $(R_0 - R)/R_0$ of PAN/MO_3 nanocomposite and AA doped PAN with NH_3 concentrations (adapted from Refs. [74,76]).

film. The electrons of the NH_3 gas act as the donor to the p-type semiconductor polypyrrole, with the consequence of reducing the number of holes in the polypyrrole and increasing the resistivity of the submicrometer film.

A polypyrrole–poly(vinyl alcohol)(PVA) composite prepared by electropolymerizing pyrrole in a cross-linked matrix of pyrrole was found to posses significant NH_3 sensing capacity [78]. The ammonia-sensing mechanism of the polypyrrole electrode has been addressed by Lähdesmäki et al. [79], with evidence that a mobile counter ion may be required for proper sensor operation. Such evidence supports the idea that polypyrrole undergoes a reversible redox reaction when ammonia is detected at submillimolar concentrations.

Quartz Crystal Microbalance (QCM) sensors are a kind of piezoelectric quartz crystal with a selective coating deposited on the surface to serve as an adsorptive surface. The QCM is a very stable device, capable of measuring an extremely small mass change [80]. Fig. 2 presents a schematic diagram for a QCM. The natural resonant frequency of the QCM is disturbed by a change in mass from the adsorption of molecules onto the coating. For example, a shift in resonance frequency of 1 Hz can easily be measured for an AT-cut quartz plate with a resonance frequency

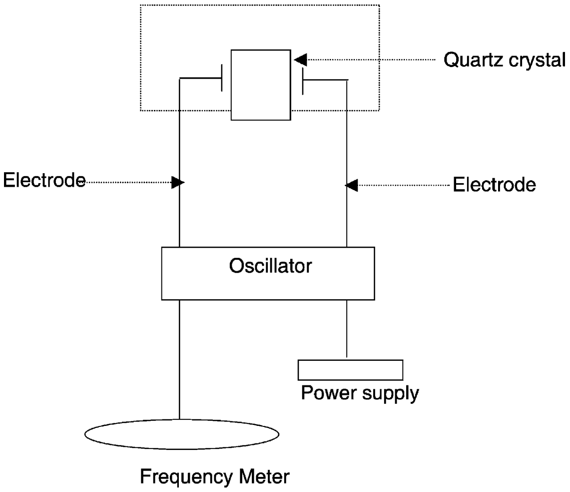


Fig. 2. Basic representation of a quartz crystal microbalance (QCM) sensor.

Table 4
Adsorption of strychnine (a pesticide) and β-ionene (an odor) at 45 °C by various films immobilized on a QCM surface

Immobilized film	Strychnine Δ*m* (ng)	β-Ionene Δ*m* (ng)
Uncoated	2	2
$2C_{18}N^{+}2C_{1}$/poly (styrene sulfonate) (PSS)	533	610
Dimylistoylphosphatidyl ethanolamine (DMPE)	560	540
Poly (vinyl alcohol)	4	4
Poly (methyl glutamate)	5	6
Poly (styrene)	7	7
Bovine plasma albumin crosslinked with glutaraldehyde	5	6
Keratin	7	6

Adapted from Ref. [81].

of 5 MHz, which corresponds to a change in mass of just 17 ng/cm^2 [81]. Table 4 shows how exposure of 19 ppm strychnine (a pesticide) or β-ionine (an odor) affects the absorption masses of QCM coated with various chemically sensitive films.

A number of materials have been investigated as coatings for QCM sensors, including phthalocyanine [82], polymer–ceramic composite [83], epoxy resin for estimation of ethanol in commercial liquors [84] and cellulose [85]. The general trend observed shows that polymer-coated QCMs are most sensitive towards volatiles possessing a complimentary physicochemical character, e.g. hydrogen bond forming acidic volatiles was best detected by hydrogen bond forming basic polymers [86,87]. Alkanes could be distinguished from alkenes by the use of strongly hydrogen bond forming acidic polymers that could interact with the weak hydrogen bond basicity of the alkenes, the alkanes having no such hydrogen bonding capacity.

If a piezoelectric substance is incorporated in an oscillating electronic circuit a surface acoustic wave (SAW) is formed across the substance. Any change in velocity of these waves, due to the change in mass of the coating on the sensor by an absorbing species, will alter the resonant frequency of the wave [88]. The oscillations are applied to the sensor through a set of metallic electrodes formed on the piezoelectric surface, over which a selective coating is deposited. Fig. 3 [89] shows that the acoustic wave is created by an AC voltage signal applied to a set of interdigited electrodes at one end of the device. The electric field distorts the lattice of the piezoelectric material beneath the electrode, causing a SAW to propagate toward the other end through a region of the crystal known as the acoustic aperture. When the wave arrives at the other end, a duplicate set of interdigited electrodes generate an AC signal as the acoustic wave passes underneath them. The signal can be monitored in terms of amplitude, frequency and phase shift. These devices operate at ultrahigh frequencies (gigahertz range), giving them the capability to sense as little as 1 pg of material.

Similar to QCM sensors, the coating on the sensor determines the selectivity of the SAW device, for example, $LiNbO_3$ [90], fluoropolymers for sensing of a pollutant organophosphorus gas [91] and commercially available gas chromatography phases as coatings for sensing toluene in dry air [92]. In these sensors the response times can be of the order of 1 s. Although SAW sensors are very sensitive to physical changes in the sample matrix, this can be overcome by the use of a reference cell.

Opekar and Bruckenstein [93] accumulated H_2S gas on the surface of a porous silver Teflon membrane electrode at constant potential, directly determined by cathodic stripping voltammetry.

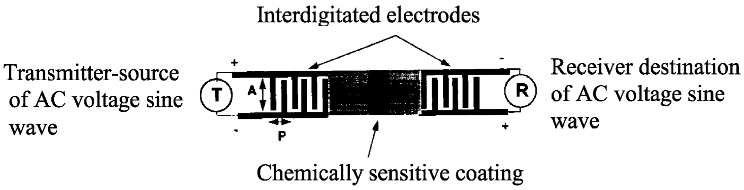
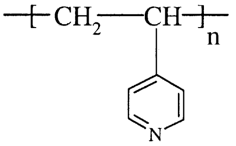


Fig. 3. Layout of a single acoustic aperture surface acoustic wave (SAW) Device [89]. Reproduced from Forster by permission of John Wiley and Sons, Inc., NJ, USA.

The sensitivity of the method, expressed by the slope of the regression line for the dependence of the stripping peak current on the amount of H_2S in the gas sample, is 357 μg of H_2S/μA. The reproducibility of the determination, expressed in terms of the relative standard deviation, is 3.2%. An ion-exchange membrane, a SPE, was used in an electroanalytical sensor [94] for the determination of hydrogen sulfide in gaseous atmospheres. The sensor, which eliminates oxygen interference, is highly sensitive and fast responding. It consists of a porous silver-working electrode (facing the sample) supported on one face of the ion-exchange membrane. The other side of the membrane faces an internal electrolyte solution containing the counter and reference electrodes. The performance of this sensor has been tested for the electroanalysis of H_2S by amperometric monitoring, cathodic stripping measurements, and flow injection analysis (FIA).

For the detection of sulfur dioxide in both gas and solution a novel electrochemical sensor has been described by Shi et al. [95]. They constructed the chemically modified electrode by polymerizing 4-vinyl pyridine (4-VP), palladium and iridium oxide (PVP(**VI**)/Pd/IrO_2) onto a platinum microelectrode, which exhibits excellent catalytic activity toward sulfite with an oxidation potential of + 0.50 V. The SO_2 gas sensor is based on the PVP/Pd/IrO_2 modified electrode as detecting electrode, Ag/AgCl electrode as reference electrode, Pt as counter electrode and a porous film, which is in direct contact with the gas-containing atmosphere. The effects of different internal electrolyte solutions of hydrochloric acid, sulfuric acid, phosphates buffer solution, mixed solution of dimethyl sulfoxide and sulfuric acid to the determination of SO_2 were also studied. The sensor was found to have a high current sensitivity, a short response time and a good reproducibility for the detection of SO_2, and showed good potential for use in the field of environmental monitoring and controlling. QCM-type SO_2 gas sensors were fabricated by Matsuguchi et al. [96] using amino-functional poly (styrene-*co*-chloromethylstyrene) derivative (**VII**) on the quartz surface. Three kinds of diamine compounds *N*, *N*-dimethyl ethylene diamine (DMEDA), *N*, *N*-dimethyl propane diamine (DMPDA) and *N*, *N*-dimethyl-*p*-phenylene diamine (DPEDA) were used to attach amine group onto the copolymer backbone. It is obvious that the basic amino group absorbs SO_2, being a strong Lewis acid gas. Sensing characteristics were affected by many factors including the mole fraction of chloromethyl styrene in the copolymers, the structure of diamine compound attached, measuring the temperature, and addition of organically modified siloxane oligomer. Among the sensors prepared the sensor using DPEDA functional copolymer shows the shortest response time ($t_{100} =$ 11 min), and complete reversibility, even at 50 °C. Fig. 4 describes the response characteristics of this SO_2 gas sensor using various amino-functional copolymers measured for 50 ppm SO_2 gas at 30 °C.



Polyvinyl Pyridine (PVP) (**VI**)

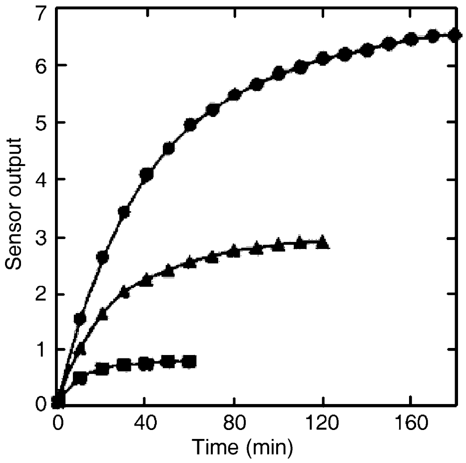
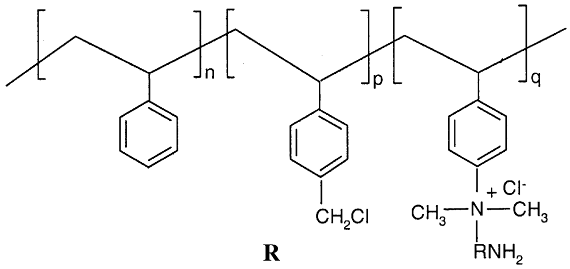


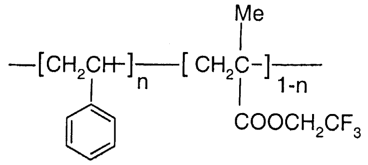
Fig. 4. Response characteristics of the sensor using amino-functional copolymers measured for 50 ppm of SO_2 at 30 °C; (●) DMEDA; (▲) DMPDA and (■) DPEDA [96]. Reproduced from Matsuguchi, Tamai and Sakai by permission of Elsevier Science Ltd, Oxford, UK.



	R
DMEDA	-$(CH_2)_2$-
DMPDA	-$(CH_2)_3$-
DPEDA	-C_6H_4-

Amino-functional poly(styrene-co-chloromethylstyrene) derivative (**VII**)

Luminescent sensors based on composites comprising transition metal complexes immobilized in polymer matrices attracted attention as oxygen sensors for both biomedical and barometric applications. Typically, phosphorescent dyes dispersed in a polymer matrix of high gas permeability are used. By using S–N–P polymers as a novel matrix material Pang et al. [97] showed that it is possible to control the sensitivity of the sensors over a wide range. Miura et al. [98] developed a concentration cell type O_2 sensor using Nafion membrane as a proton conductor. Chemically homogenous polymer layers loaded with oxygen-quenchable luminescent dyes may lead to promising applications in oxygen sensing. Hartmann et al. [99] investigated the luminescence quenching of tris (4,7′-diphenyl-1, 10′-phenanthroline) Ru (II) perchlorate dissolved in a polystyrene layer. Amao et al. [100] prepared an aluminum 2,9,16,23-tetraphenoxy-29*H*, 31*H*-phthalocyanine hydroxide (AlPc (OH))-polystyrene (PS) film and measured its photophysical and photochemical properties. They developed an optical oxygen sensor based on the fluorescence quenching of AlPc (OH)-PS film by oxygen. Later, Amao et al. [101] developed an optical oxygen sensor based on the luminescence intensity changes of tris (2-phenylpyridine anion) iridium (III) complex ([Ir(ppy)$_3$]) immobilized in fluoropolymer, poly (styrene-*co*-2,2,2-trifluoroethyl methacrylate) (poly (styrene-*co*-TFEM) (**VIII**) film. The luminescence intensity of [Ir(ppy)$_3$] in poly(styrene-*co*-TFEM) film decreased with increasing oxygen concentration.



$$-[CH_2CH(C_6H_5)-]_n-[CH_2C(Me)(COOCH_2CF_3)-]_{1-n}-$$

Poly (styrene-co-2, 2,2-trifluroethyl methacrylate) (**VIII**)

While acidic-basic gases (e.g. CO_2, NH_3) and oxygen have a long history in the development of dissolved gas sensing, a challenge has arisen in the need for rapid, sensitive detection of nitric oxide (NO). There is increasing interest in determination of NO, primarily because of its role in intra-and intercellular signal transduction in tissues [102]. Ichimori et al. [103] introduced an amperometric NO selective electrode that became commercially available. The Pt/Ir (0.2) electrode was modified with an NO-selective nitrocellulose membrane and a silicone rubber outer layer. The electrode was reported to be linearly responsive in the nM concentration range, with a time constant of $\sim$1.5 s. Sensitivity was increased $\sim$three-fold by raising the temperature from 26 °C to the physiological value of 37 °C. Measuring NO in rat aortic rings under acetylcholine stimulation was reported as an example of the use of the electrode for in vivo applications. Friedemann et al. [104] utilized a carbon-fiber electrode modified with an electrodeposited *o*-phenylenediamine (*o*-Pd) coating. They found that a Nafion underlayer provided good sensitivity to NO and that a three-layer overcoat of the Nafion optimized the selectivity against nitrite. They compared their electrode to a porphyrinic sensor of the type reported by Maliniski and Taha [105].

Christensen et al. [106] developed a novel NO_2 sensing device using a polystyrene film. When the film was exposed to a 1:10 v/v mixture of NO_2/N_2, the conductivity of the film increased irreversibly and rapidly by several orders of magnitude. They believed that the increase in conductivity of the film might be due to self-ionization of N_2O_4, the form of NO_2 within the film, to $NO^+NO_3^-$. Ho and Hung [107] developed an amperometric NO_2 gas sensor based on Pt/Nafion electrode, for the NO_2 concentration range from 0 to 485 ppm.

Recently, Xie et al. [108] reported the fabrication and characterization of a polyaniline-based gas sensor by ultra-thin film technology (Table 2). They prepared a pure polyaniline (PAN) film, PAN and acetic acid (AA) mixed films, as well as PAN and polystyrenesulfonic acid (PSSA) composite films, with various number of layers, by LB and self-assembly (SA) techniques. The authors studied the gas sensitivity of these ultra-thin films with various layers to NO_2 gas. They found that pure PAN films prepared by the LB technique had good sensitivity to NO_2, while SA films exhibited faster recovery. PAN is oxidized by contact with NO_2, a well-known oxidizing gas. Contact of NO_2 with the π-electron network of polyaniline is likely to result in the transfer of an electron from the polymer to the gas, making the polymer positively charged. The charge carriers give rise to increased conductivity of the films. They also found that PAN–AA mixed films showed reduced sensitivity, due to the fact that acetic acid molecules had occupied and chemically blocked sensitive sites responsive to NO_2. Reticulated vitreous carbon (RVC) [109] was tested as a material for the preparation of the indicator electrode in solid-state gas sensors. The tested planar sensor contained an RVC indicator, a platinum auxiliary and a Pt/air reference electrode, with a SPE of 10% PVC, 3% tetrabutylammonium hexafluorophosphate (TBAHFP) and 87% of 2-nitrophenyloctyl ether (NPOE). The analyte, gaseous nitrogen dioxide in air, was monitored by reduction at 500 mV vs. the Pt/air electrode. It was demonstrated that RVC could successfully replace noble metals in gas solid-state sensors. For hydrophobic SPE, the sensitivity decreases with increasing humidity, while for hydrophilic ones (e.g. Nafion), it usually increases. The extraordinary chemical inertness of RVC favorably affects the signal stability, not only with detection in solution, but also in sensors where RVC remains in contact with a SPE. Rella et al. [110] prepared films of poly [(3-butylthio) thiophene] by Langmuir–Blodgett (LB) deposition and casting techniques for applications in gas sensor devices. The preparation of the sensing layer is described for both methods: the LB deposition of the polymer in mixture with arachidic acid and direct casting from a solution of the polymer in chloroform. In both cases, alumina substrates equipped with gold interdigitated electrodes have been used. The samples so prepared showed a variation in the electrical conductivity when exposed to NO_2-oxidizing or NH_3-reducing agents, at a working temperature of about 100 °C.

Otagawa et al. [111] fabricated a planar miniaturized electrochemical CO sensor comprising three platinum electrodes (sensing, counter, and reference) and a solution cast Nafion as a SPE. The response was linear with the CO concentration in air. The sensitivity was about 8 Pa/ppm with a 70 s response time.

A CO_2 gas sensor, consisting of K_2CO_3-polyethylene glycol solution supported on porous alumina ceramics, was investigated by Egashira et al. [112–114]. The resistance of the device increased after exposure to CO_2 under an applied voltage. A linear relationship existed between the sensitivity (the ratio of resistance in CO_2 to that in air) and the CO_2 concentration from 1 to 9%. Sakai et al. [115] improved this type of sensor by solidifying the sensing layer. They used a solid polyethylene glycol of high molecular weight doped with a solution comprised of liquid polyethylene glycol and K_2CO_3. The change in resistance is attributed to the change in concentration of the charge carrier K^+ ion. Opdycke and Meyerhoff [116] reported the development and analytical performance of a potentiometric pCO_2 (partial pressure of CO_2) sensing catheter. The sensor geometry consists of an inner tubular PVC pH electrode in conjunction with an outer gas-permeable silicone rubber tube. Continuous pCO_2 values obtained with the sensor during 6 h in vitro blood pump studies correlated well with conventional blood-gas instruments. The preliminary results of a study with this sensor implanted intravascularly in a dog demonstrated its suitability for continuous in vivo monitoring of pCO_2.

Methane gas was determined via pre-adsorption on a dispersed platinum electrode backed by a SPE membrane (Nafion) in contact with 10 M sulfuric acid [117]. The adsorption process is strongly temperature dependent, with an activation energy of 8.7 kcal mol^{-1}. The determination of ethane, propane and butane was also found possible by this scheme and the cross-sensitivity to carbon monoxide and hydrogen could be significantly reduced by means of suitable chemical adsorption filters. Nanto et al. [118] chose a copolymerized propylene–butyl film, as a material for the gas sensing membrane coated on a quartz resonator microbalance; the ‘solubility parameter’ for the polymer almost coincides with that of harmful gases such as toluene, xylene, diethyether, chloroform and acetone. It was found that copolymerized propylene-butyl-film-coated quartz resonator microbalance gas sensor exhibited high sensitivity and excellent selectivity for these harmful gases, especially for toluene and xylene gas, suggesting that the solubility parameter is an effective parameter for use in the functional design of the sensing membrane of quartz resonator gas sensors.

Fuel cells using a polymer electrolyte membrane were successfully fabricated and tested by Kim et al. [119] for the detection of ethanol gas concentration. Nafion 115 membrane was used as the polymer electrolyte and 10% Pt/C sheets with 0.5 mg/cm^2 Pt loading were used as catalyst electrodes. The peak height of electrical signal obtained from the fuel cells was found to be quite linear with the ethanol gas concentration.

Torsi et al. [120] doped electrochemically synthesized conducting polymers, such as polypyrrole and poly-3-methylthiophene, with copper and palladium inclusions. These metals were deposited potentiostatically, either on pristine conducting films or on partially reduced samples. Exposure of PPy and Cu-doped PPy sensors to H_2 and CO reducing gas produced an expected enhancement of the film resistance. On the other hand, the electrical response of the Pd–PPy sensor to H_2, and CO was a drastic drop in resistivity (Fig. 5a), while a resistivity enhancement is produced upon ammonia exposure (Fig. 5b). Moreover, the CO and H_2 responses of Pd–PPy sensor are highly reversible and reproducible. Roy et al. [121] has reported the hydrogen gas sensing characteristics of doped polyaniline and polypyrrole films. A thin film of 1,4-polybutadiene has been used to construct a small and very sensitive (< 10 ppb) ozone sensor [122].

3.2. pH sensor

The pH indicates the amount of hydrogen ion in a solution. Since the solution pH has a significant effect on chemical reactions, the measurement and control of pH is very important in chemistry, biochemistry, clinical chemistry and environmental science. Munkholm et al. [123] used photochemically polymerized copolymer of acrylamide-methylenebis(acrylamide) containing fluoresceinamine covalently attached to an optical fiber surface (core dia 100 μm) in a pH sensor device. Amongst various organic materials, polyaniline has been found as most suitable for pH sensing in aqueous medium [124–127]. The use of conducting polymers in the preparation of optical pH sensor has eliminated the need for organic dyes. Demarcos and Wolfbeis [128] developed an optical pH sensor based on polypyrrole by oxidative polymerization. Since the polymer film has suitable optical properties for optical pH sensor, the immobilization step for an organic dye during preparation of the sensor layer was not required. Others [129–131] have also developed optical pH sensors based on polyaniline for measurement of pH in the range 2–12. They reported that the polyaniline films synthesized within a time span of 30 min are very stable in water. Jin et al. [132] reported an optical pH sensor based on polyaniline (Table 2). While they prepared polyaniline films by chemical oxidation at room temperature, they improved the stability of the polyaniline film significantly by increasing the reaction time up to 12 h. The film showed rapid reversible color change upon pH change. The solution pH could be determined by monitoring either absorption at a fixed wavelength or the maximum absorption

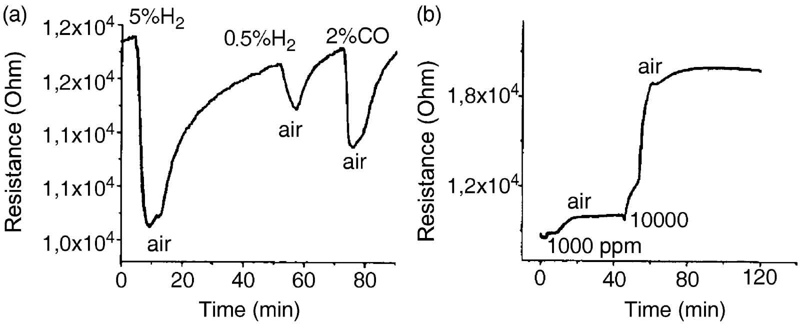
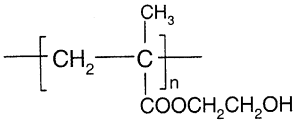


Fig. 5. Responses of Pd-Ppy based gas sensor to different reducing gases; (a) H_2 and CO; (b) NH_3 [120]. Reproduced from Torsi, Pezzuto, Siciliano, Rella, Sabbatini, Valli and Zambonin by permission of Elsevier Science Ltd, Oxford, UK.

wavelength of the film. The effect of pH on the change in electronic spectrum of polyaniline polymers was explained by the different degree of protonation of the imine nitrogen atoms in the polymer chain [133] The optical pH sensors could be kept exposed in air for over 1 month without any deterioration in sensor performance.

Ferguson et al. [134] used a poly(hydroxyethyl methacrylate) (**IX**) hydrogel containing acryloyl fluorescein as pH indicator. Shakhsher and Seitz [135] exploited the swelling of a small drop of aminated polystyrene (quaternized) on the tip of a single optical fiber as the working principle of a pH sensor.



$$-\left[CH_2 - \overset{CH_3}{\underset{COOCH_2CH_2OH}{C}} \right]_n-$$

Poly (hydroxyethyl methacrylate) (**IX**)

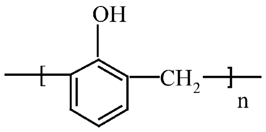
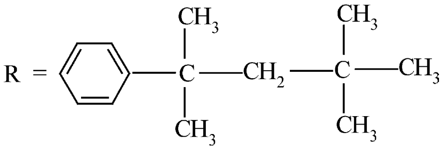
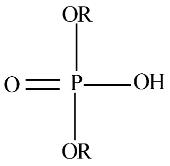
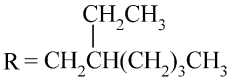
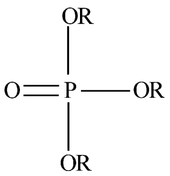
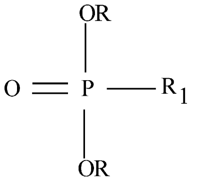
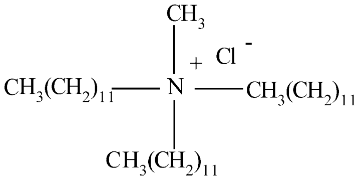
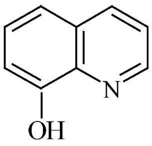
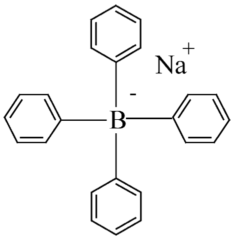
Other pH sensor devices using polymers have also been developed [131,136,139]. Leiner [140] developed a commercial blood pH sensor in which the pH-sensitive layer was obtained by reacting aminoethylcellulose fibers with 1-hydroxy-pyrene-3,6,8-trisulfochloride, followed by attachment of the sensitive layer to the surface of a polyester foil, and embedding the composite in an ion-permeable polyurethane (PU) based hydrogel material. Hydrogen ion selective solid contact electrodes based on *N*,*N*′-dialkylbenzylethylenediamine (alkyl = butyl, hexyl, octyl, decyl) were prepared. Solid contact electrodes and coated wire electrodes had been fabricated from polymer cocktail solutions based on *N*,*N*′-dialkylbenzylethylenediamine (alkyl = butyl, hexyl, octyl, decyl). They showed that the response range and slopes were influenced by the alkyl chain length. Solid contact electrodes showed linear selectivity to hydrogen ion in the pH ranges 4.5–13.0, 4.2–13.1, 3.4–13.0 and 3.0–13.2, with Nernstian slopes of 49.7, 50.8, 51.5 and 53.7 mV pH^{-1} at 20 ± 0.2 °C, respectively. Stability was also improved, especially when compared with coated wire electrodes. The 90% response time was <2 s, and their electrical resistance varied in the range 2.37–2.76 MΩ. Solid contact electrodes with *N*,*N*′-didecylbenzylethylenediamine showed the best selectivity and reproducibility of e.m.f. [139]. Pandey et al. [140] developed a solid state poly(3-cyclohexyl)thiophene treated electrode as pH sensor, and subsequently, urea sensor. Later, Pandey and Singh [141] reported the pH sensing function of polymer-modified electrode (a novel pH sensor) in both aqueous and non-aqueous mediums. The sensor was derived from polymer-modified electrode obtained from electrochemical polymerization of aniline in dry acetonitrile containing 0.5 M tetraphenyl borate at 2.0 V versus Ag/AgCl. The light yellow color polymer modified electrode was characterized by scanning electron microscopy (SEM). They used weak acid (acetic acid) and weak base (ammonium hydroxide) as analytes. The acetic acid was analyzed in both aqueous and dry acetonitrile, whereas ammonium hydroxide was analyzed only in aqueous medium.

3.3. Ion selective sensors

There is a vast literature covering the theory and design of ion selective devices. Generally, ion sensors have been developed taking the polymer as the conductive system/component, or as a matrix for the conducting system. When such systems come in contact with analytes to be sensed, some ionic exchange/interaction occurs, which in turn is transmitted as an electronic signal for display. Ion selective electrodes (ISE) are suitable for determination of some specific ions in a solution in the presence of other ions. The quantitative analysis of ions in solutions by ISEs is a widely used analytical method, with which all chemists are familiar. Commercial potentiometric devices of varying selectivity for both cations and anions are common in most laboratories [142]. Ion sensors find wide application in medical, environmental and industrial analysis. They are also used in measuring the hardness of water. Potentiometric ISEs for copper ions have been prepared by screen-printing, with the screen-printing paste composed of methyl and butyl methacrylate copolymer, copper sulphides and graphite [143] (Table 2).

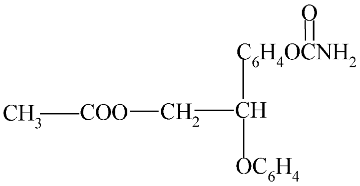
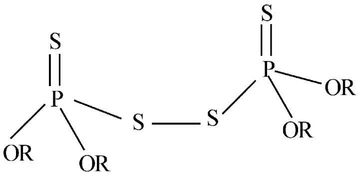
Ion-sensitive chemical transduction is based on ion selectivity conveyed by ionophore—ion-exchange agents, charged carriers and neutral carriers—doped in polymeric membranes. In addition to organic salts, several macrocyclics, such as antibiotics, crown ethers and calixerenes, are used as neutral carriers, functioning by host–guest interactions [144–147]. The chemical structures of some ionophores are shown in Table 5. The polymeric membrane-based

Table 5
Structures of some ionophores used in ion selective sensor devices

Ionophore	Structure
Calix[n]arene	
Bis[4-(1,1,3,3-tetramethylbutyl)phenyl]phosphoric acid (DTMBP-PO_4H) 	
Tris(2-ethylhexyl)phosphate  $R = CH_2\underset{}{\overset{CH_2CH_3}{\overset{\vert}{C}}}H(CH_2)_3CH_3$	
Dioctyl phenylphosphonate R = $(CH_2)_7{-}CH_3$ R = $(CH_2)_7$-CH_3 R_1 = 	
Tridodecylmethylammonium chloride	
8-Hydroxyquinoline	
Sodium tetraphenyl borate	

(*continued on next page*)

Table 5 (*continued*)

Ionophore	Structure
Ethyl-2-benzoyl-2-phenylcarbamoyl acetate	
Bis diethyldithiophosphate	

device consists of an internal electrode and reference solution, the selective membrane across which an activity-dependent potential difference develops, and an external reference electrode to which the membrane potential is compared in the potential measurement. The response and selectivity of an ion-selective device depend on the composition of the membrane. Polyvinyl chloride (PVC) is the most commonly used as polymeric matrix. A typical membrane composition for the usual cations and anions consists of polymer (~33 wt%), plasticizer (~65 wt%), ion carrier (~1–5 wt%), and ionic additives (~0–2 wt%) [148]. In ion-selective sensors, polymers have been utilized to entrap the sensing elements. Table 6 describes various sensor components, which are entrapped in polymer films for the detections of different ions, and their sensing characteristics.

Silicone rubber and a PU/PVC copolymer were reported [149] to be good screen-printable ion-selective membranes for sensing arrays. Silicone rubber-based membrane [147] containing a modified calyx (4) arene was used for detection of Na^+ in body fluids. Teixeira et al. [150] studied the potentiometric response of a λ-MnO_2-based graphite-epoxy electrode for determination of lithium ions. The best potentiometric response was obtained for an electrode composition of 35% λ-MnO_2, 15% graphite and 50% epoxy resin. The response time of the proposed electrode was lower than 30 s and its lifetime greater than 6 months. Further, they discussed the possibility of miniaturization of the electrode by putting the composite inside a capillary tube. Such an electrode requires a conditioning time in a Li^+ solution prior to the measurement of its equilibrium potential. Since the epoxy resin absorbs significant amount of water, it is possible that the first layer of epoxy resin on the electrode surface absorb the Li^+ solution, and thus time is necessary to attain equilibrium.

A new Ca^{2+}-selective polyaniline (PANI)-based membrane has been developed [151] for all-solid-state sensor applications. The membrane is made of electrically conducting PANI containing bis [4-(1,1,3,3-tetramethylbutyl) phenyl] phosphoric acid (DTMBP-PO_4H), dioctyl phenylphosphonate (DOPP) and cationic (tridodecylmethylammonium chloride, TDMACl) or anionic (potassium tetrakis (4-chlorophenyl) borate, KTpClPB) as lipophilic additives. PANI is used as the membrane matrix, which transforms the ionic response to an electronic signal. Artigas et al. [152] described the fabrication of a calcium ion-sensitive electrochemical sensor. This sensor device consists of a photocurable polymer membrane based on aliphatic diacrylated polyurethane instead of PVC. Moreover, these polymers are compatible with the photolithographic fabrication techniques in microelectronics, and provide better adhesion to silanized semiconductor surfaces, such as the gate surfaces of ion selective field effect transistors (ISFETs). Membranes sensitive to calcium ions were optimized according to the type of plasticizer and the polymer/plasticizer ratio. Such sensors are stable for more than 8 months, and the resulting sensitivities

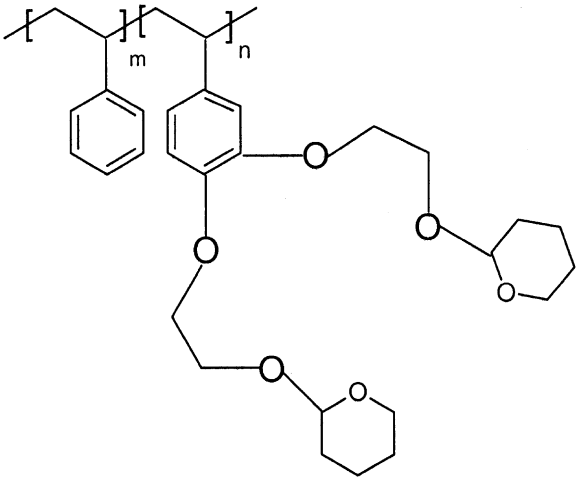
Table 6
Polymers used in different ion-selective sensors

Ion	Polymer	Membrane components	Sensor properties	Refs.
Calcium	Aliphatic diacrylated polyurethane, epoxy resin	1. Ionophore: Bis-di (4-1,1,3,3-(tetra-methyl butyl) phenyl) phosphate ionophore 2. Plasticizers: DOPP, TOP and o-NPOE	Quasi-Nernstian Sensitivity (26–27 mV/dec) in a range of $5 \times 10^{-6} - 8 \times 10^{-2}$ M, more than 8 months stability	[152]
Zinc	PVC	1. Ionophore: Dimethyl-8,13-divinyl-3, 7,12,17-tetramethyl-21H,23H-porphine-2,18-dipropionate (Proto-porphyrin IX dimethyl ester) 2. Anion excluder: NaTPB 3. Plasticizer: DOP	Working concentration range: $1.5 \times 10^{-5} - 1.0 \times 10^{-1}$ M with a slope of 29.0 ± 1 mV/decade of activity, fast response time (10 s), more than 5 months stability	[172]
	PVC	Zinc salt of HDOPP as ligand, DOPP-n as solvent	Life-time at least 3 months	[173]
Nickel (II)	PVC	Neutral carrier: DBzDA18C6	Nernstian response over a wide concentration range ($5.5 \times 10^{-3} - 2.0 \times 10^{-5}$ M), fast response time, stability of at least 6 weeks, good selectivity	[171]
Calcium and magnesium	Lipophilic acrylate resin	Calcium salt of bis [4-(1,1,3,3-tetramethylbutyl) phenyl] phosphate as ionophore, 1-decylalcohol as plasticizer	Nernstian response with a slope of 29 mV/decade in the concentration range 10^{-5}–10^{-1} M, stability of 1 year	[167]
Phosphate ($H_2PO_4^-$)	PVC	o-NPOE (plasticizer), uranyl salophene III (ionophore), TDAB (lipophilic salt)	Linear response in the range 1–4 of $pH_2PO_4^-$ with a slope 59 mV/decade	[158]

DOPP, Dioctyl phenylphosphonate; TOP, tris(2-ethylhexyl)phosphonate; 2-nitrophenyl octyl ether; DOP, dioctyl phthalate; NaTPB, sodium tetra phenyl borate; HDOPP, di-*n*-octylphenylphosphoric acid; DOPP-n, di-octylphenylphosphonate; DBzDA18C6, 1,10-dibenzyl-1, 10-diaza-18-crown-6; *o*-NPOE, *o*-nitro phenyl octylether; TDAB, tetradecyl ammonium bromide.

were quasi-Nernstian (26–27 mV/dec) in a range of 5×10^{-6}–8×10^{-2} M. These sensors were used to measure calcium activity in water samples extracted from agricultural soils. The authors claimed their results to be well correlated with those obtained by standard methods.

For successful determination of beryllium in a mineral sample, a beryllium-selective PVC-based membrane electrode was prepared [153] using 3,4-di[2-(2-tetrahydro-2*H*-pyranoxy)] ethoxy styrene–styrene copolymer (**X**) as a suitable ionophore. The membrane was prepared using oleic acid (OA) and sodium tetraphenylborate (STB) as anionic additives, and dibutyl phthalate (DBP), dioctyl phthalate (DOP), acetophenone (AP) and nitrobenzene (NB), as plasticizing solvent mediators. A membrane having the composition PVC: NB:I:OA of 3%: 55%: 10%: 5% ratio gave the best performance. The sensor having such a composition works well over the concentration range (1.0×10^{-6} to 1.0×10^{-3} M), with a Nernstian slope of 29 mV per decade of Be^{2+} activity over a pH range 4.0–8.0. The detection limit of the electrode is 8.0×10^{-7} M (7.6 ng ml^{-1}). The proposed electrode shows excellent discrimination toward Be^{2+} ion with regard to alkali, alkaline earth, transition and heavy metal ions. A fast and simple analytical method has been applied successfully by Liu et al. [154] for the selective determination of silver ions in electroplating wastewater by poly(vinyl chloride) (PVC) membrane electrodes with 5% bis(diethyldithiophosphates) ionophore and 65% 2-nitrophenyl octyl ether (*o*-NPOE) plasticizer. A suitable lipophilicity of the carrier and appropriate co-ordination ability were found to be essential for designing an electrode with good response characteristics. This electrode exhibits a linear response over the concentration range 10^{-1}–10^{-6} mol l^{-1} Ag^+, with a slope of 57.3 mV/dec. A poly(vinyl chloride) matrix membrane sensor [155] incorporating 7-ethylthio-4-oxa-3-phenyl-2-thioxa-1,2-dihydropyrimido[4,5-d]pyrimidine (ETPTP) ionophore exhibits good potentiometric response for Al^{3+} over a wide concentration range (10^{-5}–10^{-1} M), with a slope of 19.5 mV per decade. The sensor provided a stable response for at least 1 month, good selectivity for Al^{3+} in comparison with alkali, alkaline earth, transition and heavy metal ions and minimal interference from Hg^{2+} and Pb^{2+}, which are known to interfere with other aluminum membrane sensors.



3,4-[Di-(2-tetrahydro-2H-pyranoxy)ethoxy-styrene-styrene] copolymer (**X**)

The potential response of a cadmium (II) ISE based on cyanocopolymer matrices and 8-hydroxyquinoline as ionophore has been evaluated by Gupta and Mujawamariya by varying the amount of ionophore, plasticizer and the molecular weight of the cyanocopolymer [156]. They found a significant dependence of sensitivity, working range, response time, and metal ions interference on the concentration of ionophore, plasticizer and molecular weight of cyanocopolymers. The cyano groups of the copolymers contributed significantly to enhance the selectivity of the electrode, such as an appreciable selectivity for Cd^{2+} ions in presence of alkali and alkaline earth metal ions in the pH range 2.5–6.5. The electrodes prepared with 2.38×10^{-2} mol kg^{-1} of ionophore, 1.23×10^{-2} mol dm^{-3} plasticizer and 2.0 g of cyanocopolymer (molecular wt, 59365) showed a Nernstian slope of 29.00 ± 0.001 mV per decade activities of Cd^{2+} ions, with a response time of 12 ± 0.007 s. The electrode showed an average life of 6 months and was found to be free from leaching of membrane ingredients. New lipophilic tetraesters of calyx(6)arene and calyx(6)diquinone were investigated [157] as cesium ion-selective ionophores in poly(vinyl chloride) membrane electrodes. The selectivity coefficients for cesium ion over alkali, alkaline earth and ammonium ions were determined. This PVC membrane electrode based on calyx(6)arene tetraester showed good detection limit, excellent selectivity coefficient in pH 7.2 (0.05 M Tris–HCl) buffer solution and linear response in Cs^+-ion concentrations of 1×10^{-6}–1×10^{-1} M.

Wróblewski et al. [158] reported the anion selectivities of poly(vinyl chloride) (PVC) plasticized membranes containing uranyl salophene derivatives. They investigated the influence of the membrane components on its phosphate selectivity (e.g. ionophore structure, the dielectric constant and structure of the plasticizer, and the amount of incorporated ammonium salt). The highest selectivity for H_2PO_4 over other anions tested was obtained for lipophilic uranyl salophene III (without *ortho*-substituents) in PVC/*o*-nitrophenyl octylether (*o*-NPOE) membrane containing 20 mol% of tetradecylammonium bromide (TDAB). The introduction of *ortho*-methoxy substituents in the ionophore structure decreased the phosphate selectivity of potentiometric sensors. Ma et al. [159] described polyion sensitive membrane electrodes for detection of the polyanionic anticoagulant heparin, employing a PVC membrane, formulated with tridodecylmethylammonium chloride (TDMAC), a classical lipophilic anion exchanger, as the membrane active component. Ohiki et al. [160] showed that a PVC membrane doped with alkyldiphosphonium type exchangers yields significant response to PSS (polystyrene sulphonates). According to Hattori and Kato [161], PVC membranes doped with tetradecyldimethylbenzylammonium chloride show EMF response towards PSS.

For satisfactory determination of fluoroborate in electroplating solution, a poly(vinyl chloride) membrane electrode based on chloro[tetra(*m*-aminophenyl)porphinato]-manganese (T(*m*-NH_2)PPMnCl) and 2-nitrophenyl octyl ether (*o*-NPOE) in the composition 3:65:32 [T(*m*-NH_2)PPMnCl:*o*-NPOE: PVC] was prepared by Zhang and coworkers [162]. They obtained a Nernstian response to fluoroborate ion in the concentration range 5.1×10^{-7}–1.0×10^{-1} mol l^{-1}, with a wide working pH range from 5.3 to 12.1, and a fast response time of 15 s. An improved selectivity towards BF_4^- with respect to common coexisting ions was obtained in comparison with reports in the literature. Torres et al. [163] developed five different types of membranes for anion selective electrodes. They prepared the membranes by solubilizing poly(ethylene-*co*-vinyl-acetate) copolymer (EVA) and tri-caprylyl-trimethyl-ammonium chloride (Aliquat-336S) in chloroform without using any plasticizer, followed by film casting. The ISEs prepared using these membranes were used for the detection of iodide, periodate, perchlorate, salicylate and nitrate determinations, in the concentration range of 10^{-5} and 10^{-1} mol l^{-1} under steady-state. The membrane performance was also evaluated for salicylate and iodide in a FIA using a tubular electrode in which the electrode exhibited a Nernstian response for salicylate in the concentration range of 2.5×10^{-3} and 1.0×10^{-1} mol l^{-1}, while for iodide the range is 5.0×10^{-4} to 1.0×10^{-1} mol l^{-1}. The systems have been employed for the salicylate and iodide determination in pharmaceutical samples, with a relative deviation of 1.6% from the reference method.

5,7,12,14-Tetramethyldibenzotetraazaannulene (Me_4BzO_2TAA) has been explored as an electroactive material for preparing poly(vinyl chloride) (PVC)-based membrane electrodes selective to Ni^{2+} [164]. A membrane with constituents Me_4BzO_2TAA, sodium tetraphenyl borate (NaTPB) and PVC in the optimum ratio 2:1:97 (w/w) gave the best working concentration range (7.9×10^{-6}–1.0×10^{-1} M), with a Nernstian slope (30.0 ± 1.0 mV/decade of activity) in the pH range 2.7–7.6. The sensor exhibited a fast response time of 15 s and a good selectivity for nickel (II) over a number of mono-, bi- and tri-valent cations. The electrode has been used for the quantitative determination of Ni^{2+} in chocolates and the sensor has been successfully used as an indicator electrode in the potentiometric titration of Ni^{2+} against EDTA.

Hassan et al. [165] developed a mercury (II) ion-selective PVC membrane sensor based on ethyl-2-benzoyl-2-phenylcarbamoyl acetate (EBPCA) as novel nitrogen containing sensing material. The sensor shows good selectivity for mercury (II) ion in comparison with alkali, alkaline earth, transition and heavy metal ions. The sensor was applied for the determination of Hg (II) content in some amalgam alloys. Mahajan and Parkash [166] observed a high selectivity for Ag^+ ions over a wide concentration range (1.0×10^{-1}–4.0×10^{-5} mol l^{-1}) over that for Na^+, K^+, Ca^{2+}, Sr^{2+}, Pb^{2+} and Hg^{2+} with a PVC membrane containing bis-pyridine tetramide macrocycle. The electrode showed a relatively fast response time, and was used for more than 5 months without observing any change in response. A divalent catISEs, which utilizes a lipophilic acrylate resin as a matrix for the sensing membrane with a long-term stability has been developed by Numata and coworkers [167]. The acrylate resin was impregnated with a solution of 1-decylalcohol and the calcium salt of bis [4-(1,1,3,3-tetramethylbutyl) phenyl] phosphate at concentrations of 0.08 g ml^{-1} each. The electrode exhibited nearly equal selectivity to Ca^{2+} and Mg^{2+} ions and could be used as a water hardness sensor. The initial performance of the electrode was maintained for 1 year in a lifetime test of the electrode conducted in tap water at a continuous flow rate of 4 ml min^{-1}. The hardness of tap water and upland soil extracts were determined using the electrode, with results in good agreement with those obtained by chelatometric titration using an EDTA solution as the titrant. The long-term stability of the electrode was found to be due to strong affinity of 1-decylalcohol to the lipophilic acrylate resin.

Hassan et al. [168] described two novel uranyl PVC matrix membrane sensors responsive to uranyl ion. The first sensor contains tris (2-ethylhexyl) phosphate (TEHP) as both the electroactive material and plasticizer, and sodium tetraphenylborate (NaTPB) as an ion discriminator. The sensor displays a rapid and linear response for UO_2^{2+} ions over the concentration range 1×10^{-1}–2×10^{-5} mol l^{-1} UO_2^{2+}, with a cationic slope of 25.0 ± 0.2 mV $decade^{-1}$ at working pH range of 2.8–3.6 and a life span of 4 weeks. The second sensor contains *O*-(1,2-dihydro-2-oxo-1-pyridyl)-*N*,*N*,*N*′,*N*′-bis (tetra methylene) uranium hexa fluoro phosphate (TPTU) as a sensing material, sodium tetra phenyl borate as an ion discriminator and dioctyl phenylphosphonate (DOPP) as a plasticizer. Linear and stable response for 1×10^{-1}–5×10^{-5} mol l^{-1} UO_2^{2+} with near-Nernstian slope of 27.5 ± 0.2 mV $decade^{-1}$ was obtained with the sensor at working pH range of 2.5–3.5 and a life span of 6 weeks. Direct potentiometric determination of as little as 5 μg ml^{-1} uranium in aqueous solutions showed an average recovery of 97.2 ± 1.3%. A potentiometric method has been described by Abbas et al. [169] for the determination of cetylpyridinium (CP) cation using a PVC powder membrane sensor based on CP-iodomercurate ion pair as an electroactive material. The CP electrode has been utilized as an end point indicator electrode in potentiometric titration of some anions, and applied for the determination of anionic surfactants in some commercial detergents and wastewater.

In vitro platelet adhesion studies were used by Espadas-Torre and Meyerhoff [170] to compare the thrombogenic properties of various polymer matrices useful for preparing implantable ion-selective membrane electrodes. Incorporation of high molecular weight block copolymers of poly(ethylene oxide) and poly(propylene oxide) within ion-selective membranes reduces platelet adhesion. A more marked decrease in platelet adhesion was, however, observed when the Tecoflex (plasticized PVC)-based membranes were coated with a thin photo-cross-linked layer of poly(ethylene oxide). Such surface-modified membranes were shown to retain potentiometric ion response properties (i.e. selectivity, response times, response slopes, etc.) essentially equivalent to untreated membranes.

Mousavi et al. [171] constructed a PVC membrane nickel (II) ISEs using 1,10-dibenzyl-1, 10-diaza-18-crown-6 (DbzDA18C6) as a neutral carrier. The sensor exhibits a Nerstian response for Ni (II) ions over a wide concentration range (5.5×10^{-3}–2.0×10^{-5} M). The proposed sensor exhibited relatively good selectivity for Ni (II) over a wide variety of other metal ions, and could be used in a pH range of 4.0–8.0. It was used as an indicator electrode in potentiometric titration of nickel ions (Fig. 6). Gupta et al. [172] constructed an ion-selective sensor using PVC based membrane containing dimethyl-8,13-divinyl-3,7,12,17-tetramethyl-21H,23H-porphine-2,18-dipropionate as the active material, along with sodium tetraphenyl borate (NaTPB) as an anion excluder and dioctyl phthalate (DOP) as solvent mediator, in the ratio 15:100:2:200 (w/w) (I:DOP:NaTPB:PVC). The sensor properties are presented in Table 6. The working pH range is 2.1–4.0, and the sensor could be successfully used in partially non-aqueous medium (up to 40% v/v). It has been used as an indicator electrode for end point determination in the potentiometric titration of Zn^{2+} against EDTA. Gorton et al. [173] constructed a zinc-sensitive polymeric membrane electrode. The membrane composition (by weight) was 8% ligand (zinc salt of di-*n*-octylphenylphosphoric acid (HDOPP)), 62% solvent (di-octylphenylphosphonate (DOPP-n) and 30% polymer (PVC). The life-time of the electrode was found to be at least 3 months. Poly(octadec-1-ene maleic anhydride) was used as a matrix for ion-channel sensors [174].

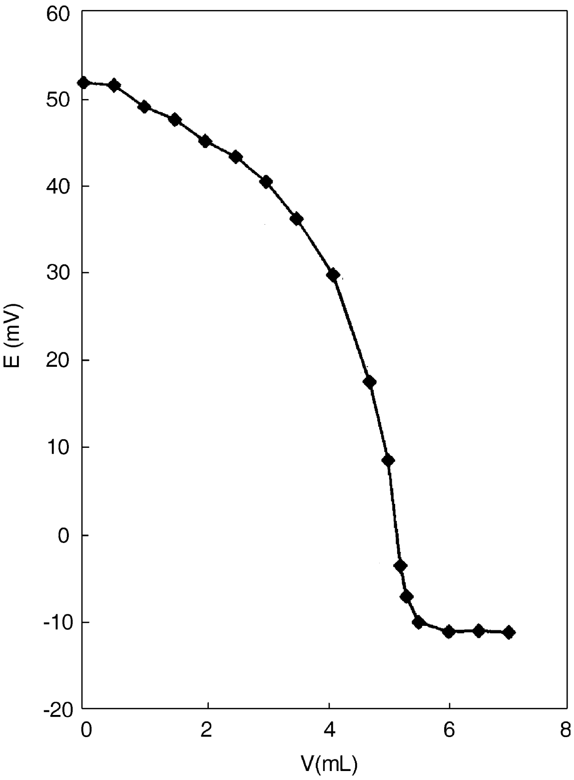


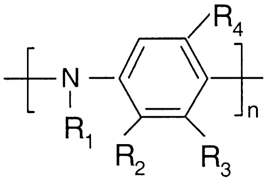
Fig. 6. Potentiometric titration curve of 20 ml of 0.01 M Ni (II) solution with 0.04 M EDTA in trice buffer (pH = 8), using the proposed sensor as an indicator electrode [171]. Reproduced from Mousavi, Alizadeh, Shamsipur and Zohari by permission of Elsevier Science Ltd, Oxford, UK.

Bakker and Meyerhoff [175] reviewed the latest developments on ionophore-based membrane electrodes providing new analytical concepts and non-classical response mechanisms. Some of these developments are: a dramatic lowering of the detection limits; direct potentiometric determination of total ion concentrations; identification of ionophore systems; ion-exchanger-based membranes that respond to important polyion species (e.g. heparin); the potentiometric response of membranes to neutral species, including surfactants, etc.

3.4. Alcohol sensors

The determination of alcohol is important in industrial and clinical analyses, as well as in biochemical applications. Ukeda et al. [176] presented a new approach in the coimmobilization of alcohol dehydrogenase and nicotinamide adenine dinucleotide (NAD) using acetylated cellulose membrane on glutaraldehyde activated Sepharose and its application to the enzymatic analysis of ethanol. Since conducting polymers gained popularity as competent sensor material for organic vapors, few reports are available describing the use of polyaniline as a sensor for alcohol vapors, such as methanol, ethanol and propanol [177,178]. Polyaniline doped with camphor sulphonic acid (CSA) also showed a good response for alcohol vapors [179–182]. These reports discussed the sensing mechanism on the basis of the crystallinity of polyaniline.

Polyaniline and its substituted derivatives (**XI**) such as poly(*o*-toluidine), poly(*o*-anisidine), poly(*N*-methyl aniline), poly(*N*-ethyl aniline), poly(2,3 dimethyl aniline), poly(2,5 dimethyl aniline) and poly(diphenyl amine) were found by Athawale and Kulkarni [183] to be sensitive to various alcohols such as methanol, ethanol, propanol, butanol and heptanol vapors (Table 2). All the polymers respond to the saturated alcohol vapors by undergoing a change in resistance. While the resistance decreased in presence of small chain alcohols, viz. methanol, ethanol and propanol, an opposite trend in the change of resistance was observed with butanol and heptanol vapors. The change in resistance of the polymers on exposure to different alcohol vapors was attributed to their chemical structure, chain length and dielectric nature. All the polymers showed measurable responses (sensitivity ~60%) for short chain alcohols, at concentrations up to 3000 ppm, but none of them are suitable for long chain alcohols. They explained the results based on the vapor-induced change in the crystallinity of the polymer. The polypyrrole was also studied as a sensing layer for alcohols. Polypyrrole [184] incorporated with dodecyl benzene sulfonic acid (DBSA) and ammonium persulfate (APS) showed a linear change in resistance when exposed to methanol vapor in the range 87–5000 ppm. Bartlett et al. [185] also detected methanol vapor by the change in resistance of a polypyrrole film. The response is rapid and reversible at room temperature. They investigated the effects of methanol concentration, operating temperature and film thickness on the response.



Polymer	R_1	R_2	R_3	R_4
Polyaniline	H	H	H	H
Poly(o-toluidine)	H	CH_3	H	H
Poly(o-anisidine)	H	OCH_3	H	H
Poly(N-methyl aniline)	CH_3	H	H	H
Poly(N-ethyl aniline)	C_2H_5	H	H	H
Poly(2,3-dimethylaniline)	H	CH_3	CH_3	H
Poly(2,5-dimethyaniline)	H	CH_3	H	CH_3
Poly(diphenyl amine)	C_6H_5	H	H	H

Polyaniline derivatives (**XI**)

Mayes et al. [186] reported a liquid phase alcohol sensor based on a reflection hologram distributed within a poly(hydroxyethyl methacrylate) (**IX**) film as a means to measure alcohol induced thickness changes. Blum et al. [187] prepared an alcohol sensor in which two lipophilic derivatives of Reichardt's phenolbetaine were dissolved in thin layers of plasticized poly(ethylene vinylacetate) copolymer coated with micro porous white PTFE in order to facilitate reflectance (transflectance) measurements. The sensor layers respond to aqueous ethanol with a color change from green to blue with increasing ethanol content. The highest signal changes are observed at a wavelength of 750 nm, with a linear calibration function up to 20% v/v ethanol and a detection limit of 0.1% v/v. These layers also exhibit strong sensitivity to acetic acid, which affects effective measurements on beverages. However, this limitation was overcome by adjusting the pH of the sample solution.

3.5. Process control

Modern industrial process control devices utilize various efficient sensors for fast and reliable on-line detection of organic vapors. That has presented a challenge for newer types of analytical sensor systems based on an array of differently selective chemical sensors. Stahl et al. [188] reported the use of mass-sensitive coated SAW sensors. The sensors were initially coated with a standard set of polymers. Since this first approach did not meet all of the requirements, they developed a new class of commercially available polymer coatings, namely adhesives. The polymers used in the coating were butylacrylate–ethylacrylate copolymer, styrene–butadiene–isoprene terpolymer, polyurethane alkyd resin, ethylacrylate–methylmethacrylate–methacrylic acid terpolymer, polyurethane, ethylene–vinyl acetate copolymer, vinylchloride–vinylacetate–maleic acid terpolymer and polyvinyl acetate. After optimizing the coating procedure, they investigated the aging of the adhesives, and applied the system in a real testing environment at a chemical plant: the fast on-line control of a preparative reversed phase process HPLC (RP-PHPLC). Mulchandani and Bassi [189] reviewed the principles and applications for biosensors in bioprocess control. There is also report on biosensors in process monitoring and control and environmental control [190].

3.6. Detection of other chemicals

3.6.1. Drugs

The construction and electrochemical response characteristics of poly(vinyl chloride) (PVC) membrane sensors were described by El-Ragehy et al. [191] for the determination of fluphenazine hydrochloride and nortriptyline hydrochloride. The method is based on the formation of ion-pair complexes between the two drug cations and sodium tetraphenylborate (NaTPB) or tetrakis (4-chlorophenyl) borate (KtpClPB). A novel plastic poly(vinyl chloride) membrane electrode based on pethidine-phosphotungstate ion association as the electroactive material was developed by Liu et al. for the determination of pethidine hydrochloride drug in injections and tablets [192] (Table 2).

3.6.2. Amines

The absorbance-based chromoreactand 4-(*N*,*N*-dioctylamino)-4′-trifluoroacetyl azobenzene (ETH^{T} 4001) has been investigated [193] in different polymer matrices for the optical sensing of dissolved aliphatic amines. Sensor layers containing ETH^{T} 4001 and different polymer materials generally showed a decrease in absorbance at around 500 nm and an increase in absorbance at around 420 nm wavelengths upon exposure to dissolved aliphatic amines. The change in absorbance was caused by conversion of the trifluoroacetyl group of the reactant into a hemiaminal or a zwitterion. The polymers used for optical amine sensing are plasticized poly(vinyl chloride), copolymers of acrylates, polybutadiene, and silicone. The sensitivity of the sensor layer depends on the choice of the polymer. The polarity of the polymer matrix has a strong influence on the diol formation caused by conditioning in water, and the absorbance maximum of the solvatochromic reactant. However, the selectivity of the sensor layers for primary, secondary and tertiary amines remains nearly unaffected by the polymer matrix. Although it was possible to vary sensitivity towards amines and humidity by choosing the appropriate polymer matrix, it was not possible to modify the sensor's selectivity among amines.

3.6.3. Surfactant

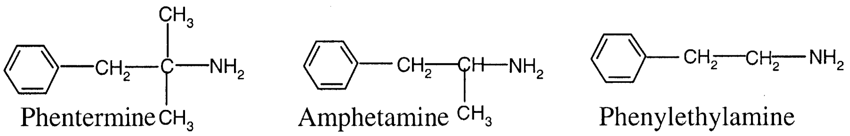
Sometimes it becomes necessary to determine the surfactant concentration in product formulations of industrial samples or food samples and in environment. Comprehensive reviews have been published on surfactant analysis [194–196]. Tanaka [197] reported an alkyl benzenesulfonate ISE with plasticized PVC membrane. Ivaska et al. [144,198] made stable neutral carrier type ISEs by placing an electrochemically prepared or solution cast conducting polymer layer as a charge-transfer mediator between the ISE membrane and the solid substrate. A single-piece all-solid-state electrode was also made by Bobacka et al. [199] by dissolving an appropriate conducting polymer in PVC matrix of the ISE. An all-solid-state anionic surfactant electrode was developed [200] using teflonized graphite rods coated with an electrochemically deposited polypyrrole film as the electric connector support. The measuring membrane of the electrodes was made of ion-pairs formed with the appropriate anionic and cationic surfactants incorporated into a plasticized poly(vinyl chloride) film. The surfactant electrode showed good stability due to the well-defined charge transfer mechanisms at the graphite–polypyrrole-membrane interfaces.

3.6.4. Herbicide

Panasyuk-Delaney et al. [201] used the technique of graft polymerization to prepare thin films of molecularly imprinted polymers (MIPs) on the surface of polypropylene membranes and on hydrophobized gold electrodes, for the detection of a herbicide. The herbicide desmetryn was used as a template. The solid supports used were hydrophobic, while the polymer was hydrophilic. On irradiation by UV-light an adsorbed layer of benzophenone initiated a radical polymerization near the surface. The electrodes coated with the MIPs displayed specific binding of desmetryn, as detected by the decrease in the capacitance of the electrode. Only small capacitive effects were observed on addition of terbumeton or atrazine, while metribuzine displayed capacitance decrease similar to desmetryn. These results demonstrate the compatibility of capacitive detection with a chemically sensitive polymer layer obtained by polymer grafting.

3.6.5. Stimulants

Katsu et al. [202] reported a poly(vinyl chloride) membrane electrode responsive to a stimulant, phentermine, in combination with an ion exchanger, sodium tetrakis[3,5-bis(2-methoxyhexafluoro-2-propyl)phenyl]borate (NaHFPB). Phentermine is a stimulant, the structure of which is similar to that of amphetamine, a phenyl alkylamine (**XII**):



Structures of a series of phenylalkylamines (**XII**)

This electrode discriminated between phentermine and analogous compounds, and showed remarkably little interference by lipophilic quaternary ammonium ions, as well as inorganic cations, to almost the same degree as an electrode using the recently developed phentermine ionophore, *N*,*N*-dioctadecyl-*N*′, *N*′-dipropyl-3,6-dioxaoctanediamide.

3.6.6. Aromatic compounds

Patra and Mishra [203] developed a possible optical sensor for various nitro aromatic compounds such as nitrobenzene, m-dinitrobenzene, *o*-nitrotoluene, *m*-nitrotoluene, *p*-nitrobromobenzene, *o*-nitroaniline, *p*-nitrophenol, etc. by fluorescence quenching of benzo[k]fluoranthene (BkF) in poly(vinyl alcohol) film. The fluorescence spectra of BkF doped PVA films in various solvents are shown in Fig. 7. From Fig. 7, it is seen that the sensor film gives good fluorescence quantum yield in methanol compared to other solvents, because of enhanced swelling of the film in methanol. Although the PVA film swells more in water compared to methanol, the lower quantum yield of BkF in water makes the sensor film less fluorescent in water. Polypyrrole–nitrotoluene copolymer responds selectively to aromatic hydrocarbons [204].

3.6.7. Hydrazine

Wang et al. [205] described a trifunctional electrode coating based on a mixture of cobalt phthalocyanine (CoPC) and cellulose acetate for the detection of hydrazine (detection limit, 0.64 ng) and other compounds in a FIA. Later a novel composite electrode coating with a mixture of cobalt phthalocyanine and Nafion was described by Wang and Li [206]. The coated film has better properties than either of the two components alone, resulting in several potential applications. In particular, the sensor exhibits electrocatalytic, preconcentration and permselective properties simultaneously. The practical

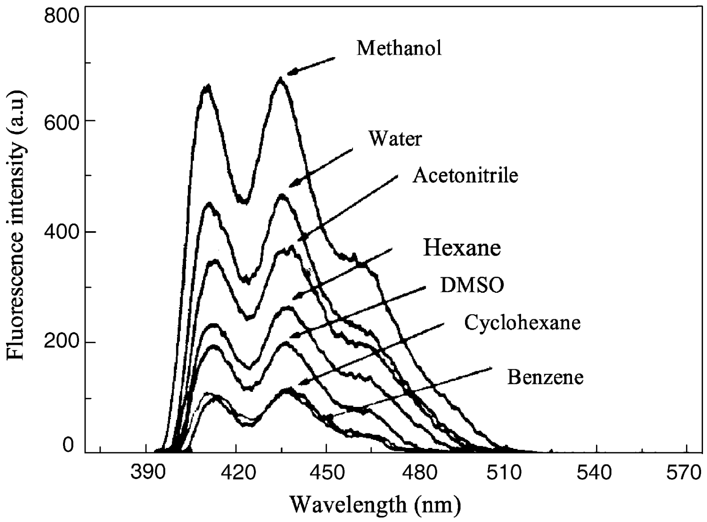


Fig. 7. Emission spectra of PVA film doped with benzo [k] fluoranthene in different solvent media ($\lambda_{ex} = 308$ nm) [203]. Reproduced from Patra and Mishra by permission of Elsevier Science Ltd, Oxford, UK.

analytical utility of the sensor was established by selective flow-injection measurements of hydrazine (detection limit 5.7 ng) or hydrogen peroxide in the presence of oxalic or ascorbic acids, respectively. In another paper, Hou and Wang [207] described a Nafion film coated on top of a Prussian Blue-modified glassy carbon electrode (GCE) for the detection of hydrazine in FIA with a detection limit of 0.6 ng. A Nafion/ruthenium oxide pyrochlore ($Pb_2Ru_{2-x}Pb_xO_{7-x}$)-modified GCE exhibited excellent electrocatalytic activity in the oxidation of hydrazine in neutral media. Zen et al. [208] synthesized the catalyst directly inside the Nafion thin film matrix, which is spin coated onto a GCE. Hydrazine is detected with excellent sensitivity in a FIA at the modified electrode, with a detection limit of 0.048 ng. A polypyrrole layer was used as a sensing layer for ammonia and hydrazine [209].

3.7. Humidity sensor

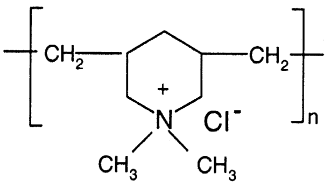
Humidity sensors are useful for the detection of the relative humidity (RH) in various environments. These sensors attracted a lot of attention in the medical and industrial fields. The measurement and control of humidity are important in many areas, including industry (paper, food, electronic), domestic environment (air conditioner), medical (respiratory equipment), etc. Polymer, polymer composites and modified polymers with hydrophilic properties have been used in humidity sensor devices. Table 7 describes the polymers used, as well as the sensor properties of humidity sensors based on different working principles. Ion conducting polymeric systems has been used in humidity sensor devices based on variation of the electrical conductivity with water vapor. Polymer electrolytes containing polymer cation/polymer anion with its counter ions and mixtures or complexes of inorganic salts with polymer are the major materials for fabrication of humidity sensor. For example, lithium chloride dispersed in hydrophobic polyvinyl acetate held in the pores of polyvinyl alcohol film [210] and $LiClO_4$ doped polyethylene oxide [211] are reported for humidity sensors. Polyethylene oxide doped with alkali salts provides low resistivity and low activation energy for electrical conduction. Sorption of water molecules increases the free volume, causing a hopping migration of smaller cations [212]. Mixtures of poly(styrene-*co*-quaternized-vinylpyridine) and perchlorates such as $HClO_4$, $LiClO_4$, $KClO_4$ were used by Xinet al. [213] in a humidity sensor, reporting that the conductivity of the sensor due to sorbed water varied in the order $HClO_4 > KClO_4 > LiClO_4$. A very low humidity, down to 2 ppm,

Table 7
Different polymers used in humidity sensors

Polymer	Principles	Sensor Properties	Refs.
2-Acrylamido-2-methyl propane sulfonate modified with tetraethyl orthosilicate	Electrical property measurement	Less hysteresis $<2\%$, good linearity, 30–90%working range humidity, long-term stability of at least 31days	[243]
Iron oxide-polypyrrole nanocomposite	Electrical property measurement	Sensitivity increases with increasing concentration of polypyrrole	[247]
Nano-$BaTiO_3$-quaternary acrylic resin (RMX) composite	Electrical property measurement	Maximum humidity hysteresis is 3% RH, 7–98%working humidity range, 15 and 120 s response and recovery time, respectively, in 33–98% RH, about 1 year long term stability	[242]
Quaternized and cross-linked poly (chloromethyl styrene)	QCM sensor	Degree of hysteresis decreases with increase in quaternization	[248]
Crystal violet and methylene blue incorporated in PVA/H_3PO_4 SPE	Optical humidity sensor	Shows linearity of response	[244]
PVA (polyvinyl alcohol)	SAW sensor	60%RH measured as a frequency change of about -11.5 MHz at room temperature	[246]

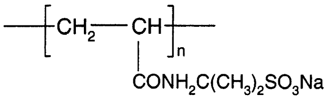
can be measured by a composite film of perfluorosulfonic ionomer-H_3PO_4 [214].

Although polymer electrolytes containing hydrophilic groups such as $-COOH$, $-SO_3H$, $-N^+(R)_3Cl$, etc. are potentially excellent materials for sensing low humidity, these cannot operate at high humidity because of their solubility in water. Such problems have been overcome by blending with a hydrophobic polymer, or preparing hydrophobic polymers with hydrophilic branches, copolymerization of a hydrophobic monomer with a hydrophilic monomer, crosslinking of hydrophilic polymers with a suitable crosslinking agent or by grafting a hydrophilic monomer onto a hydrophilic polymer backbone. Sodium polystyrene sulfonate (PSSNa) [215], poly(*N*,*N*-dimethyl-3,5-dimethylene piperidinium chloride) (DpiC) (**XIII**) [216] are used as humidity sensitive polymer electrolyte.



Poly(N,N-dimethy1-3,5-dimethylene piperidinium chloride) (DpiC) (**XIII**)

Aliphatic ionene polymers having quaternary nitrogens, $-N^+(CH_3)_2-(CH_2)_x-N^+(CH_3)_2-(CH_2)_y-$, show good sensitivity to humidity between 30 and 90% RH [217]. A thin film of a copolymer of 2-hydroxy-3-methacryloyloxypropyl trimethylammonium chloride (HMPTAC) showed a resistivity change from 10^6 to 10^3 Ω when the RH varied from 20 to 100% [218]. Kinjo and coworkers [219–221] prepared humidity sensors using a variety of ionic and non ionic monomers, such as methyl methacrylate (MMA), styrene, methyl acrylate (MA), and 2-hydroxyethyl methacrylate (HEMA) as the nonionic monomers and sodium styrene sulfonate (NaSS), sodium 2-acrylamide-2-methyl-propane sulfonate (NaAMPS) (**XIV**), sodium methacrylate, ethacrylolyloxy-ethyldimethylammonium chloride (MEDMACl), methacrylolyloxyethyltrimethylammonium chloride (METMACl), and methacryloyloxy-ethyldimethyloctylammonium chloride (MEDMOcACl) as the ionic monomers. The response time obtained was in the order $-SO_3^- > -CO_2^- > -C_2H_4N^+H(CH_3)_2 > -C_2H_4N^+(CH_3)_3 > -C_2H_4N^+(C_8H_{17})(CH_3)_2$ when the RH was changed quickly from 40 to 60%.



$$-\!\left[CH_2-\underset{CONH_2C(CH_3)_2SO_3Na}{CH}\right]_n\!-$$

Sodium salt of poly(2-acrylamide-2-methyl propane sulphonic acid) (**XIV**)

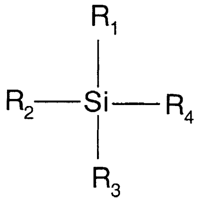
Humidity sensitive, but water-insoluble copolymers, were produced by grafting hydrophilic monomer on hydrophobic polymers such as grafting of polystyrene on PTFE followed by sulfonation of polystyrene branch [222], grafting of 4-vinylpyridine on PTFE film followed by quaternization with alkyl halide

[223]. Microporous polyethylene film with thickness and porosity 100 μm and 70%, respectively, was also used as the base polymer. 2-Acrylamide-2-methylpropane sulfonic acid (AMPS) [224] or 2-hydroxy-3-methacryloyloxypropyl trimethylammonium chloride (HMPTAC) [225,226] was grafted onto the microporous polyethylene by conventional catalytic initiation with benzoyl peroxide or ultraviolet irradiation, using benzophenone as a sensitizer.

Chemical modification of hydrophobic polymers has been done to generate ionic groups to obtain a material sensitive to humidity. Sulfonation of polyethylene [227], polysulfone [228] provided good sensitivity to humidity. Yamanaka et al. [229] used Nafion with sulfonic acid groups for sensing humidity in the range 20–70% RH, while Huang [230] used Nafion with both sulfonic and carboxyl groups for the RH range of 40–95%. Plasma polymerization was also used as an important tool to make polymers suitable for humidity sensing. Plasma polymerization of organosilicone containing amino or amine oxide groups such as trimethylsilyldimethyl amine, tertramethylsilane plus ammonia, bis (dimethyl amino) methyl silane, bis(dimethyl amino) methyl-vinyl silane, followed by treatment with methyl bromide, was used to fabricate humidity sensing devices [231, 232]. Various silane derivatives are shown in structures **XV**.

Surface functionalized polyethylene (PE) and polypropylene (PP) have been prepared by sulfonation by treatment with oleum to form a sulfonated derivative, followed by either reaction with lithium hydroxide to form a lithiated PE/PP or the anchoring of gold nanoclustures on the surface of the sulfonated PE/PP [233]. After controlled sulfonation these surface functionalized polymers show promising humidity-dependent resistance changes ($10^9-10^6\ \Omega$ with a change in the RH from 30 to 95%), and a short response time. The sensitivity can be controlled by surface structure and the extent of functionalization, causing a change in carrier concentration and the mobility of protons and counter ions.

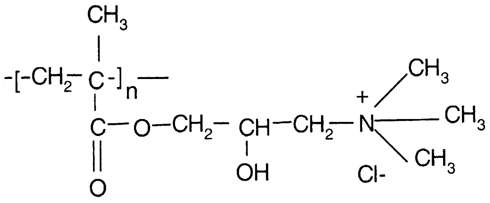
Crosslinkable polymers are also used to generate ionic sites, in the crosslinked state, for sensing humidity. Hijikigawa et al. [234] measured the humidity sensing characteristics of polystyrene sulfonate, crosslinked with *N*,*N*′-methylene bisacrylamide by UV. Poly-4-vinyl pyridine was quaternized and crosslinked simultaneously with α, ω-dichloroalkane for use in a humidity sensing device [235]. Poly(chloromethyl styrene) simultaneously crosslinked and quaternized by *N*, *N*,*N*′,*N*′-tetramethyl-1,6-hexanediamine on similar substrate is also another humidity sensing film [236]. Otsuki and Dozen [237] prepared water resistive film by quaternizing the copolymers of 4-vinylpyridine or 2-dimethylaminoethylmethacrylate with 4-methacryloyloxychalcon and crosslinking by



	R_1	**R_2**	**R_3**	**R_4**
Silane	H	H	H	H
Trimethylsilyldimethyl amine	CH_3	CH_3	CH_3	$(CH_3)_2NH$
Tetramethylsilane	CH_3	CH_3	CH_3	CH_3
Bis(dimethyl amino)methyl silane	CH_3	$(CH_3)_2NH$	$(CH_3)_2NH$	H
Bis(dimethyl amino)methyl-vinyl silane	CH_3	$(CH_3)_2NH$	$(CH_3)_2NH$	$CH_2{=}CH$

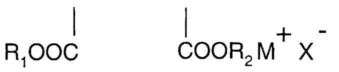
Silane derivatives (**XV**)

UV. Crosslinked organopolysiloxane having hydrophilic groups such as NH_2, $N^+(CH_3)_3Cl^-$, SO_3H, OH were grafted on a pressed silica gel or a sintered alumina plate [238] to make humidity sensor. Raven et al. [239] fabricated a humidity sensor by spin coating the ionic conductive polymer poly(dimethyldiallylammonium chloride) on a ceramic wafer, followed by crosslinking with gamma-irradiation. Humidity-sensitive poly(2-hydroxy-3-methacryloxypropyl-trimethyl ammonium chloride)(HMPTAC) (**XVI**) has a hydroxy as well as a quaternary ammonium group. The hydroxy group can also be crosslinked by diisocynate to fabricate a humidity sensor [240]. An IPN film composed of crosslinked HMPTAC polymer and crosslinked ethylene glycol dimethacrylate (EGDMA) polymer was formed on a substrate with interdigited electrodes [240]. The impedance of the sensor thus prepared decreased from 10^7 to10^2 Ω with 0–90% RH.



Poly(2-hydroxy-3-methacryloxypropyl-trimethyl ammonium chloride) (**XVI**)

Sun et al. [241] reported the humidity sensitivity of the polymer RMX (**XVII**), which is a kind of electrolytic organic humidity sensing material, where R denotes the carbon chain of the polymer and M and X represent anode ion NH_4^+ and cathode ion Cl^-, respectively:



$$-(R)_m-(R)_n- \quad \text{with } R_1OOC \text{ on } (R)_m,\ COOR_2M^+X^- \text{ on } (R)_n$$

RMX (**XVII**)

Later Wang et al. [242] prepared a composite material of nanocrystalline $BaTiO_3$ with quaternary acrylic resin of the RMX type for use as humidity sensor. They investigated the electrical property of this humidity sensor, including the resistance versus RH (see Fig. 8), humidity hysteresis, response-recover time and long-term stability.

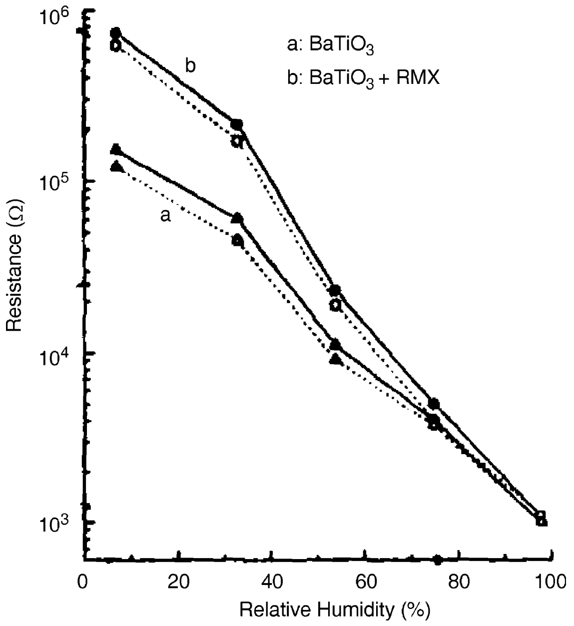


Fig. 8. Resistance-relative humidity (RH) properties of the sensors [242]. Reproduced from Wang, Lin, Zhou and Xu by permission of Elsevier Science Ltd, Oxford, UK.

Su Pi et al. [243] fabricated a resistive-type humidity sensor by thick film deposition using poly(2-acrylamido-2-methylpropane sulfonate) (poly-AMPS) modified with tetraethyl orthosilicate (TEOS) as the sensing material, without a protective film or complicated chemical procedures. They investigated the effect of adding triethylamine (TEA) or diethylamine (DEA), the dosage of TEOS on the capacity resistance to high humidity atmosphere, and the thickness of film. They also further studied the response time, response linearity, working range, hysteresis, and effect of temperature and long-term stability of the sensor. They reported that such a humidity sensor possesses <2% hysteresis, good linearity ($R^2 = 0.9989$) over the humidity working range of 30–90% RH, long-term stability (at least 31 days) and satisfactory resistance to high humidity atmosphere (95% RH) on addition of TEOS (16.25%, w/w) and TEA (0.4 ml) into poly-AMPS as the sensing material. Somani et al. [244] demonstrate that certain dyes can serve as excellent candidates for optical humidity sensing when incorporated in SPEs. Thus, either crystal violet (CV) or methylene blue (MB) will form association–dissociation complexes as the basis for an optical humidity sensor when incorporated separately in poly(vinyl alcohol) PVA/H_3PO_4; the latter SPE is a good proton conductor. The change in the optical properties of the films could possibly be due to either association/dissociation complex that the CV dye must be forming with the polymer or due to change in the pH value. MB forms a charge transfer complex with the PVA/H_3PO_4 SPE and thereby change its optical property due to change in humidity

A luminescence lifetime-based fiber-optic sensor can be used to measure the water content in organic solvents and the RH of air [245]. The sensor is based on the luminescence lifetime quenching of ruthenium (II) bisphenanthrolinedipyrido phenazine (Rudppz) immobilized in a Nafion™ membrane that is mechanically attached to the distal tip of an optical fiber. Treatment of the Nafion™ membrane with lithium hydroxide prior to doping with Rudppz provides a stable sensor response with intense, long-lived luminescence. The response of the sensor to RH was characterized using dry air, room air, and water saturated air. The sensor can be used to measure the water content of organic solvents below 4% (v/v), with detection limits of 0.06, 0.07, and 0.006% (v/v) in DMSO, ethanol, and acetonitrile, respectively.

A hygroscopic polymer should be simultaneously highly sensitive and resistive to water molecules. A highly sensitive SAW sensor system has been developed by Penza and Cassano [246] for RH measurements using a chemically interactive poly (vinyl alcohol) (PVA) film. They reported that the PVA film provided high RH sensitivity, as well as high water resistance, as desired. The SAW response toward 60% RH has been measured as a frequency change of about 11.5 MHz, at room temperature. They also reported cross-sensitivity of the PVA film toward organic vapors with bonded OH groups. The room temperature RH sensing characteristics of such PVA-based dual SAW sensor has been analyzed in terms of sensitivity, calibration curve, detection limit, noise, water-resistance, short-medium term repeatability, aging, and sensing performances comparison.

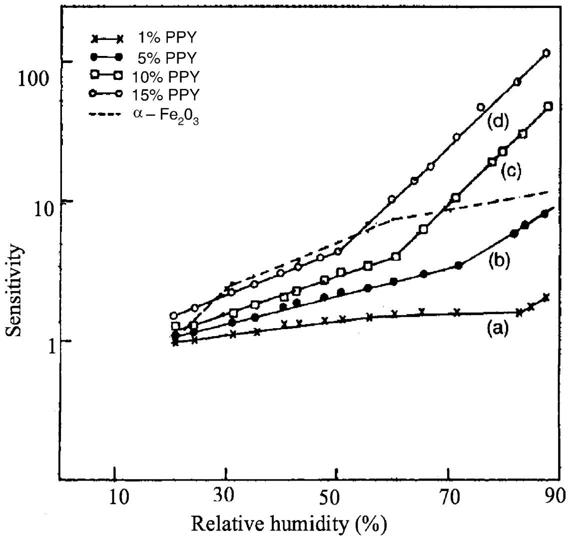


Fig. 9. Variation of sensitivity with humidity for sensors having (a) 1%, (b) 5%, (c) 10% and (d) 15% polypyrrole [247]. Reproduced from Suri, Annapurni, Sarkar and Tandon by permission of Elsevier Science Ltd, Oxford, UK.

Suri et al. [247] prepared nanocomposite pellets of iron oxide and polypyrrole for humidity and gas sensing by a simultaneous gelation and polymerization process. This resulted in the formation of a mixed iron oxide phase for lower polypyrrole concentration, stabilizing to a single cubic iron oxide phase at higher polypyrrole concentration. Sensitivity to humidity increased with increasing polypyrrole concentration (see Fig. 9). Gas sensing was performed for CO_2, N_2, and CH_4 at varying pressures, with the highest sensitivity to CO_2. Sakai et al. [248] prepared a resistive-type humidity sensor using a poly(chloromethyl styrene) (PCMS) film, which was simultaneously cross-linked, and quaternized (**XVIII**). The sorption isotherm curves of water vapor in various cross-linked films were obtained using a QCM. It was found that the degree of hysteresis depended on the density of the quaternary ammonium group, which affects the diffusion coefficient of the water molecules in the film (see Fig. 10). Su et al. [249] fabricated a resistive-type humidity sensor by a thick film method using the poly(2-acrylamido-2-methylpropane sulphonate) (poly-AMPS) modified with tetraethyl orthosilicate (TEOS) as the sensing material, without protective film or complicated chemical procedures. The sensitivity of the sensor to humidity was affected by adding triethylamine (TEA) or diethylamine (DEA), the dosage of TEOS on

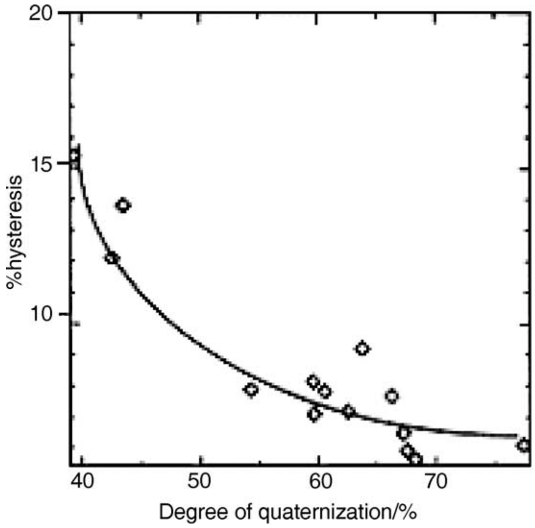
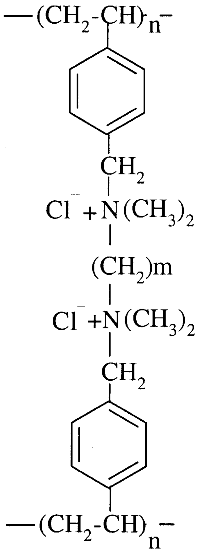


Fig. 10. Plot of % hysteresis at 40% RH as a function of degree of conversion [248]. Reproduced from Sakai, Matsuguchi, Hurukawa by permission of Elsevier Science Ltd, Oxford, UK.



Cross-linked and quaternized poly(chloromethyl styrene) (**XVIII**)

the capacity resistance to high humidity atmosphere, and the thickness of film. The humidity sensor has low hysteresis ($<2\%$), good linearity ($R^2 = 0.9989$) at the humidity working range of 30–90% RH, long-term stability (at least 31 days) and satisfactory resistance to high humidity atmosphere (95% RH) with the addition of TEOS (16.25%, w/w) and TEA (0.4 ml) to poly-AMPS as the sensing material. Sun and Okada [250] simultaneously investigated the interaction between methanol, water and Nafion®(Ag), and determined the concentration of methanol and water (RH) using a QCM coated with Nafion® film recast from Nafion®(Ag) complex solution. Due to the larger association constant of water than methanol, the frequency shift caused by methanol and water adsorbed onto Nafion®(Ag) was in the order: water $>$ methanol. Binding rate constant analysis showed that methanol demonstrates larger binding and dissociation rate constants than water, due to the higher vapor pressure of methanol. The binding energy change between Nafion®(Ag) and methanol or water molecules was also evaluated using a molecular mechanics calculation. Polyimide film has been used to design humidity sensor [251,252].

3.8. Biosensor

A biosensor may be considered as a combination of a biorecepter, the biological component, and a transducer, the detection method. The total effect of a biosensor is to transform a biological event into an electrical signal. Biosensors found extensive applications in medical diagnostics, environmental pollution control for measuring toxic gases in the atmosphere and toxic soluble compounds in river water. Applications of different sensors are summarized in Table 2. These pollutants include heavy metals, nitrates, nitrites, herbicides, pesticides, polychlorinated biphenyls, polyaromatic hydrocarbons, trichloroethylene etc. Pollutant sensitive biocomponents have been used with a variety of detection modes for their quantitative estimation [253,254]. The estimation of organic compounds is very important for the control of food manufacturing process and for the evaluation of food quality. The online analysis of raw materials and products is also necessary in industrial fermentation processes. The use of enzyme sensors can help in the direct measurement of such compounds, including organic pollutants for environmental control. Since hydrogen peroxide, used in food, textile and dye industries for bleaching and sterilization purposes, can be directly measured by

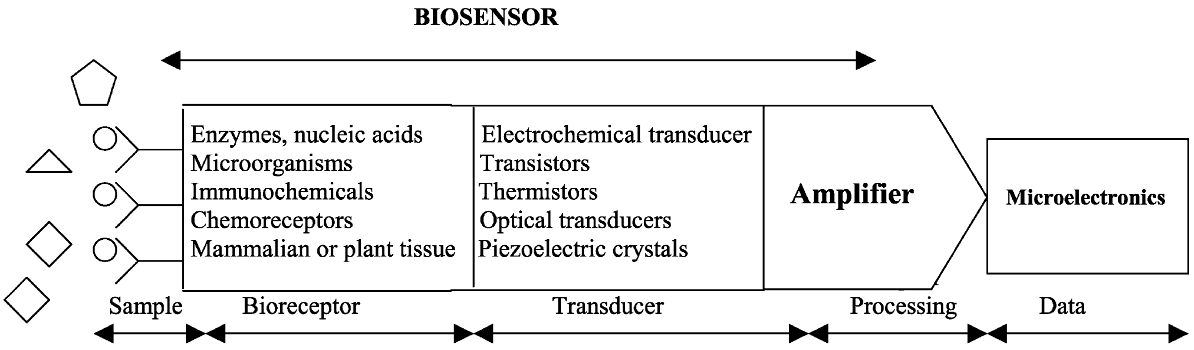


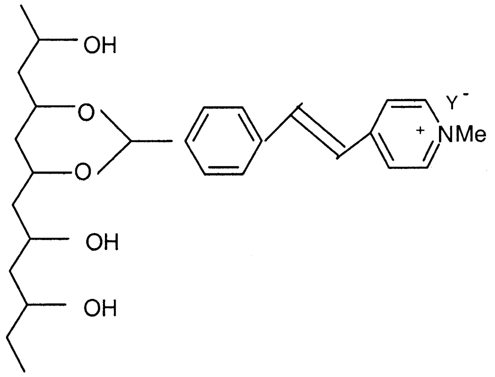
Fig. 11. Major stages of measurements of analytes with a biosensor.

enzyme sensors as per the following equation, with the liberated oxygen detected by oxygen electrode:

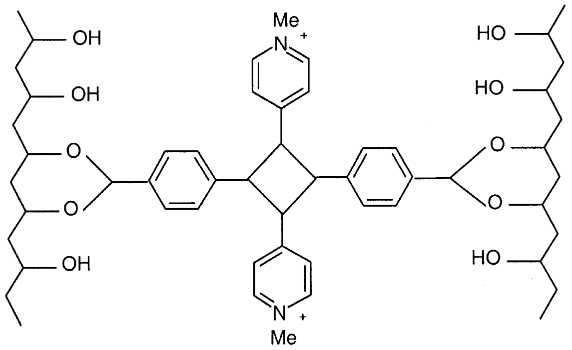
$$H_2O_2 \xrightarrow{\text{Catalase}} H_2O + \frac{1}{2}O_2$$

This technique is faster and more convenient than the classical colorimetric and volumetric methods. Fig. 11 shows the principle of the operation of a biosensor [255], which starting from the analyte can provide all the information needed for its evaluation. By far the largest group of direct electron-transfer biosensors is based on coimmobilization of the enzyme in a conducting polymer, namely polypyrrole [256–265]; and polyaniline [266]. Various epoxy cements are somewhat similar [267–269].

Ichimura and coworkers [270] reported a method to photochemically immobilize enzymes in photocrosslinkable poly(vinyl alcohol) (**XIX**) bearing stilbazolium groups. **XX** represents the structure of photocrosslinked poly(vinyl alcohol) through stilbazolium group.



Photocrosslinkable poly(vinyl alcohol) bearing stilbazolium group (**XIX**)



Photocrosslinked poly(vinyl alcohol) through stilbazolium group (**XX**)

Such a film of the photosensitive polymer, containing the enzyme, gave water-insoluble, cellophane-like transparent film, with a high enzyme activity. The dissolution of enzymes from the film was dependent upon the molecular weight of the proteins and the fraction of the photocrosslinking units in the polymer. Various enzymes remain sufficiently entrapped in the photocrosslinked polymer matrix with a photosensitive group content more than about 1.0 mol%.

The use of stable synthetic polymers having a specific receptor structure is important in biology, medicine and biotechnology. Methacrylic polymers, selective for nucleotides, amino acids and herbicides have been prepared by Piletsky et al. [271] using the molecular imprinting technique. The selectivity of template polymers is dependent on the amount and nature of the interactions between the substrate and the stationary polymer phase, as well as on the shape of the imprinting molecules and the polymer cavities. Nagels and Staes [272] reviewed the penetration of polymer-based electrode coatings for amperometric detection in continuous flow systems of analysis. Redox hydrogels, loaded ionomers, and conductive electroactive polymers form the basis of such materials. They can improve the detectability of electroactive substances with slow kinetics on classical electrode materials. Conductive electroactive polymers can detect electroinactive ions amperometrically, via an indirect mechanism. When combined with immobilized enzymes, the above materials can detect otherwise electroinactive substances in LC and FIA methods. Gros and coworkers [273] prepared a polypyrrole-containing $Fe(CN)_6^{3-}$modified electrode by anodic electropolymerization at 0.8 V versus SCE of an aqueous solution containing only pyrrole and $K_4Fe(CN)_6$. A high degree of reversibility of the $Fe(CN)_6^{3-}/Fe(CN)_6^{4-}$redox system made it possible to use the modified electrode as a pseudo-reference in a weakly polarized two-electrode device for the design of amperometric biosensors involving NAD-dependent dehydrogenases. D-lactic acid was estimated using D-lactate dehydrogenase and diaphorase. The modified electrode exhibits a sensitivity of 20 μA mM^{-1} cm^{-2}, a stable potential for currents lower than 100 nA and an operating life of more than 2 months. Peng et al. [274] fabricated a new bulk acoustic wave (BAW) sensor modified with a MIP, poly(methacrylic acid-*co*-ethylene glycol dimethacrylate), for the determination of pyrimethamine in serum and urine media. This sensor exhibited high selectivity and sensitive response to pyrimethamine. They investigated and optimized the factors such as pH and the amount of coating influencing sensor properties. They obtained a linear calibration curve in the range 6.0×10^{-7}–1.0×10^{-4} M, with a determination limit of 2.0×10^{-7} M. The sensor exhibits long-term stability, even in harsh chemical environments, such as high temperature, organic solvents, bases, acids, etc.

3.8.1. Enzyme sensor

An enzyme sensor may be considered as the combination of a transducer and a thin enzymatic layer, which normally measures the concentration of a substrate. The enzymatic reaction transforms the substrate into a reaction product detectable by a transducer. A schematic representation of an enzyme sensor is given in Fig. 12. The sensitive surface of the transducer remains in contact with an enzymatic layer, and it is assumed that there is no mass transfer across this interface. The external surface of the enzymatic layer is kept immersed in a solution containing the substrate under study. The substrate migrates towards the interior of the layer and is converted into reaction products when it reacts with the immobilized enzyme [275].

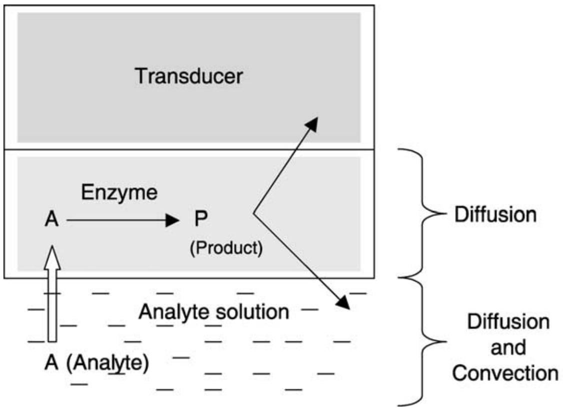


Fig. 12. Diffusions of the analyte A from solution to enzyme layer and the product P via enzymatic reaction to the transducer.

Different strategies are followed for the immobilization of molecular recognition agent in sensor devices particularly in biosensors. Polymers are the most suitable materials to immobilize the enzyme, the sensing component, and hence to increase the sensor stability. Table 8 includes the polymers used in different enzyme sensors, as well as their senor characteristics.

Glucose biosensor. The determination of glucose is one of the most frequently performed routine analyses in clinical chemistry, as well as in the microbiological and food industries. Diabetes is now a serious global problem that has attracted continuous interest for the development of an efficient glucose sensor (Table 2). An artificial pancreas has come to a reality for dynamically responding to glucose level and controlling insulin release based on the sensor's response. Clark and Lyons [276] first developed an enzyme sensor for glucose analysis and Updike and Hicks [277] used glucose oxidase immobilized in polyacrylamide gel and an oxygen electrode. Enzymatic reaction consumes oxygen and decreases the concentration of dissolved oxygen around the enzyme membrane, resulting marked decrease in electrode

Table 8
Polymers used in different enzyme biosensors

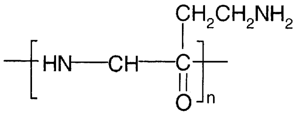
Analyte	Polymer	Sensing elements	Sensor properties	Refs.
Glucose	Polypyrrole	Glucose oxidase (GOD)	Long-term stability is 7days	[289]
	Poly-*N*-methylpyrrole	GOD	Detect analyte within the concentration range 0–0.22 mol/dm^3	[293]
	Poly(*o*-amino phenol)	GOD	Response time <4 s, lifetime $>$ 10 months	[278]
	5-(1-pyrrolyl) pentyl-2-(trimethylammonium) ethyl phosphate, Nafion or poly (*o*-phenylenediamine) (PPD) as inner membrane.	GOD	Influence of ascorbic acid eliminated, stability of 200 days	[301]
	Polyphenol	GOD	Short response time <4 s, high sensitivity ~ 1200 nA/mM cm^2, low interference from endogenous electroactive species, long term stability ~ 50 days	[294]
L-Amino acids	Polytyramine	L-amino acid oxidase (L-AAOD)	Lower limit of detection is 0.07 mM. Stability is more than 1 month	[330]
Peroxides	Poly (anilino methyl-ferrocene)	Horseradish peroxidase	–	[344]
Brain glutamate	Poly (*o*-phenylenediamine)	Glutamate oxidase	Fast response time, lower detection limit ~ 0.3 μM, sensitivity is 4 nA/μM	[372]
Creatinine	Poly (1,3-diaminobenzene)	Creatininase, creatinase, sacrosine oxidase	Fast response time ~ 1 min, detection limit of 10–20 μM	[320]
Sulfite	Chitosan	Sulfite oxidase (SOX)	Current responses are directly proportional to the concentration of ions in the range 0.5–2.5 mM	[371]
Glucose, lactate, pyruvate	Poly [4-vinyl pyridine Os (bis-pyridine)$_2$Cl]-*co*-allylamine	GOD, lactate oxidase (LAX), pyruvate oxidase (PYX)	Sensitivities are 0.26, 0.24, 0.133 μA/(cm^2 mM), respectively. Concentration ranges are (0–20 mM), (0–10 mM), (0–2 mM), respectively	[295]
Glucose, urea, triglycerides	Polyaniline	GOD, urease, lipase	–	[280]

current, until a steady state is reached. Zhang et al. [278] developed a glucose biosensor based on immobilization of glucose oxidase in an electropolymerized o-aminophenol film on a platinized GCE. The device offered excellent characteristics, including high sensitivity, long-term stability, very short response time, and significantly reduced interference. Jung and Wilson [279] developed a miniaturized, potentially implantable amperometric glucose sensor with a sensing area of 1.12 mm^2 based on the enzymatically catalyzed reaction used by Clark and others. Sangodkar et al. [280] reported a biosensor array based on polyaniline. They fabricated polyaniline based microsensors and microsensor arrays for the estimation of glucose, urea, and triglycerides. Microelectronics technology was used to produce gold interdigitated microelectrodes on oxidized silicon wafers. Polymer deposition and enzyme (glucose oxidase, urease, and lipase) immobilization was done electrochemically. They claimed that an analyte containing a mixture of three substances can be analyzed in a single measurement using a single sample of a few microliters, and also claimed this as a general technique that may be extended to other enzyme-substrate systems, eventually leading to the development of an ‘electronic tongue’.

Geise and coworkers [281] constructed electrochemical biosensors by all-chemical means for the determination of serum glucose in a flow-injection analysis. They immobilized glucose oxidase on the surface by crosslinking with glutaraldehyde, followed by deposition of an electropolymerized film of 1,3-DAB (Diaminobutane)/resorcinol. The electrode is protected from interference and fouling by electropolymerized films. The biosensor, with poly(1,3-DAB/resorcinol), was reported to be effective for 5 months of periodic use, a linear response over the human physiological range (2.5–10 mM), and an accuracy of ± 3% for standard serum samples. Rohde et al. [282] described a reagentless glucose oxidase-based biosensor for application in a flow system. They first codeposited the enzyme with the redox polymer $[Os\ (bipyridyl)_2(poly\text{-}4\text{-}vinylpyridine)_{10}Cl]Cl$ and glutaraldehyde on the surface of a platinum electrode with subsequent covering with an electropolymerized layer of pyrrole containing oxidase. Due to the high permeability of both layers, β-D-glucose was directly detected amperometrically.

A sol–gel silicate-based biosensor responded rapidly (ca. 15 s) to glucose at 0.6 V (versus Ag/AgCl), without any interference from electroactive species such as L-ascorbate and urate below 0.2 mM. Such a glucose biosensor [283] was made by utilizing a composite membrane of sol-gel enzyme film and electrochemically generated poly(1,2-diaminobenzene) film to improve the selectivity of the sol–gel enzyme sensors. Reliable results were obtained in assays of glucose in controlled human sera, for both steady state and flow-injection measurements. Similar sensors were also developed for galactose and cholesterol, although the sensitivity of these sensors was inferior to that of glucose sensor. Reagentless enzyme electrodes were prepared by covalent binding of enzymes and redox mediators on the sensor surface to prevent contamination of the sample by sensor components [284]. Miniaturization and mass production of enzyme electrodes are carried out by electrochemical deposition of conducting polymer layers, e.g. polypyrrole, at the surface of an electrode independent of its size and form. Through the functionalization of conducting polymer films the electrode surfaces are made suitable for the binding of enzymes or redox mediators.

Glucose-sensing electrodes were constructed using polydimethylsiloxane (PDMS) [285]. A PDMS/GOx-bilayer electrode was fabricated by placing an enzyme layer on a PDMS-coated electrode, prepared by dip coating from an aqueous dispersion of the siloxane polymer. Another enzyme electrode with a PDMS layer containing lipid-modified Gox was prepared by placing aqueous dispersions of the polymer and the modified enzyme on the base electrode surface, and drying. This modified Gox electrode is suitable for measuring glucose in high concentrations (around 5 mM), compared to the bilayer-based system. The permselectivity of PDMS made it possible to monitor the oxygen consumption rate without serious electrochemical interferences. Myler et al. [286] used an ultra-thin-polydimethyldichlorosiloxane film composite membrane as the outer covering barrier in an amperometric glucose oxidase enzyme electrode biosensor. Polysiloxane composite membranes offer some screening functionality towards anionic biological interferents such as ascorbate. While an approximate 25% signal drift was observed during the first 2 h exposure to blood, the responses was nearly stable thereafter. Whole blood glucose determinations showed a close correlation to results performed via standard hospital analyses. Ghosh et al. [287] developed a glucose biosensor with a cellulose acetate butyrate microencapsulated enzyme, with glucose oxidase as the model enzyme. The encapsulation was achieved by a multiple emulsion technique. Mandal and Sarkar [288] reported screen printed electrodes for glucose biosensor using non-conducting polymers such as Nafion, poly-L-lysine (**XXI**) and polyethyleneimines with tetrabutylammonium tetrafluoroborate (TBF) and tetracyanoquinodimethane (TCNQ) as electron mediator.



$$-\!\!\left[HN-CH-\underset{\underset{\displaystyle O}{\|}}{\overset{\overset{\displaystyle CH_2CH_2NH_2}{|}}{C}} \right]_n\!\!-$$

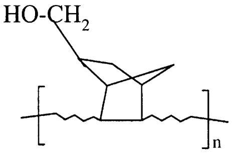
Poly(L-lysine) (**XXI**)

Umana and Waller [289] reported a glucose biosensor by immobilizing glucose oxidase enzyme with electropolymerized polypyrrole, whereby the enzyme becomes entrapped by the polypyrrole film growing on the electrode surface.

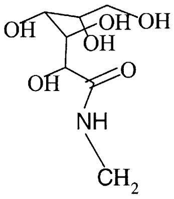
Tian and Zhu [290] developed a novel amperometric biosensor for the cathodic detection of glucose utilizing the two enzymes glucose oxidase (GOD) and horseradish peroxidase (HRP). They constructed this glucose biosensor by electrochemical deposition of a polypyrrole (PPy) membrane in the presence of GOD on the surface of a HRP-modified sol–gel derived-mediated ceramic carbon electrode, using ferrocenecarboxylic acid (FCA) as mediator to transfer electron between the enzyme and electrode. In the hetero-bilayer configuration of the electrode, all enzymes remain well immobilized in the electrode matrices, and showed favorable enzymatic activities. They carried out the amperometric detection of glucose at +0.16 V (versus saturated calomel reference electrode (SCE)) in 0.1 M phosphate buffer solution (pH 6.9), with a linear response range between 0.08 and 1.3 mM glucose. Miniaturized disposable amperometric biosensors [291] were developed based on a poly(pyrrole) film with immobilized glucose oxidase for glucose determination in serum. A commercially available three-electrode system created on a planar corundum ceramic base was used as biosensor substrate, and a working Pt electrode was modified by an electrogenerated overoxidized poly(pyrrole) film (PPYox). Glucose oxidase (GOD) was immobilized, either by enzyme entrapment into the electropolymerized film by an 'all-electrochemical' procedure (PPYox/GOD), or by gel-entrapment over the PPYox modified electrode by co-crosslinking with glutaraldehyde/bovine serum albumin (BSA) (PPYox/GOD-gel). A comparison of the glucose sensitivity, done by dropping 50 μl of the sample solutions onto the relevant electrode systems, showed that both sensors were linear up to 10 mM, though the Pt/PPYox/GOD-gel sensor is the more sensitive of the two (168 ± 15 versus 53 ± 7 nA/mM). The two sensors showed remarkable anti-interferent selectivity, moreover the PPYox/GOD-gel sensor also had good stability and could be used for FIA of glucose, with a linearity range extending up to 25 mM. Various copolymers of 3,4-ethylenedioxythiophene (EDOT) and modified EDOT containing hydroxyl groups were electrochemically prepared by Kros and coworkers [292]. These copolymers have the ability to bind proteins at the surface through the covalent coupling of glucose oxidase, which were used as working electrodes and were able to amperometrically detect glucose under aerobic and anaerobic conditions. Bartlett et al. [293] had done electrochemical polymerization of *N*-methylpyrrole in buffered aqueous solution containing glucose oxidase to produce adherent films at the electrode surface containing the active enzyme. This electrode can detect glucose in the range 0–0.22 mol dm^{-3}. Electropolymerization of phenol was employed to form an anti-interference and protective polyphenol film within the enzyme layer. The enzyme layer was formed by electrodeposition on a Pt electrode. In addition, Chen et al. [294] constructed a stability-reinforcing membrane derived from (3-aminopropyl) trimethoxysilane by electrochemically assisted cross-linking. The hybrid film outside the enzyme layer contributed to the improved stability and permselectivity. Revzin et al. [295] reported glucose, lactate and pyruvate biosensor arrays based on redox polymer/oxidoreductase nanocomposite thin-films deposited on photolithographically patterned gold microelectrodes.

Xu and Chen [296] prepared an amperometric glucose sensor by polymerizing ethacridine at a Pt electrode by potentiostatic and cyclic voltammetric methods. They incorporated glucose oxidase as doped anions into a thin poly(ethacridine) matrix (PETD), to fabricate an amperometric glucose sensor. This enzyme electrode exhibited a fast amperometric response to glucose (within 2 s) and good stability.

Two different biodegradable synthetic polymers functionalized by hydroxyl (**XXII**) or gluconamide (**XXIII**) groups proved to be good immobilization matrices for glucose oxidase [297]. The responses of these biosensors to glucose additions were measured by potentiostating the modified electrodes at 0.6 V/SCE in order to oxidize the hydrogen peroxide generated by the enzymatic oxidation of glucose in the presence of oxygen. The response of such electrodes was evaluated as a function of film thickness, pH and temperature. They reported a linear relationship between current response and glucose concentration up to 2 mM. The current response saturated at ~15 mM concentration of glucose. The above polymers (**XXII**) and (**XXIII**) were synthesized by emulsion polymerization following the methods developed by Rico-Lattes et al. [298,299].



Poly(5-hydroxymethyl-bicyclo-2,2,1-hept-2-ene) (**XXII**)



Poly(N-methylnorbornylgluconamide) (**XXIII**)

Matsumoto et al. [300] developed an amperometric glucose sensor with electrodes coated with a four layered membrane: 3 aminopropyltriethoxysilane (γ-APTES), Nafion®, glucose oxidase (GOX), and perfluorocarbon polymer (PFCP). This sensor determines accurately and successively glucose concentrations between 2.8 and 167 mM, over a 66-day period with no increase in response time, while maintaining imperviousness to the interference species (2.8 mM ascorbic acid, 0.3 mM uric acid, 0.3 mM *p*-acetaminophen). Furthermore, tests on diabetic urine samples showed an excellent correlation between the sensor results and those of a glucose-dehydrogenase clinical laboratory analyses.

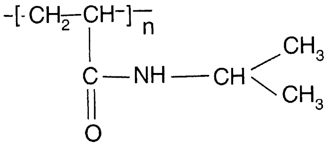
Electropolymerized pyrrole derivatives with phosphatidylcholine, 5-(1-pyrrolyl)pentyl-2-(trimethylammonium)ethyl phosphate in the presence of glucose oxidase (GOD), and an inner-membrane of Nafion or poly(*o*-phenylenediamine) (PPD) were developed as new hemocompatible glucose sensors [301]. The presence of these membranes not only eliminated the influence of ascorbic acid on the sensor response, but also increased the electrode stability. The electrode responses using the PPD inner-membrane were shown to be relatively constant for more than 200 days, or three times as long as the electrode responses without the inner membranes. A heterobilayer configuration for in situ biochemical reduction of interference in the amperometric glucose biosensor was constructed by electrochemically formed polypyrrole in the presence of horseradish peroxidase (HRP), on top of an immobilized glucose oxidase (GO) film [302]. The biosensor showed a good suppression of interference, and less than 5% deviation in the amperometric detection, especially when the glucose concentration was higher than 50 mM. Selective amperometric glucose sensors were prepared by immobilization of glucose oxidase in a layer of polyaniline, made by electropolymerization using phosphate buffer on a Prussian Blue-modified platinum electrode. The influence of ascorbic acid and acetaminophen was completely eliminated due to the impermeability of polyaniline to these substances [303]. A simple electropolymerization process is described by Adeloju and coworkers [304] for the fabrication of an ultra-thin polypyrrole (PPy)-glucose oxidase (GOD) film (~55 nm) in a supporting electrolyte-free monomer solution for potentiometric biosensing of glucose, using 0.1 M pyrrole, 55–110 U/ml GOD, current density of 0.05 mA/cm^2 and an electrical charge of 25 mC/cm^2. Long-term storage of the biosensor in acetate buffer improved the sensitivity of the biosensor by a factor of approximately two. They reported that the biosensor could be repeatedly used for over 2 months with little or no loss in sensitivity. The interference of ascorbic acid was successfully reduced by inclusion of an outer PPy–Cl layer.

A new dipyrrolic derivative linked with a long hydrophilic spacer has been synthesized [305]. The electrooxidation of this monomer in water, either in its solubilized or adsorbed state, leads to the formation of a polymer film on the electrode surface. These procedures have been applied to the immobilization of glucose oxidase as an enzyme model. The amperometric response of the resulting biosensors to glucose has been studied at 0.6 V (vs. SCE), through the oxidation of the generated H_2O_2. The glucose sensitivity of the optimized configuration of enzyme electrode was 3.93 mA M^{-1} cm^{-2}. A new miniaturized glucose sensor with good selectivity and stable current response has been fabricated by simultaneous electropolymerization of *m*-phenylenediamine (MPD) and entrapment of glucose oxidase (GOx) as an inner layer covered by a poly(*m*-phenylenediamine) (PMPD) film without GOx. The inner layer was covered by an outer bilayer of poly(tetrafluoroethylene) (Teflon) and polyurethane (PU) films. The inner layer maintained less than 1% permeability to acetaminophen for 12 days. The fairly adhesive outer layer allowed stable current response. Due to high permeability, the information about enzyme activity can be obtained without serious error in spite of the outer layer intervening between enzymes and solution [306].

Schuhmann [307] used polypyrrole/glucose oxidase electrodes, with the enzyme covalently bound to the outer surface of the functionalized polymeric network, together with a similarly prepared non-enzyme electrode to determine glucose in the presence of cooxidizable compounds in fruit juices and wines. For discriminating the interfering compounds, the thickness of the polypyrrole layers, having size exclusion properties, was kept equal at the two electrodes. They obtained a significant improvement with respect to both the reliability of glucose measurements in real samples and the number of analyses with time. A glucose biosensor, based on glucose oxidase immobilized in a non-conducting (overoxidized) polypyrrole film, has been described [308]. This biosensor has been used for continuous subcutaneous monitoring of glucose in a rabbit implanted with a microdialysis probe. Later a glucose amperometric biosensor based on glucose oxidase immobilized on an overoxidized polypyrrole (PPy_{ox}) platinum modified electrode, by glutaraldehyde co-crosslinking with BSA was reported [309]. In this biosensor the advantages of covalent immobilization techniques (e.g. high loading and long-term stability of the enzyme) were coupled with the excellent interferent rejection of electrosynthesized non-conducting polymers. This sensor was tested for glucose determination of untreated serum samples from both normal and diabetic subjects. The results of amperometric assay compared well with those obtained by a standard enzymatic-colorimetric method. A film of poly *N*-methylpyrrole was adhered at the electrode surface by electrochemical polymerization of *N*-methylpyrrole in buffered aqueous solution containing the enzyme glucose oxidase [293]. Electrodes prepared in this manner were used to detect glucose in solution in the range 0–0.22 mol dm^{-3}. The observed response as a function of glucose concentration, enzyme loading, and film thickness was claimed to be in excellent agreement with theory.

A polyacrylonitrile thin film composite membrane has been used by Bridge and Higs [310] as the outer covering barrier in an amperometric glucose oxidase enzyme electrode. Glucose determinations within whole blood patient samples performed using the enzyme electrode sensor compared favorably to standard hospital analyses. A disposable glucose sensor based on a differential amperometric measurement has been fabricated by Cui et al. [311] on activated carbon paste electrodes, with the use of a glucose oxidase (GOx)-immobilized in nitrocellulose (NC) membrane. Two identical three-electrode cells are screen-printed symmetrically on both faces of a single polyester (PE) substrate. Both electrodes of the two-sided sensor strip are covered with NC membranes incorporating a mediator ($K_3[Fe(CN)_6]$), one membrane with GOx and the other with BSA (i.e. no GOx): the former serves as a glucose-sensing cell and the other as a reference cell. Estimated glucose values in normal and abnormal serum samples using such glucose sensor strip are: 5.08 ± 0.52 (found) vs. 5.10 ± 0.46 (listed), and 16.56 ± 1.71 (found) vs. 16.92 ± 1.72 (listed).

The swelling and shrinking of poly(N-isopropylacrylamide) (**XXIV**) aqueous gel in response to a variation in temperature was utilized to construct a micro sampling device by Kobayashi and Suzuki [312]. They incorporated the sampling mechanism in a micro system with a micro glucose sensor based on the detection of hydrogen peroxide. After the gel was shrunk at 40 °C making contact with a buffer solution, the inlet of the sampling mechanism was placed in contact with a sample solution at 30 °C. It was observed that the sample solution was introduced and moved into the interior of the system following the swelling of the gel. The micro glucose sensor showed a distinct response-accompanying peak with a 90% response time between 2 and 10 s.



Poly(N-isopropylacrylamide) (**XXIV**)

Urea biosensor. Urea is the most important end product of protein degradation in the body. The urea content of blood serum depends on protein catabolism and nutritive protein intake and is regulated by renal excretion [313]. The concentration of urea in blood is important in clinical chemistry in the assessment of kidney functioning [314].

Mizutani et al. [315] prepared an amperometric urea-sensor by immobilizing a tri-enzyme system of pyruvate oxidase (PyOx), pyruvate kinase (PK) and urea amidolyase (UA) on a polydimethylsiloxane (PDMS)-coated electrode. The oxygen consumption was monitored using a PDMS-coated electrode without interference from the PyOx-reaction product, hydrogen peroxide. Thus, the urea was determined in a test solution (5 μM–0.35 mM) containing ATP (adenosine-5′-diphosphate) and PEP (phosphoenolpyruvate) with the tri-enzyme system, without error from coexisting species, such as acetaminophen, uric acid, phosphate in the sample measured.

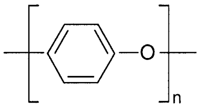
Pandey and Singh [316] described the application of a polymer-modified electrode for the construction of a urea biosensor based on immobilized urease within a poly vinyl alcohol (PVA) matrix, and also within organically modified sol-gel glass on the surface of polymer-modified electrode. This new urea sensor showed a maximum response of 160 mV at 25 °C, with a lowest detection limit of 20 μM urea. A polyvinylbutyral resin membrane was applied to the surface of a silicon nitride-coated silicon wafer for urease immobilization. The membrane (23 μm thick) exhibited good adhesive properties. Immobilized urease activity in this membrane was approximately 24% higher than when a urease-cellulose triacetate membrane was used. [317]

Komaba et al. [318] prepared a urea biosensor by immobilizing urease enzyme in an electropolymerized electroinactive polypyrrole (PPy) on a platinum electrode. The urase-immobilized PPy electrode showed a stable potential response to urea based on the pH response of the electroinactive PPy film electrode. This biosensor showed a Nernstian response, with a slope of 31.8 mV decade^{-1} over concentration range of 1×10^{-4}–0.3 mol dm^{-3} urea. Osaka and coworkers [319] constructed a highly sensitive and rapid flow injection system for urea analysis, with a composite film of electropolymerized inactive polypyrrole (PPy) and a polyion complex incorporating urease. Their system showed a sensitivity of 120 mV decade^{-1} and a lifetime of more than 80 assays. They attributed the high sensitivity of the system to an additional potential response of inactive PPy to ammonia or ammonium ion superimposed on the response to pH change. If a concentrated buffer solution is injected immediately after the sample injection, the system shows a capability of assaying more than 15 samples per hour.

Creatinine biosensor. Measurement of the creatinine levels in serum and determination of the renal clearance of creatinine are widely used for laboratory diagnosis of renal and muscular function [320]. The first reversible chemosensor for creatinine based on artificial chemoreceptors has been reported by Panasyuk-Delaney et al. [321]. They prepared the receptor layer by molecularly imprinted photopolymerization of acrylamidomethylpropanesulfonic acid and methylenediacrylamide. They grafted the polymer layer onto a gold electrode surface coated with an alkanethiol monolayer. Creatinine binding was detected by a decrease in the electrode capacitance. While the sensor response is reversible and highly selective, no response to addition of sodium chloride, creatine, urea or glucose was observed. The detection limit for creatinine is 10 μM, which is optimal for medical applications.

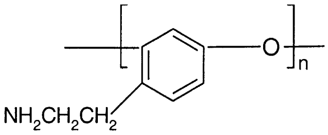
Mădăras et al. [320] constructed miniaturized, disposable amperometric biosensors for determination of creatinine in human serum using thin a electropolymerized permselective film of poly(1,3-diaminobenzene). The polymer film greatly diminished the electrochemical interferences from ascorbate, urate, acetaminophen, and other oxidizable species. A multienzyme system of creatininase, creatinase and sarcosine oxidase was immobilized on top of the permselective layer through cross-linking of the proteins (active enzymes and BSA) with gluteraldehyde. A composite polymeric outer membrane [Nafion + poly-(2-hydroxy-ethyl methacrylate)] was used for diffusion control, and to protect the enzyme layer from fouling. Subrahmanyam et al. [322] devised a new 'bite-and-switch' approach for the design of an imprinted polymer-recognition material useful for the development of a sensor for creatine. They explored the ability of polymerizable hemithioacetal, formed by allyl mercaptan and o-phthalic dialdehydes, to react with primary amines to form a fluorescent isoindole complex, which gives a fluorescence signal. As claimed, this approach could be used for development of sensors for detection of a broad range of amino compounds.

Amino acid biosensor. Amino acids are important in the food industry and in biotechnology, and the concentration of amino acids can be used as a measure of the nutritive value of the food. Single amino acids are measured to gain access to particular enzyme activities, e.g. transaminases and peptidases [323]. Also the determination of total serum amino acids can provide valuable clinical information [323]. Although a few reports for the determination of amino acids are available, no mention has been made for the use of polymers in sensor devices. A general strategy is that either enzymes are physically immobilized in a polymer matrix or a series of chemical/electrochemical modifications are done to generate amine groups on the polymer for covalent attachment of the enzyme. Polymers such as polypyrrole [324,289,260], polyaniline [325,326], polyphenylenediamine [327,328], and polyphenol (**XXV**) [329] were used for the physical entrapment of the enzyme during electrodeposition of the polymer. Such polymers can also be used as a matrix for covalent enzyme immobilization.



Polyphenol (**XXV**)

Cooper and Schubert [330] demonstrated the electrodeposition of polytyramine (poly-4-(2-aminoethyl)phenol) (**XXVI**) as a simple and conventional procedure for electrode modification through generating amine groups on which L-amino acid oxidase (L-AAOD) can be covalently bound (Table 2). They used a L-AAOD-polytyramine electrode for detection of L-amino acids, via current due to oxidation of enzymatically produced hydrogen peroxide.



Polytyramine (**XXVI**)

Pyruvate sensor. Situmorang and coworkers [331] constructed a biosensor by covalently attaching pyruvate oxidase (PyOx) at the surface of electrodeposited polytyramine. They showed that the resulting biosensor is sensitive to pyruvate with a linear calibration plot in the concentration range 0.1–3.0 mM pyruvate, a slope 0.42 μA mM^{-1} and a detection limit of 0.05 mM pyruvate ($S/N = 3$). They claimed that the use of polytyramine produces a stable biosensor with excellent reproducibility. Mascini and Mazzei [332] reported several procedures for immobilization of PyOx by chemical bonding. While they found unsatisfactory attachment of PyOx to nylon net in terms of yield and stability, polyazetidine, a new commercially available prepolymer and a new nylon membrane with surface carboxyl groups, provided good long-term stability, up to 30 days in the case of the nylon membrane. Amperometric sensors based on these membranes are suitable for application to blood serum. In a recent report [333] the preparation of an amperometric sensor has been described for the detection of pyruvate in biological fluids. This sensor was formed by modifying the tip of a 0.25 mm gold wire with a layer of electrically ‘wired’ recombinant PyOx. The sensor did not require O_2 for its operation. The electroactive area of the microwire tip was increased by electrodeposition of platinum black. The PyOx was adsorbed on the platinum black and then wired with the subsequently deposited cross-linked poly(4-vinylpyridine). A part of the pyridine functions were complexed with $[Os(bpy)_2Cl]^{+/2+}$ and part quaternized with 2-bromoethylamine. When the electrode was set at 0.4 V vs Ag/AgCl, the sensitivity at pH 6 was 0.26 A cm^{-2} M^{-1} and the current increased linearly with the pyruvate concentration through the 2–600 μM range. In calf serum, the detection limit was 30 μM, suggesting that the electrode might be used in the continuous monitoring of pyruvate in hypoxic organs. Mizutani et al. [334] prepared an amperometric pyruvate-sensing electrode by immobilizing PyOx on a polyion complex membrane. For polyion complex membrane preparation, aqueous solutions of poly-L-lysine and poly(4-styrenesulfonate) were successively placed on a mercaptopropionic acid-modified gold surface, followed by drying. A photocrosslinked poly(vinyl alcohol) layer containing PyOx was then formed on the poly-L-lysine/poly(4-styrenesulfonate)-complex layer. The polyion complex layer eliminates electrochemical interferents such as L-ascorbic acid, uric acid, L-cysteine and acetaminophen, whereas the hydrogen peroxide produced in the PyOx-catalyzed reaction permeates easily through the layer. A high sensitivity (detection limit, 50 nM) and a low interference level were obtained (e.g. a ratio of the response for L-ascorbic acid to that for the same concentration of pyruvic acid was 0.18). The electrode could be used for determining phosphoric acid (detection limit, 0.2 μM).

Cholesterol sensor. A cholesterol biosensors was constructed [335] by entrapment of cholesterol oxidase (ChOx) within a composite poly(2-hydroxyethyl methacrylate) (*p*(HEMA))/polypyrrole (*p*(pyrrole)) membrane. Platinum electrode-supported polymer films were prepared by UV polymerization of the hydrogel component containing dissolved enzyme, followed immediately by electrochemical polymerization of entrapped pyrrole monomer (Py) within the performed hydrogel network. A linear response range from 0.5 to 15 mM and detection limit of 120 μM toward cholesterol were obtained. With a response time of 30 s, about 60 samples/h were reported to be manually analyzed with this cholesterol biosensor, which retained 80% of the initial activity after 12 months, when stored desiccated in the absence of buffer. Cholesterol biosensors were also constructed [336] by entrapment of cholesterol oxidase within a polypyrrole (PPy) film electropolymerized in a flow system. This method enables adjustment of the biosensor characteristics and features low reagent consumption. The proposed cholesterol oxidase based biosensor, named Pt/PPy–ChOx, was applied to the determination of cholesterol in reference serum samples, with results consistent with certified values.

Another approach [337,338] is the immobilization of the enzyme and laponite particles in a polypyrrolic matrix in order to greatly enhance the sensitivity and stability of a cholesterol oxidase-based biosensor. Such a biosensor was constructed by electropolymerization of a laponite nanoparticle-amphiphilic pyrrole derivative-enzyme mixture preadsorbed on the electrode surface. Compared to a similar biosensor without laponite, the biosensor sensitivity increased from 5.1 to 13.2 mA M^{-1} cm^{-2}. The authors showed that the presence of hydrophilic laponite additive in the polymeric matrix containing cholesterol oxidase and cholesterol esterase is essential for the successful determination of total cholesterol. Yon Hin and Lowe [339] constructed a bienzyme electrode for the detection of total cholesterol by incorporating cholesterol esterase and cholesterol oxidase in polypyrrole films. They claimed that in situ deposition of both enzymes during the electrochemical polymerization of pyrrole provides a simple procedure for the immobilization of biomolecules at electrodes and a fast amperometric response to cholesterol and good storage stability. Kajiya et al. [263] also incorporated cholesterol oxidase and ferrocenecarboxylate ions in polypyrrole films by electro-polymerization of pyrrole in an aqueous solution containing these substances. They obtained a remarkable amperometric response to cholesterol using such polymer films, correlating the current response with the apparent enzymatic activity of polypyrrole films.

Peroxide sensor. The measurement of peroxides in samples involves conventional methods, such as spectrophotometry, colorimetric, chemiluminescence, etc. which are complicated, and suffer from various interferences. The determination of hydrogen peroxide and organic peroxides in clinical samples and the environment is rapidly gaining practical importance. Measurement of lipid peroxides in food products and biological tissues is necessary in establishing a relationship between diseases such as breast cancer and the level and type of fat in the diet [340]. It is necessary to monitor the level of organic peroxides released in the environment from many industrial processes [341], produced during ozonation of drinking water [342] and ozonation reactions in air [343].

An amperometric enzyme electrode having covalently attached horseradish peroxidase to GCE and a ferrocene-modified polyaniline film (poly(anilinomethylferrocene)) deposited by the electrochemical polymerization of *N*-(ferrocenylmethyl)aniline monomer has been reported for measurement of peroxide in real sample [344]. This enzyme electrode gave rapid responses to micromolar concentrations of peroxides in the order: hydrogen peroxide > cumene hydroperoxide > tert-butyl hydroperoxide. García-Moreno et al. [345] prepared a biosensor by immobilization of the horseradish peroxidase (HRP) enzyme during the electropolymerization of *N*-methylpyrrole for use in the determination of organic peroxides in a predominantly nonaqueous medium, such as reversed micelles. They prepared the reversed micelles using ethyl acetate as the continuous phase, 4% of 0.05 mol l^{-1} phosphate buffer solution of pH 7.4 as the dispersed phase, and 0.1 mol l^{-1} AOT (dioctyl sulphosuccinate) as the emulsifying agent. Optimization of the working variables involved in the polymer biosensor preparation are discussed in the paper. They obtained amperometric measurements in the reversed micellar medium for 2-butanone peroxide and *tert*-butylhydroperoxide, respectively. The authors used the poly-*N*-methylpyrrole-HRP amperometric biosensor for the determination of the organic peroxide content in body lotion samples, employing 2-butanone peroxide as a standard. Optimization of the peroxide extraction step from the sample was carried out, and recoveries approximating 100% are reported.

A novel and stable amperometric biosensor was developed [346] for the detection of hydrogen peroxide. The biosensor device was constructed by electrodepositing HRP/PPy membrane on the surface of ferrocenecarboxylic acid mediated sol–gel derived composite carbon electrode. The response time of this biosensor to hydrogen peroxide is a few seconds, with detection limit of 0.05 mM. Chen et al. [347] made a hydrogen peroxide biosensor with sol–gel-derived glasses doped with poly(ester sulfonic acid) Eastman AQ 55D in the presence of thionine (TH), as a mediator. They evaluated the response time and sensitivity (11.36 μA mM^{-1}), with a detection limit of 5.0×10^{-7} M H_2O_2 and storage stability. The sensor achieved 95% of the steady state current within 20 s. A hydrogen peroxide biosensor was fabricated by Wang and Dong [348] by coating a sol–gel-peroxidase layer on a Nafion-methylene green modified electrode, where the methylene green (MG) was immobilized by the electrostatic force between MG^+ and the negatively charged sulfonic acid groups in Nafion polymer. The performance of the sensor was evaluated with respect to response time, sensitivity and operational stability. The enzyme electrode has a sensitivity of 13.5 μA mM^{-1} with a detection limit of 1.0×10^{-7} M H_2O_2, and the sensor achieved 95% of the steady-state current within 20 s.

Acetaminophen has been one of the most serious electrochemical interferences to oxidase-based amperometric biosensors that measure H_2O_2. A study was carried out by Zhang et al. [349] to explore various polymer materials for their selectivity as the sensor inner membrane. They found that a composite membrane of cellulose acetate and Nafion eliminated acetaminophen and other electrochemical interferences effectively, while at the same time maintaining reasonable diffusivity for hydrogen peroxide. They attributed the excellent in vivo performance of the sensor not only to significantly reduced steady-state sensitivity to acetaminophen, but also to a very slow acetaminophen response. Tatsuma et al. [350] proposed a substrate-purging enzyme electrode carrying a sensing enzyme and a substrate-purging catalyst on its surface. Thus, by coating it with a cross-linked film of catalase and albumin, the upper sensing limit of a peroxidase-incorporated polypyrrole membrane electrode as an H_2O_2 sensor was increased by approximately two orders of magnitude.

Fish freshness. Maintenance of freshness of products of food industry should be given prime attention. Various compounds, such as amines, carboxylates, aldehydes, ammonia, sulfur compounds and carbon dioxide, are produced during putrefying, especially for fish, meat and green vegetables. Conventional methods for their measurement require complicated operations, such as extraction, centrifugation, steam distillation, and titration, all of which seriously lack reproducibility and continuity. On the contrary, an enzyme sensor can measure the freshness of food products by estimating putrefaction products in an easy and simple manner. Karube et al. [351] developed an enzyme sensor consisting of a monoamine oxidase-collagen membrane and an oxygen electrode for the determination of monoamines for food analysis including the determination of monoamines in meat pastes. In 1998, Ghosh et al. [352] developed a biosensor system for quantitative measurement of fish freshness by determining the ATP degradation products, hypoxanthine (HX), inosine (INO) and inosine monophosphate (IMP) metabolites in fish-tissue. Freshness is indicated by an index K_1 or Hypoxanthine index (H) that depends on the amount of these ATP degradation products in the fish meat. The biosensor system consists of ferrocene carboxylic acid (FCA) mediator incorporated conducting polypyrrole enzyme electrodes with immobilized xanthine oxidase, nucleoside phosphorylase and nucleotidase enzymes for quantitative measurement of HX, INO and IMP respectively by amperometric method. This simple, fast and ready to use biosensor has been used to measure the H values of fresh water fish Catla-Catla over days of storage. Results show that the fish degrades very rapidly after 7 days, even when stored at −12 °C.

Lactate sensor. At present, the determination of lactate does not belong to a frequently performed analyses in clinical chemistry; but its popularity in the diagnosis of shock and myocardial infarction and in neonatology and sports medicine is increasing. Strong efforts were made to develop sensor-based lactate analyzers, which might be readily used at the bedside [353]. A lactate electrode with a lactate oxidase from *Mycobacterium smegmatis* immobilized in a nylon net fixed on an oxygen probe was developed for the determination of L-lactate in blood serum samples in flow systems. The reaction is given by

$$\text{Lactate} + O_2 \xrightarrow{\text{Lactate oxidase}} \text{Acetate} + CO_2 + H_2O$$

The high activity of the enzyme obtained with this immobilization process permits the use of only 20–100 μl of plasma diluted with citrate buffer [354]. Weigelt et al. [355] immobilized lactate monooxygenase by gelatin entrapment, and fixed it to a Clark-type oxygen probe. The resulting enzyme sensor detected L-lactate in the linear range between 0.01 and 60 mM, and has stability of 55 days. The sequential determination of lactate and lactate dehydrogenase activity was possible by addition of NADH and pyruvate to the measuring solution. The linear measuring range for the latter was 0.045–0.9 $\mu mol\ s^{-1}\ l^{-1}$. For lactate determination in diluted serum by FIA, lactate oxidase was electrochemically immobilized in a poly-*o*-phenylenediamine film for the one-step and all-chemical construction of a lactate amperometric biosensor, prepared in situ, i.e. in the FIA system by simply injecting a plug of a solution containing the monomer and the enzyme [356]. Results obtained by FIA-amperometric detection compared well with those obtained by a standard enzymatic colorimetric assay (according to a proper *t*-test at a 95% confidence level). At a flow rate of 1 ml/min a sample throughput higher than 70 samples h^{-1} was achieved. A 75% decrease in biosensor sensitivity was observed after 1 week of continuous use in the FIA system. Chaube et al. [357] reported the co-immobilization of lactate oxidase and lactate dehydrogenase on conducting polyaniline films by physical adsorption for the estimation of l-lactate in cells and fermentation. Later Chaube et al. [358] immobilized lactate dehydrogenase (LDH) on electrochemically polymerized polypyrrole–polyvinylsulphonate (PPy-PVS) composite films, via cross--linking technique using glutaraldehyde, for application to lactate biosensors. These PPy–PVS–LDH electrodes were shown to have a detection limit of 0.1 mM, a response time of about 40 s, and a shelf-life of about 2 weeks and these were used for L-lactate estimation from 0.5 to 6 mM.

Fructose sensor. The fructose biosensor is very useful in determination of fructose in fruits or juices or for detection of lactulose after enzymatic hydrolysis in milk samples. It has been reported [359] that ferrocene/Nafion® modified cellulose acetate (Fc-CA)/Nafion membrane is the most useful fructose biosensor, because of its acceptable analytical characteristics, operational stability, etc. The prevention of ferrocene leakage from the electrode by physical retention of a mediator such as 2,6-dichlorophenolindophenol in a cellulose acetate membrane matrix is reported here for the first time. Five cellulose acetate membranes were prepared, four containing 1.8, 5.3, 8.5, and 20.0% ferrocene and one containing 1.8% of ferrocene and 0.05% of Nafion® in the matrix. All the membranes were much more resistant to ascorbate interference (12–69 nA mM^{-1}) than an uncovered GCE (1152 nA mM^{-1}). With increasing ferrocene in the membrane, a decreasing ability of the membrane to retain mediator was observed. The biosensor with a membrane containing 20.0% of ferrocene in the matrix exhibited the lowest detection limit (3 μM), the shortest response time (45 s) and the highest sensitivity (232 nA mM^{-1}). However, this biosensor was unstable because of ferrocene leaching, whereas the membrane containing 1.8% of ferrocene and 0.05% of Nafion® showed better stability characteristics, and retained almost 40% of the initial response after 8 h of continuous use, with similar sensitivity (226 nA mM^{-1}) and response time (75 s).

Garcia et al. [360] reported a new fructose biosensors utilizing a polypyrrole film and D-fructose 5-dehydrogenase immobilized by different processes. They employed the occlusion enzymatic immobilization technique for enzyme immobilization in the polypyrrole film and crosslinked covalent bond method as another technique for immobilization of the enzyme in the polypyrrole film. Such biosensors were utilized for fructose determination in three different samples of dietetic products, with 200 analyses performed in 2 weeks continuously. An amperometric biosensor for fructose determination was fabricated by Khan et al. [361] by co-immobilizing a pyrrolo quinoline quinone (PQQ) enzyme (fructose dehydrogenase, FDH) with mediator in a thin polypyrrole membrane. They described two methods of sensor preparation. In one, FDH was potentiostatically adsorbed as a monolayer on a transducer electrode, and a very thin (equivalent to a monolayer of FDH) polypyrrole membrane containing a mediator was electrodeposited on the adsorbed FDH. In the other, FDH and mediator [hexacyanoferrate (II) or ferrocene] were co-immobilized on an electrode by electrochemical polymerization of pyrrole. In the former case, highly sensitive and selective response was obtained for fructose, with a wide detection range of up to 30 mM and a linear range from 10 μM to 10 mM. However, the stability of the sensor was poor due to easy leaching of the mediator. In the latter case, the stability of the sensor was significantly better with a dynamic range for fructose detection from 50 μM to 5 mM.

Monophenolase activity of apple polyphenol oxidase. Polypyrrole matrix was used for the immobilization of tiron for the enzyme activity determination of tyrosinase enzyme. A polypyrrole-tiron film was used for the determination of the monophenolase activity of apple polyphenol oxidase [362]. Curulli et al. [363] synthesized different nonconducting polymers on the surface of a platinum (Pt) electrode to assemble fast-response and sensitive amperometric biosensors for choline, butyrylcholine, and acetylcholine, based on choline oxidase (ChOx) and acetylcholinesterase (AchE) or butyrylcholinesterase (BuchE), co-immobilized by crosslinking with BSA and glutaraldehyde (GLT).

Multianalyte biosensor. Very recently Brahim et al. [364] physically entrapped polypyrrole and various oxidoreductase enzymes in poly(2-hydroxyethyl methacrylate) (pHEMA) for the construction of clinically important amperometric biosensors. Glucose oxidase, cholesterol oxidase and galactose oxidase biosensors were constructed. Electrode-supported hydrogel films were prepared by UV polymerization of the HEMA component (containing the dissolved enzyme) followed immediately by electrochemical polymerization (+0.7 V vs. Ag/AgCl) of the pyrrole component within the interstitial spaces of the pre-formed hydrogel network. The optimized glucose oxidase biosensor displayed a wide linear glucose response range (0.05–20 mM), a detection limit ($3S_{y/x}$/sensitivity) of 25 μM and a response time of 35–40 s. This linear glucose response range covers the physiological glucose levels in nondiabetic patients (between 4.5 and 6.0 mM). Tinkilic et al. [365] prepared miniaturized urea and glucose sensors by immobilization of glucose oxidase or urease directly on solid-state contact PVC–NH_2 membrane ammonium and hydrogen ISEs. The resulting biosensing membranes function equivalently to normal PVC membranes in terms of potentiometric response properties. The most important features of the glucose and urea sensors were high sensitivity, long life-time, easy, low-cost micro-construction and short response time. The urea electrode showed a linear response between 0.5 and 50 mM urea, while the glucose electrode showed a linear response between 0.1 and 50 M glucose. Mao and Yamamoto [366] demonstrated that an electropolymerized film of Meldola's blue (MB) act as electron shuttle between an immobilized horse peroxidase (HRP) and a GCE for sensing hydrogen peroxide (H_2O_2) produced by enzyme catalyzed reactions. They carried out the electrochemical polymerization of Meldola's blue by cyclic voltammetry (CV) in a phosphate buffer solution (pH 7.00) at −0.60 to +1.30 V (versus AgCl/Ag). They used H_2O_2 sensing system for the construction of on-line biosensors for glucose and choline. H_2O_2 reaction.

An interference and cross-talk free dual electrode amperometric biosensor integrated with a microdialysis sampling system has been described for simultaneous monitoring of glucose and lactate by FIA [367]. The biosensor is basically a conventional thin layer flow-through cell equipped with a Pt dual electrode, with each Pt disk modified by a composite bilayer consisting of an electrosynthesized overoxidized polypyrrole (PPYox) anti-interference membrane, covered by an enzyme entrapping gel consisting of glutaraldehyde co-crosslinked glucose oxidase or lactate oxidase with BSA. The advantages of covalent immobilization techniques are coupled with the excellent interference-rejection capabilities of PPYox. The potential of the described biosensor was demonstrated by the simultaneous determination of lactate and glucose in untreated tomato juice samples. The flow injection responses for glucose and lactate were found to be linear up to 100 mM and 20 mM, with typical sensitivities of 9.9 ± 0.1 and 7.2 ± 0.1 nA/mM, respectively. The biosensor has a self-life of at least 2 months. Urban et al. [368] produced an integrated thin-film glucose and lactate sensors using thin photo-patternable multi-enzyme membranes for the measurement of undiluted biological fluids in a clinical analyzer. The principle of the glucose and lactate sensors are based on the Pt electrode measurement of H_2O_2 produced by the enzymes GOD and LOD, respectively, entrapped in photo-patterned pHEMA hydrogel membranes. An electropolymerized semipermeable membrane was used to prevent electrochemical interferences and fouling of the Pt electrode. A second enzyme membrane layer containing the enzyme catalase was immobilized above the oxidase enzymes. To separate the two enzyme layers and introduce an additional diffusion barrier a third pHEMA membrane without enzyme was placed between the oxidase and catalase enzyme membranes. Optimization of the covalent attachment of enzymes such as glucose oxidase, lactate, tyrosinase (polyphenol oxidase), cholesterol oxidase and alcohol oxidase to copolymers of methyl and glycidyl methacrylates has been explored by Hall and coworkers [369]. Crosslinked polyacrylamide has been employed [370] as the matrix material for the immobilization of the enzyme (by entrapment) in the construction of enzymatic microsensors based on semiconductor technology and photo-curable membranes. A planar three-microelectrode cell and a pH-sensitive Ion Selective Field-Effect Transistor (ISFET) with a Si_3N_4 membrane has been used as transducers for glucose and urea measurements, respectively. This hydrogel permits membrane deposition and patterning by photolithographic techniques, which are compatible with semiconductor technology. Glutaraldehyde was introduced in the membrane for inter-enzyme cross-linking to develop long-term stability of the sensor. Both the membranes with the cross-linker and without it, have been compared, observing an increase of the long-term stability of around two-fold for glucose and urea sensors.

Sulphite ion sensor. Sulphite ions are commonly used as oxygen scavengers to prevent oxidation reactions from taking place in foods and beverages. Its various forms have been used extensively as antimicrobials and for prevention against the enzymatic browning reactions in foods. Ng et al. [371] covalently immobilized enzyme sulphite oxidase (SO_x) on a matrix of chitosan-poly(hydroxy-ethyl methacrylate) (chitosan-pHEMA), a natural/synthetic polymer hybrid obtained via UV curing. *p*-Benzoquinone, which served as an electron transfer mediator, was coupled to the polymer network for activation of the chitosan-pHEMA copolymer, after completion of the photo-induced polymerization reaction.

Brain glutamate sensor. Glutamate acts as one of the main excitation neurotransmitters, and is essential for the functioning of the nervous system. Berners et al. [372] studied on-line measurement of brain glutamate in brain microdialysate with an enzyme/polymer coated tubular electrode based on enzyme glutamate oxidase and the detection of H_2O_2 on a platinum electrode at 600 mV vs Ag/AgCl. the enzyme was immobilized in poly(*o*-phenylenediamine). The glutamate sensor shows a fast response time, with a lower detection limit of 0.3 μM and a sensitivity of 4 nA/μM. A novel capillary biosensor was developed by Cosford and Kuhr [373] for the analysis of glutamate, allowing biological transduction of glutamate signal during transport of analyte from the sampling site to the detector. Detection was accomplished using laser-induced fluorescence. They demonstrated the successful attachment of glutamate dehydrogenase to the inner wall of a small diameter fused silica capillary, while retaining enzymatic activity. The high sensitivity of this biosensor and the fast response time demonstrate its suitability for in vivo application to neurochemical purposes.

3.8.2. *Odor sensor*

Sensor arrays coupled with pattern recognition are useful in the discrimination of the aromas of certain foods and beverages. Several examples are available in the literature, demonstrating the success of using polymeric array of sensors for the detection of food and beverage odors [65,374–376]. Doleman and Lewis [377] made a quantitative comparison between the electronic nose and mammalian olfaction as a contribution towards the ambitious goal of designing an electronic analogue to the mammalian olfactory sense. The quantitative and statistical discrimination performance of an electronic nose made of conducting polymer composite is significantly higher than that of the monkey or human olfactory system studied for a particular pair of odorants used in the investigations done by Doleman and Lewis. Guadarrama et al. [378] described a sensor array based on thin films of conducting polymers with an objective to discriminate among different virgin olive oils (Table 2). They constructed an array using eight polymeric sensors deposited electrochemically using monomers such as 3-methylthiophene, pyrrole and aniline and doping agents. In a later publication, Guadarrama et al. [379] reported an electronic nose for the organoleptic characterization of olive oil. The instrument consists of an array of electrodeposited conducting polymer-based sensors able not only to distinguish among olive oils of different qualities (extra virgin, virgin, ordinary and lampante) but also among Spanish olive oils prepared from different varieties of olives and even different geographic origins.

For the identification of wines, Guadarrama and collaborators [380] tested a set of 12 polymeric sensors as an artificial olfactory system. The set of sensors were prepared by electrochemical deposition of various conducting polymers, such as polypyrrole, poly-3-methylthiophene and polyaniline. The array of 12 sensors, which were located in a stainless steel chamber, was exposed to the aromas of Spanish white and red wines from different regions, and the system was able to differentiate among the tested samples. In another development by Meijerink and his coworkers [381], polyaniline dispersion was used to prepare chemoresistors by spin-coating on a wafer, with an interdigited electrode array (IDA). The array was successfully used for the recognition of a series of diluted organic vapors over a period of 8 weeks. Polymer-carbon black composite films were used by Zee and Judy [382] in a miniaturized polymer-based chemical gas sensor array on silicon, prepared using micromachining technology. The polymers were poly(ethyl methacrylate), chlorinated polyisoprene, polyepichlorohydrin, styrene/butadiene ABA block copolymer, chlorinated polypropylene (isotactic) and styrene/ethylene/butylenes block copolymer. The composite films were made by dispersing carbon black in the respective solutions of the polymers in suitable solvents. The sensors, which swell reversibly, cause resistance change on exposure to a wide variety of gases. Devices were fabricated which can measure the resistance change using a 'well' design. These wells contain the polymer-carbon black-solvent liquid volume present during deposition and allow the sensor film to be placed reproducibly in a specific and well-constrained area. Since the composite film sensors are not specific to any one gas, an array of these sensors, each with a different sensing film, is used to identify gases and gas mixtures through a pattern response of the array. The sensors were able to uniquely detect methanol, methyl ethyl ketone and methylene chloride vapors, and demonstrated a linear response to concentration levels between 2000 and 10,000 ppm (Fig. 13).

A novel ChemFET sensor array was also developed by Covington and coworkers [383] utilizing carbon black composite polymers for the detection of organic vapors such as ethanol and toluene. Three vapor-sensitive carbon black polymer composites with poly(ethylene-*co*-vinyl acetate), poly(styrene-co-butadiene) and poly(9-vinyl carbazole) have been used as the gate materials in FET devices. A shift in the threshold voltage in response to toluene was observed with a linear dependence on concentration, and a voltage sensitivity of up to 2.8 μV/ppm. The authors put forward two mechanisms for the change in the threshold voltage: a partial charge transfer from the analyte to the polymer, with the polymer behaving as an acceptor or donor for electrons or a swelling effect of the polymer, that increases the distance between the conducting carbon spheres. The effects of humidity and temperature have also been examined, and the magnitude of response showed little dependence to humidity, but an exponential decrease with increasing temperature. The authors believe that this reduction in response may be primarily due to a modification in the bulk solubility of the polymer. Percival and his collaborators [384] showed that a polymer coated QCM sensor can be used to selectively detect monoterpene menthol in the liquid phase, with a sensitivity of 200 ppb. A highly specific noncovalently imprinted polymer (MIP) such as crosslinked poly(ethylene glycol dimethacrylate-*co*-methacrylic acid) was cast in situ on the surface of a gold-coated QCM electrode as a thin permeable film. The sensor was able to distinguish between the D-and

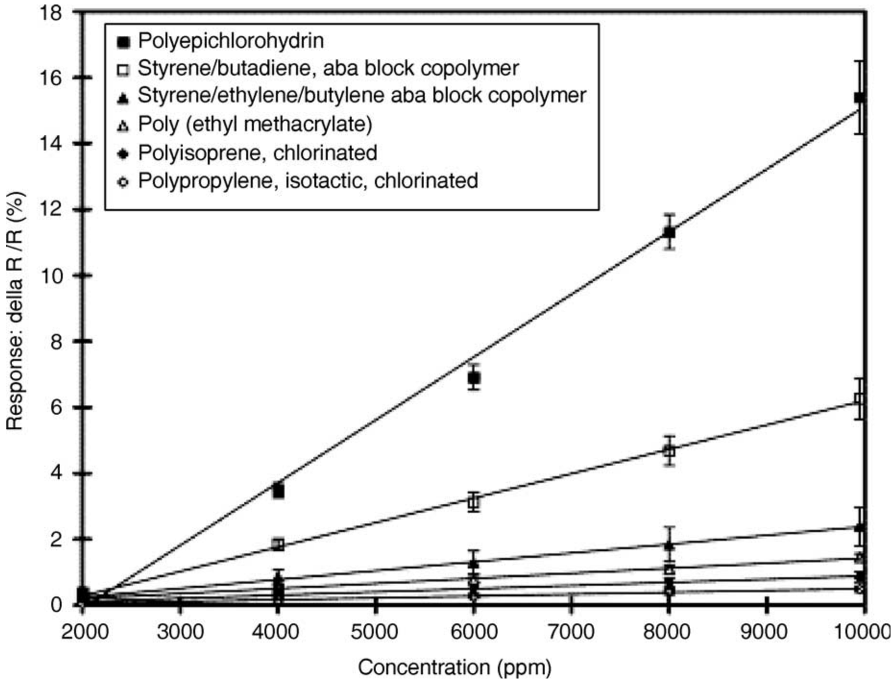


Fig. 13. Response of the six polymer sensors to increasing concentrations of methyl ethyl ketone gas [382]. Reproduced from Zee and Judy by permission of Elsevier Science Ltd, Oxford, UK.

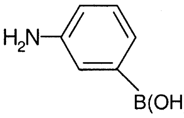
L-enantiomers of menthol owing to the enantioselectivity of the selected sites. The authors claimed this as the earliest report describing enantiometric resolution within an MIP utilizing a single monomer-functional moiety interaction. As envisaged by them, this technique could also be employed to determine the concentration of terpenes in the atmosphere. Pavlyukovich et al. [385] showed that divinyl-styrene polymer or polyisoprene could be used in piezoelectric chemical sensors for environmental control of trace organic toxicants, which react with the film of carbon chain polymer.

2-Methylisoborneol (MIB) and geosmin are off flavor compounds that cause odor in drinking water and fish. Ji et al. [386,387] used the molecular imprinting technique to create sensors with a predetermined selectivity for molecules in the gas phase. They developed piezoelectric odor sensors that exhibit selectivity for MIB by virtue of the incorporation of a MIP as the recognition element. Due to the intercalation of a layer of nylon between the QCM and the MIP, the sensitivity of these devices has been improved 20-fold, while maintaining selectivity. They first coated the piezoelectric quartz crystals with a layer of nylon from an acidic aqueous suspension by an LB technique, to provide increased sensitivity, and then applied a layer of a crosslinked polymer, such as poly(methacrylic acid-co-ethylene glycol dimethacrylate), imprinted with 2-methylisoborneol (MIB) to endow the device with selectivity. The response of the ‘imprinted’ sensor was significantly higher than the response of the ‘non-imprinted’ sensor at MIB concentrations above 10 ppb. Ema et al. [84] reported odor sensor system consisting of several QCM using different lipids or polymeric materials for the identification of 11 alcoholic drinks. They used epoxy resin, acetyl cellulose plus triolein, acetyl cellulose plus diethylene glycol etc., as membrane materials. Matsuno et al. [388] developed an odor sensor using an array of QCM coated with a mixture of lipids and PVC for identification of six odorants such as amyl acetate, ethanol, acetic acid, water, citral and nerol. Nanto et al. [389] used an epoxy-coated quartz resonator for sensing aromas from three wines (red, white and rose). Hierlemann et al. [390] detected volatile organic compounds such as hydrocarbons, chlorinated compounds and alcohols using an array of QCM coated with side-chain modified polysiloxanes. Persaud and Pelosi [391] used OCPs derived from aromatic or heteroaromatic compounds as gas and odor sensors for perfumes such as musk and ylang ylang. Baldacci et al. [392] used an odor sensor array composed of two novel conductive polymers, such as the polymers of 3,3′-dipentoxy-2,2′-bitiophene (3DPO2BT) and 3,3′-dipentoxy-2,2′:5′,2″-tertiophene (3,3′-DPTTT), for sensing wine flavor.

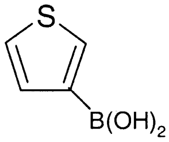
3.8.3. Immunosensor

Immunological sensors (or immunosensors) are based on the recognition involved in the coupling of an antigen with an antibody, with immunoagents immobilized in a polymer matrix such as PVC, polyacrylamide gel, etc. Either an immobilized antigen detects an antibody, or an immobilized antibody detects an antigen. Due to the interaction between an antibody and an antigen, a variation in electric charge, mass or optical properties, is detected directly with a variety of transducers [393]. Holt et al. [394] reported the fabrication of a capillary immunosensor in poly(methylmethacrylate) for environmental monitoring and remediation, which can provide on-site, real-time, semiquantitative or quantitative measurement of contaminant levels. The military sector is in need of such devices for monitoring environmental levels of 2,4,6-trinitrotoluene (TNT) and hexahydro-1, 3,5-trinitro-1,3,5-triazine (RDX) introduced into soils and water supplies and absorbed by plants, causing toxic to animal and human life. The conventional continuous flow displacement immunosensors (CFI) constructed with fused-silica microcapillaries are fragile. So most rugged, tough and low density polymers, such as PMMA, PS or PE, are used after surface activation through alkoxysilane sol-gel technology for attachment of the chemical or biochemical sensing elements. The key feature of the technique described by the authors is the use of sol-gel technology to deposit a glass-like (Si···OH) film on surfaces of the plastic capillary channels to facilitate antibody immobilization. These sensors exhibited sensitivity to low (μg/l) RDX concentrations, and peak-to-peak signal variations that were generally less than 10% for multiple injections at a single RDX concentration. The useful lifetime of the coupons in these experiments was greater than 10 h, even after multiple exposures to high (1000 μg/l) RDX levels (Table 2).

Piletsky et al. [395] presented a new technique for coating microtitre plates with MIP, specific for low-molecular weight analytes such as epinephrine, atrazine and proteins. They polymerized 3-aminophenylboronic acid (APBA) (**XXVII**), 3-thiopheneboronic acid (TBA) (**XXVIII**) and aniline in water by oxidative polymerization, and grafted the polymers onto the polystyrene surface of the microplates.



3-Aminophenylboronic acid (**XXVII**)



3-Thiopheneboronic acid (**XXVIII**)

They reported that this process results in the creation of synthetic materials with antibody-like binding properties. The high stability of the polymers and good reproducibility of the measurements made MIP coating an attractive alternative to conventional antibodies or receptors used in enzyme linked immunosorbent assay (ELISA). A new quartz crystal thickness-shear-mode (TSM) biomimetic sensor has been described using a MIP coating and its application for the determination of nicotine (NIC) in human serum and urine [396]. The MIP was synthesized using NIC as the template molecule and methacrylic acid (MAA) as the functional monomer. The sensor showed high selectivity and a sensitive response to NIC in aqueous system.

Ying-Sing and collaborators [397] deposited a polymer sorbent at the surface of a gold-plated piezoelectric crystal by anodic oxidation of *m*-aminophenol for antibody coupling after activation by divinylsulphone. Also, a novel film was obtained with increased capacity for immobilizing antibodies, using phloroglucinol to modify poly-*m*-aminophenol via divinylsulphone. In comparison to the dip-coating methods using polyethylenimine and (γ-aminopropyl) trimethoxysilane, this new technique gave more reproducible results for the immobilization of antibody from sample to sample due to the improved homogeneity and reproducibility of the coating. The authors developed a piezoelectric immunosensor with this modified method for the detection of *Salmonella enteritidis*, with a detection limit of 1×10^5 cells ml^{-1} and an assay time of 25 min.

Kim and coworkers [398] reported a conductimetric membrane strip immunosensor with polyaniline-bound gold colloids as signal generator. They introduced polyaniline as a conductivity-modulating agent on the gold surface after immobilizing an antibody specific to human albumin as a model analyte. This novel signal generator amplified the conductimetric signal 4.7 times compared with the plain gold, and the signal was also a maximum of 2.3-fold higher than that for the photometric system under the same analytical conditions. Sadik and Wallace [399] demonstrated pulsed potential waveforms to control antibody–antigen interactions on conducting polymer surfaces. This approach enabled detection of proteins at low levels, and the use of antibody containing electrodes for multiple analyses.

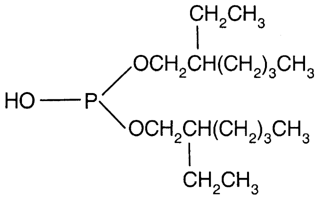
3.8.4. DNA biosensor

There has been considerable interest in the development of DNA sensors for the analysis of unknown or mutant genes, the diagnosis of infectious agents in various environments and the detection of drugs, pollutants, etc. which interact with the structure of the double stranded DNA. Single strand DNA probes are immobilized by techniques of adsorption, direct covalent binding, entrapment in a polymer matrix, etc. Dupont-Filliard et al. [400] described the design of a new versatile and reversible DNA sensor in which they immobilized single strand DNA to provide advantages of high sensitivity, versatility and ease of use. The novelty in this development lies in the reversibility of the coupling process, which enables the renewing of the sensor capability by the change of the immobilized probe. The system developed by Dupont-Filliard et al. [400] is based on biotin grafting-units, covalently linked to a polypyrrole matrix, able to anchor large biomolecules due to biotin/avidin affinity. There is a scope for regenerating the grafting-units after the 'denaturation' of the biotin/avidin link, thus allowing the matrix for the immobilization of a new assembly (new biomolecule) with the possibility to generate a new sensor. New biocomposite materials, based on the incorporation of nucleic acid dopants within an electronically conducting polypyrrole network, are described by Wang and Jiang [401]. The growth patterns and ion-exchange properties of these electropolymerized polypyrrole-oligonucleotide (PPy/ODN) films have been characterized using an in situ electrochemical quartz crystal microbalance (EQCM) [401]. Various parameters, such as the ODN length or concentration, and the potential range, have a marked effect on the properties of the new conducting biomaterials. Very favorable growth patterns are observed for biocomposites containing 20–30-mer long ODNs, while films based on shorter ODNs or chromosomal DNA display inferior properties. The composite films can be prepared using low (approximately 1×10^{-5} M) concentrations of the nucleic acid dopant, in the absence of additional electrolyte. Such biomaterials open up new opportunities, including genoelectronic devices, composite materials, bioactive interfaces, genetic analysis, or probing of DNA charge transfer.

A conjugated polymer is regarded as a three-dimensional network of intrinsically conducting macromolecular wires, able to transport electrical signals. Further functionalization of such molecules with prosthetic groups show recognition properties, and such polymer architectures mimic the nervous system in living systems. With this idea, Garn et al. [402] developed new electrochemical sensors based on electroactive polypyrrole functionalized with ODN. They analyzed the experimental conditions for building such a modified electrode, showing a high electroactivity in aqueous medium. The functionalization of polypyrrole involved a precursor polypyrrole bearing an easy leaving ester group, on which an amino-labeled ODN could be directly substituted. The electrochemical response of this polypyrrole electrode functionalized with an ODN probe was analyzed in various aqueous media, containing either complementary or noncomplementary ODN targets. The results showed that the functionalized polypyrroles act as macromolecular wires, able to transduce biological information into molecular signals. Livache et al. [403] described an ODN array constructed on a silicon device bearing a matrix of addressable 50-micron microelectrodes. Each electrode was covered by a conducting polymer (polypyrrole) grafted with ODN. The DNA chip was prepared by successive electrochemically addressed copolymerizations of 5′ pyrrole-labeled ODN and pyrrole. This technology found successful application in the genotyping of hepatitis C virus in blood samples, with results that showed good sensitivity and a high dimensional resolution.

3.8.5. Taste sensor

Lipid membranes used in combination within electrodes have been utilized to mimic some of the functionality of mammalian taste bud cells [404–411]. It is generally assumed that the primary process of chemoreception in the mammalian olfactory system takes place at the cell membrane of sensory neurons [412]. The mammalian sense of taste occurs as a result of complex chemical analyses that are completed in parallel at a series of chemically active sites called taste buds. These taste buds are located in depressions in the tongue, where the molecular and ionic analytes become restricted to allow time for their identification [413, 414]. There are five primary tastes: sweet (carbohydrate based), sour (acidity), salty (ionic), umami or savory (amino acids) and bitter (quinine and other alkaloids). A conceptual and experimental development of a chip-based microsphere array platform suitable for the digital analysis of taste of complex fluids was made by Lavigne et al. [415]. Those electronic taste chips mimic many of the features exhibited by the human sense of taste. That is, multianalyte mixtures could be analyzed and intelligent decisions related to the chemical composition of the solution-phase samples could be made rapidly and accurately [416]. Sangodkar et al. [280] described the fabrication of polyaniline-based microsensor and microsensor arrays for the estimation of glucose, urea and triglycerides. Polymer deposition and enzyme immobilization were done electrochemically. The enzyme was directly immobilized to the chosen microelectrodes by controlling the electrochemical potential, avoiding any contact of the enzyme solution to other microelectrodes. This enabled immobilization of a different enzyme on each of three closely spaced microelectrodes, resulting in a sensor array for the analysis of a sample containing a mixture of glucose, urea and triolein in a single measurement using a few microlitres of the sample. This strategy was extended to other enzyme-substrate systems intended to represent an ‘electronic tongue’. A multichannel taste sensor containing lipid membranes immobilized with PVC was developed [405,417–419]. In this taste sensor n-decyl alcohol, oleic acid, dioctyl phosphate (**XXIX**), trioctyl methyl ammonium chloride and oleyl amine lipids immobilized in PVC were used for the sensing of tastes such as sour, salty, bitter, sweet and umami.



Dioctyl phosphate (bis(2-ethylhexyl) hydrogen phosphate) (**XXIX**)

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3.8.6. Touch sensor

Although details are lacking, it is worth noting that Rinde et al. [420] developed a touch sensor system, including a substrate capable of propagating SAWs; and an array of reflective elements formed on the said substrate. The reflective array consists of a series of reflective elements, where each reflective element reflecting a portion of an incident SAW. The reflective array is formed of an organic matrix which is stable under change in RH between 0 and 60% at temperatures between 0 and 50 °C. The organic matrix is preferably a thermoset resin which is chemically bonded to the substrate.

3.8.7. Other applications

Dopamine quantification. The use of a new polymer-modified electrode has been described [421] for the quantification of highly selective dopamine in the presence of a large excess of ascorbic acid and 3,4-dihydroxyphenyl acetic acid (dopac). The electrochemical detection was performed at a GCE, modified with a melanin-type polymer obtained by polymerization of 3.0×10^{-3} M L-β-3,4-dihydroxyphenylalanine (L-dopa) in 0.050 M phosphate buffer solution (pH 7.40) by applying 1.00 V for 60 min. The polymer film exhibits attractive permselectivity, excluding anionic species such as potassium ferricyanide, ascorbic acid, dopac and uric acid. Cationic species such as epinephrine, norepinephrine and dopamine and neutral ones such as catechol and hydrogen peroxide can be oxidized at the polymer-modified electrode. The use of ascorbic acid in the measurement solution allows the amplification of dopamine oxidation signal due to the reduction of the electrochemically generated dopaminequinone. Electrochemical determination of 3-hydroxytyramine (dopamine) is associated with the problem of interference of oxidizable ascorbic acid and 3,4-dihydroxyphenyl acetic acid. The interference was overcome by the use of permselective films of Nafion and other polymeric membranes [422–427].

Cholinesterase inhibitor. Gogol et al. [428] have done an investigation with screen-printed electrodes coated with Nafion layer for a cholinesterase biosensor design. They immobilized butyrylcholinesterase (ChE) from horse serum onto the Nafion layer by cross-linking with glutaraldehyde vapors. The biosensors thus obtained showed better long-term stability and lower working potential in comparison to those obtained with no Nafion coating. The sensitivity of the biosensor toward organophosphate pesticides is not affected by the Nafion coating. The detection limits were found to be 3.5×10^{-7} M for trichlorfon and 1.5×10^{-7} M for coumaphos.

Ascorbic acid. O'Connell et al. [429] developed a sensor that selectively catalyses the oxidation of L-ascorbic acid at low potentials (+100 mV). Polyaniline was deposited on both glassy carbon and screen-printed electrodes, and the analytical behavior of both sensor types was investigated. The effects of many common electrochemical interferents were minimized at low applied potential. The common interferents found in juices and pharmaceutical preparations were tested, including 4-acetamidophenol (paracetamol), uric acid and citric acid. Florou et al. [430] developed a sensor to respond to ascorbic acid by incorporating 2,6-dichlorophenolindophenol (DCIP) in a cellulose acetate film and Groom and Luong [431] electrodeposited a mixture of DCIP and diamino benzene or resorcinol onto the surface of glassy carbon and platinum electrodes to form a permselective film. This permselective electrodeposited film showed improved selectivity for ascorbic acid.

Atropine sulphate. Peng and coworkers [432] described the development of a new atropine sulfate bulk acoustic wave sensor based on a molecularly imprinted electro synthesized copolymer of aniline with *o*-phenylenediamine. The sensor exhibited good selectivity and sensitivity to the template. They successfully applied the sensor to the determination of atropine sulfate in both serum and urine medium.

Epinephrin. Another MIP poly(ethyleneglycol dimethacrylate-co-methacrylic acid) coated bulk acoustic wave (BAW) bio-mimic sensor was developed by Liang et al. [433] for the direct determination of epinephrine. This sensor exhibited a highly selective and sensitive response to epinephrine. A linear relationship between 5.0×10^{-8} and 2.0×10^{-5} M epinephrine was revealed, with a detection limit and recovery of 2.0×10^{-8} M and 93.2–108.7%, respectively.

Hypoxanthine. An amperometric biosensor was developed by Mao and Yamamoto for use in a thin-layer radial flow cell in an on-line continuous measurement of hypoxanthine, based on osmium-polyvinylpyridine gel polymer (Os-gel-horseradish peroxide (HRP)) and xanthine oxidase (XOD) bienzyme-modified GCE [434]. Os-gel-HRP was first coated by casting on GCE with a surface coverage of 7.1 μl/cm^2 to sense hydrogen peroxide produced from XOD catalytic enzyme reaction based on HRP catalytic reduction mediated by osmium, followed by crosslinking of BSA/XOD to the Os-gel-HRP-coated GCEs with glutaraldehyde vapor for the measurement of hypoxanthine at 0.0 mV (versus Ag/AgCl). The resulting HRP and XOD bienzyme-based sensors (Os-gel-HRP/XOD/GCEs) were tested with CV, on-line amperometry in a flow system and FIA. They reported minimal interference from higher than physiological levels of dopamine (DA), norepinephrine (NE), serotonin, their principal metabolites, and uric acid.

Reaction monitoring. An interesting piezoelectric method has been reported by Bunde et al. [435] to monitor formaldehyde induced crosslink formation between poly-lysine and poly-deoxyguanosine. Such an experimental technique is highly beneficial for real-time monitoring of DNA-protein crosslink formation, which is important in the elucidation of the underlying chemical mechanisms associated with the reaction process.

Biomimetic. Kugimiya and Takeuchi [436] developed a surface plasmon resonance (SPR) sensor using a MIP-coated sensor chip for the detection of sialic acid. The thin polymer coating was prepared by co-polymerizing *N*, *N*, *N*-trimethylaminoethyl methacrylate, 2-hydroxyethyl methacrylate and ethyleneglycol dimethacrylate in the presence of *p*-vinylbenzeneboronic acid ester with sialic acid. The sensor showed a selective response to ganglioside with sialic acid located at the non-reducing end, and gave a linear relationship from 0.1 to 1.0 mg of ganglioside.

4. Trends in sensor research

A consolidated picture of the development of sensors and their applications is presented in Table 2, indicating the wide range of sensor research. Some insight into recent trends in sensor research is obtained from the number of papers being published per year in various analytical journals, which are useful indicators of systems that are directly applied to solving real problems. Fig. 14 shows the number of hits for various subgroups of sensors, including ISEs, optical sensors, amperometric, biosensor, acoustic, and solid-state sensors, as a percentage of the total number of sensor papers published each year [461]. A survey of the sensor market [462] identified medical applications as a major driving force for the development of the emerging sensor technologies: fiber-optic sensors, smart sensors, silicon micromachined sensors, and thin film devices.

The state-of-the-art in sensor research indicates that over the years multiple sensors have been developed for analytes, either as sensor arrays designed for multiple analytes or for specific analytes in specific sensing environments. But accurate, reliable, selective, sensitive, rapid, miniaturized, reagentless and stable devices have only been achieved in a few cases. Consequently, an assessment of the successes and failures in these developments can provide a useful guide for further research. In that context, the following trends are notable for shaping the future of sensor research:

- Improvement in the methods of immobilization of receptor components through chemical modifications, fine tuning molecular recognition for selectivity and the use of new materials for both transducers and chemical transduction strategies.
- Innovations for multianalyte sensors, sensing arrays and chemometric approaches for non-selective or partially selective sensing, e.g. an implantable multianalyte sensor array for sensing pH and K^+ in a beating heart [463].
- Miniaturization and integration of components for combined separation and detection. For example, an amperometric microsensor array has been developed with 1024 individually addressable elements for two dimensional concentration mapping [464].
- The use of microtechniques and the development of theories on physicochemical phenomena in

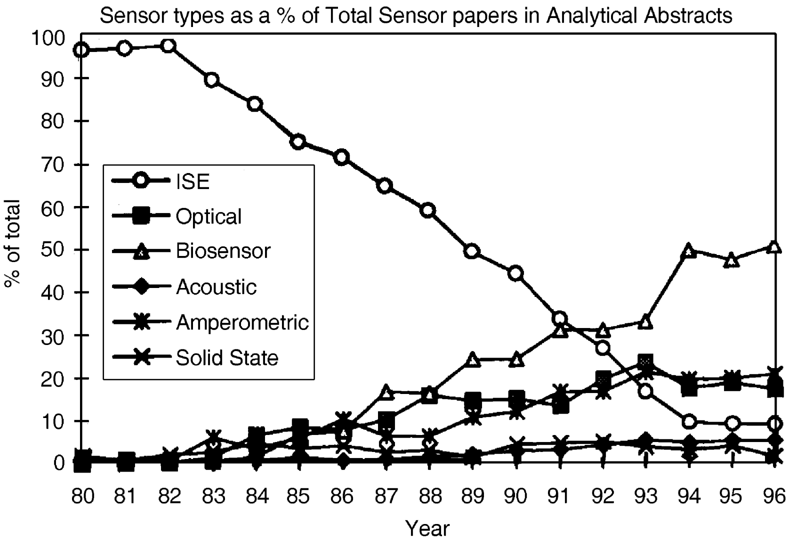

Fig. 14. Trends in the absolute numbers of papers for each sensor type abstracted from *Analytical Abstracts* over the period 1980 to 1994 [461]. Reproduced from Diamond by permission of John Wiley and Sons, Inc., NJ, USA.

dimensionally confined spaces in biosensor research, for adapting miniaturization of sensor devices involving small sample volumes.
- Studies of biochemical phenomena in non-aqueous media, to open more biosensing opportunities [465].

A significant progress in chemical modification of biosensor devices is apparent in four major areas: the molecular design of chemically selective and biospecific agents, improved immobilizations for molecular recognition, studying the actual interfaces between sample and energy transducer and designing the energy transducers. Although arrays for multicomponent biochemical analysis have been reported, the development of arrays for all energy transduction modes should accelerate with miniaturization of devices, improvements in immobilization methods and the use of chemometrics.

5. Challenges in sensor research

Following the discussion in Section 4, several challenges to the future sensor devices may be considered:

1. The search and selection of proper materials, as well as improved and novel recognition mechanisms necessary for instant identification of a target component, and the mechanism to create the signal that will be obtained from the sensor.
2. The development of new materials for use as matrices to effectively immobilize receptor molecules to obtain stable and reproducible sensor function, including new polymers.
3. The development of solid-state versions of pH and ion-selective sensors.
4. Novel sensor substrates and internal electrodes for new planar fabrication designs to facilitate the use of advanced fabrication for automated sensor manufacturing, with the help of printing or semiconductor technologies for miniaturized sensor arrays, and improvements in signal processing technologies and instrumentation [466].

6. Conclusion

The majority of sensor devices utilize many polymers with definite roles, either in the sensing mechanism or through immobilizing the species responsible for sensing of the analyte component. This has become possible only because polymers may be tailored for particular properties, are easily processed, and may be selected to be inert in the environment containing the analyte. While some polymers are intrinsically responsible for a sensor function, other polymers are made to augment the sensing operation through modification of the polymer by functionalization. Polymeric thin film deposition technology and the design of more active and sensor-specific polymers will lead to successful miniature, multiple sensor arrays. The collaboration of polymer scientists and technologists in sensor research will accelerate the availability of durable and cheap artificial sensor devices for human consumption.

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