Electrochemical sensor based on biomimetic recognition utilizing molecularly imprinted polymer receptor

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1. Introduction

Biological recognition elements such as antibodies, enzymes and aptamers have been utilized as specific receptors to a target molecule in a wide variety of assays and sensors. However, many difficulties for their practical use exist as they lack stability and reusability. Moreover, it is not easy to obtain and prepare sufficient natural bioreceptors. Since practically there are many extraneous inhibitors against biological receptors, scientists have attempted to develop specific recognition elements alternative to bioreceptors.

One approach was the synthesis of hosts which possess a structure capable of binding complementary guests. The synthesis of specific recognition sites has been accomplished by coordinating functional monomers around the target molecule, and then cross-linking to position functional monomers around the target molecule (Fig. 1). Such receptors are

Fig. 1. Synthetic procedure of molecularly imprinted polymer

synthesized from non-biomolecules and are termed “molecularly imprinted polymers (MIPs)”.

MIPs have been synthesized to suit a large variety of templates and intensively investigated in the last decade. The application of MIPs has been demonstrated by mimicking antibody/receptor binding sites in immunoassays, chemical sensors and biosensors, while MIPs were utilized as tailor-made separation material in solid-phase extraction and screening drugs (Mosbach, 1994). Such attractive techniques using MIPs have provided a promising alternative to biological recognition elements. So far, more than 1,000 papers on
the use of MIPs in a wide range of application areas have recently been reported. Therefore, MIPs have already been used as alternatives to biological elements. Among the application of MIPs, solid-phase extraction (SPE) has been utilized to clean-up environmental and biological samples and to exchange sorbents in liquid chromatography (Matsui et al., 1995). The application of SPE reduced the drawbacks of chromatography such as peak broadening and tailing. In addition, the application of MIPs to chromatography has been continually studied as a chiral stationary phase for enantiomer separations or to change the sorbent of capillary electrochromatography. These applications were intensively investigated and reported since molecular imprinting techniques began to attract interest among many researchers in the 1990s. In the late 1990s, due to these high affinities and selectivities, MIPs also began to be considered as alternatives to selective receptors in biosensors. The substitution of MIPs for biological receptors is frequently reported. Although biological receptors are extremely selective as a molecular recognition element, they are labile and expensive. On the other hand, molecular imprinting-based biomimetic recognition has physical/chemical stability, tailor-made preparation and is cheaper, and also includes binding affinity comparable to a biological receptor. So, it has been expected to be a breakthrough in the limitations of biosensor technology and has thus attracted attention through studies on how to utilize MIP materials as the sensor elements more effectively. Sensors based on electrochemical determination are potentially sensitive and inexpensive, and electrodes are easily miniaturized in the development of a sensor system. So, electrochemical sensors have been useful devices in the monitoring of a wide range of analytes. Electrochemical sensors play a crucial role in medical and clinical analysis, and in environmental and industrial monitoring. The electrochemical modes of measurements are amperometry, voltammetry, potentiometry and conductometry. Generally speaking, electrochemical analysis is sensitive and bears a reasonable cost. Since these various modes lead to several applications of sensor fabrication, electrochemical sensors are becoming important transducers in the development of sensors utilizing MIP receptors. MIP receptors are considered as promising and inexpensive alternatives to bioreceptors. Biomimetic sensors composed of electrochemical transducers and MIPs are significantly attractive sensing devices substituting biosensors. This chapter reviews recent research on biomimetic sensors utilizing MIP receptors and electrochemical transducers. The article begins by outlining general MIP preparation and various methods of applying MIPs to recognition elements in biomimetic sensors. The article further describes recently-reported biomimetic sensors utilizing MIP materials. It focuses on electrochemical sensors that show promising practical use by utilizing MIPs, which are selective to toxic compounds such as triazine herbicides and bisphenol A, which have attracted international attention as endocrine disrupting chemicals. After the overview of biomimetic sensors, the article concludes by outlining the current state-of-the-art and issues to overcome.

2. General MIP preparation

2.1 Concept of molecular Imprinting

Great efforts to develop a specific recognition system for target molecules have been made. One approach has been the synthesis of host molecules possessing a three-dimensional structure to bind complementary guests. The synthesis of specific recognition sites has been
accomplished to coordinate functional monomers around a target molecule, and then to provide cross-linkers for positioning functional monomers around the target molecule. It is said that the origin of molecular imprinting began from a hint by Pauling’s notion regarding the working of an immune system, to assemble an antibody around the foreign intruder as a template (Pauling, 1940). Then, on the basis of this hypothesis, creation of the shape of selective sites in a silica gel was attempted using organic dyes by Dickey et al., and these silicates exhibited slight affinity (Shea, 1994). The essential force of interaction to imprint target molecules has been either covalent or noncovalent, including electrostatic, hydrogen bonding and hydrophobic interactions. An approach based on covalent bonds has been mainly demonstrated by the Shea and Wulff groups (Shea, 1994; Wulff, 1995). On the other hand, an approach based on noncovalent bonds has been mainly demonstrated by Mosbach (Mosbach, 1994).

2.2 MIP Preparation

The recognition mechanism in a polymer network is particularly important for its great potential of molecular imprinting in the separation and purification of various biomolecules. Feasibility studies and attempts to optimize MIP-based systems have been performed. In order to investigate interactions between substrate and the polymer stationary phase, a chromatographic and \(^1\)H NMR study involving titration of template molecule (phenylalanine anilide) with the functional monomer methacrylic acid was performed (Sellergren et al., 1998). The results were consistent with the existence of multimolecular complexes formed by electrostatic and hydrogen-bonding interactions and allowed an estimation of their formation constants and distribution. By UV-Vis adsorption spectral studies, Infrared spectroscopy (IR) and X-ray diffraction (XRD), Daniel et al. reported the characterization of palladium ion imprinted polymer. The formation of a ternary complex of ion template with functional monomer and cross-linker was confirmed by UV-Vis absorption spectra (Daniel et al., 2003). The results of XRD showed the complete removal of palladium ion from the material and the IR spectra indicated the same polymer backbone in both unleached and leached palladium ion imprinted polymer. Solid state \(^{13}\)C-NMR and Fourier transform infrared spectroscopy (FT-IR) also have been used to investigate bonds of small molecules such as 1,3-diacetylbenzene to functionalized polymers (Shea & Sasaki, 1989). Both techniques gave a consistent picture of the manner of binding.

As the recognition mechanism of MIP was getting clearer, the application of MIP to the HPLC stationary phase began to be studied. Mosbach and co-workers extended the imprinting technique by using noncovalent bonds and optimized chiral stationary phases for degradation of amino acid derivatives in liquid chromatography (Andersson et al., 1990). The initial binding of the substrate to polymers occurred via ionic bonding between the amine group of the substrate and carboxylic residues of the polymer. The second step in the recognition process was the formation of other interactions, such as hydrogen bonds and hydrophobic forces, and it was observed that these secondary interactions gave rise to enantiomeric separations. This result suggested that it was possible to use these polymers as a chiral stationary phase in column chromatography.
Molecularly imprinting can be made against a great number of organic molecules, such as drugs, metabolites, hormones and toxins. Among them, the MIP for herbicide atrazine was reported by many researchers (a,b Matsui et al., 1995; Sieman et al., 1996; Muldoon & Stinker, 1995) (Fig. 2). Preparation of atrazine-imprinted polymers has been carried out mainly according to a protocol well-established by Mosbach, using methacrylic acid as functional monomer, ethylene glycol dimethacrylate as a cross linking agent, and chloroform or dichloromethane as solvent. They were studied using various analytical techniques including HPLC, a radio assay using radioactively-labeled ligand and investigations of template/functional monomer complexation were performed by an NMR spectra study. Atrazine-MIP was successful in several applications, while the MIP for simazine (Sim-MIP), similar in structure to atrazine, was hardly studied despite its stronger toxicity than atrazine. Therefore, we studied the Sim-MIP preparation according to atrazine-MIP and reported a simazine sensor based on biomimetic recognition utilizing the Sim-MIP receptor (a Fuchiwaki et al., 2007).

Although MIPs appear to be inexpensive, robust, and reusable materials, the preparation procedure has to be studied against each template, which are actually analytes. The factor for optimum MIP preparation is not yet understood, and continuous investigations are required.
3. Application of MIP to sensor

In the beginning of MIP research, the main purpose was the application to a stationary phase in liquid chromatography. So, over the last decade the use of MIPs as a biomimetic sensing materials has been investigated. Many studies on sensor fabrication using MIP materials have been reported since the 1990s, and alternatives to antibodies in immunosensors were most frequently reported (Lavignac et al., 2004). The advantage of MIP-based biomimetic sensors is the binding affinity of MIPs comparable to biological recognition elements as well as their robustness and stability against a wider range of environments. MIPs were easily synthesized in a tailor-made manner for template-analytes. MIPs have been developed against various templates such as herbicides, pharmaceuticals, proteins and vitamins.

In order to apply MIPs as biomimetic sensing materials, specific binding of analytes to the binding cavity in the MIP network to the sensor signal needs to be translated. This translating technique plays a key role in the application of MIPs to biomimetic materials. There tend to be two types of methods, labeling or labeling-free.

The binding sites in MIPs fit to unlabelled templates and labeled templates are not suitable for the binding site. Also, the preparation of selective MIP to labeled template is not easy. Therefore, in the labeling method, the sensor system is normally performed by competitive binding of an analyte with labeled analyte, and the labeled unbound analyte is inversely proportional to the amount of analyte. Radiolabeled and fluorescence-labeled analytes are frequently used for the MIP sorbent assay, whose results were compared with those in the enzyme-linked immunoassay (Vlatakis et al., 1993) (Figure 3). On the other hand, MIP-based sensing techniques that do not require labeling agents have been investigated and several interesting studies on the label-free method have been reported.

![Fig. 3. Correlation between a molecularly imprinted polymer-based competitive binding assay and an enzyme immunoassay for 32 samples of serum theophylline (Vlatakis et al., 1993). The correlation coefficient was calculated to be 0.98.](www.intechopen.com)
binding-site in the MIP matrix directly detect the electrochemical activity on the electrode surface if the analyte has electrochemical activity. This concept could indicate the development of sensitive and precise MIP membrane-based sensors. Also, mass sensitive sensors such as the quartz crystal microbalance (QCM) and the surface acoustic wave device (SAW) have been used to study the development of an MIP membrane-based sensor (Vila et al., 2008). Determination was based on the mass change on the conducting surface electrode. So, many applications are expected because mass is a universal property of matter.

The latter involves fluorescence and conductometric detection. For sialic acid detection, o-phthalaldehyde was used as a reagent for fluorescence measurement of the MIP matrix containing amine residues (Piletsky et al., 1996). When sialic acid bound to the binding site, the permeability of o-phthalaldehyde increased due to the swelling change by binding of the template. Fluorescence intensity increased and was proportional to the amount of bound sialic acid. Turkewitsch et al. reported a fluorescent molecularly imprinted polymer for 3', 5'-cyclic monophosphate (cAMP) that contained a fluorescent dye, trans-4-[p-(N,N-dimethylamino)styryl]-N-vinylbenzylpyridinium chloride (Turkewitsch et al., 1998). The molecularly imprinted fluorescent polymer quenched fluorescence in the presence of aqueous cAMP, whereas almost no effect was observed in the presence of structurally similar molecules.

A conductometric sensor was fabricated based on the MIP membrane-modified electrode (Sergeyeva et al., 1999; Suedee et al., 2006). In the sensing principle, the conductivity decreased with an increase of bound analyte. When a different amount of analytes was bound to MIP, the MIP membrane showed differences in the degree of shrinking. This phenomenon causes a change in electro-conductivity due to changes in ion transfer. Molecular imprinting is increasingly adopted as a biomimetic artificial receptor. Currently, many researchers have studied the improvement of MIP-based sensors by a combination of various sensing techniques for practical use.

4. Electrochemical sensor utilizing MIP

Electrochemical sensor fabrication includes various types of systems such as conductometric, voltammetric, potentiometric, capacitance, and have provided important tools to detect various analytes in environmental, clinical and biological fields due to their high sensitivity, cheapness and miniaturization.

4.1 MIP membrane-based electrochemical sensor

Membrane-based electrochemical sensor systems have become increasingly attractive for excellent affinity separation. Applications combining MIPs and membrane technology have been proposed the stable permselectivity and affinity for selective binding to analytes from a mixture containing structurally similar compounds.

4.1.1 Molecular imprinting-based conducting polymers

The application of electrosynthesis to MIP technologies is also an attractive technique. This method was first reported as a procedure for the preparation of MIPs to be utilized as a nitrate-selective potentiometric sensor by Hutchins and Bachas in 1995. By polymerizing
pyrrole in the presence of NaNO₃, in the film produced there were pores that were complementary to the size of the nitrate ion. Both the size of the pore and the charge distribution within the polymerized film formed a host cavity for nitrate, which provides additional selectivity over conventional nitrate-selective electrodes. This molecular imprinting-based electrode demonstrated improved selectivity coefficients for perchlorate and iodide as much as 4 orders of magnitude. Therefore, molecular imprinting polymers prepared with conductive polymers (MICPs) strongly adhere to the electrode of any shape and size, and the thickness of the membrane can be easily controlled. In addition, the conductive polymer is easily obtained by chemical or electrochemical techniques. However, the physical and chemical properties of the polymers are influenced by polymerization conditions such as solvent, supporting electrolyte, electrode material and electropolymerization potential. MICPs are obtained through polymerization in the presence of a template molecule. After removing the template, specific binding cavities are created in the polymer networks. And the chemical functionality and three-dimensional shape in the binding cavity are created in the MIPs. Although electrochemical sensors combining MICP with the conducting polymers are attractive concepts for the sensitive and real-time detection of a small molecule, it is not easy to form a specific binding site corresponding to template-analyte because the choices of functional monomers, crosslinking monomers, solvent and polymerization conditions are limited. Although such an electrochemical sensing system gave the possibility of direct communication between the polymer and the electrode surface in a simple way, there was also a problem. Conductive polymers are so electrochemically sensitive to ionic adsorption that nonspecific adsorption is not negligible. Because of these factors, there are few reports for MICP, although an electrochemical sensor, which enables the recognition of the herbicide atrazine, was recently described by Pardieu et al. (Pardieu et al., 2009) (Fig. 4). Poly-3,4-ethylenedioxythiophene-co-thiophene-acetic acid as the MICP was electrochemically synthesized onto a platinum electrode in two steps: (I) polymerization of comonomers in the presence of atrazine, already associated to the acetic acid substitute through hydrogen bonding, and (ii) removal of atrazine from the resulting polymer, which leaves the acetic acid substitutes open for association with atrazine. This electrochemical sensor showed selectivity towards the triazine moiety, with a wide range of detection (10⁻⁹ mol L⁻¹ to 1.5×10⁻² mol L⁻¹ in atrazine) and low detection limit (10⁻⁷ mol L⁻¹). Therefore, this report is certainly interesting in which MICP showed selectivity to the triazine moiety; however, it was difficult to distinguish between structures similar to atrazine.
4.1.2 Conductometric sensors

A conductometric sensor can be easily fabricated and its principle is very simple. Although a conductometric transducer is normally difficult to distinguish among different compounds, selectivity and sensitivity are considerably improved by introducing a recognition element on the electrode surface. Sergeyeva et al. fabricated a conductometric sensor modified with an MIP membrane for template-atrazine, and reported the characterization of changes in the MIP membrane when the solvent, pH and functional monomer in polymerization were changed (Sergeyeva et al., 1999). The membrane containing 85% tri(ethylene glycol) dimethacrylate and 15% Oligourethane acrylate (OUA) demonstrate both a rapid and selective sensor response. The detection limit for atrazine measured in 25 mM sodium phosphate buffer, pH 7.5, containing 35 mM NaCl was found to be 5 nM. The analysis can be performed within 6-15 min. The prepared MIP membrane was shown to be a very stable and flexible membrane. Suedee et al. (2006) reported an on-line conductometric monitoring system of haloacetic acids using an MIP membrane, which was synthesized by the interaction between trichloroacetic acid (TCAA) template and a functional monomer, 4-vinylpyridine (VPD), together with a cross-linking reagent, ethylene glycol dimethacrylate (EDMA). The change in conductivity in the presence of the target molecule into the imprint cavity was investigated and responded well to TCAA in a continuous flow system with relatively good linearity. The sensitivity (range 0.5-5 µg l⁻¹) and selectivity achieved with standard TCAA and five other haloacetic acids (HAAs) (dichloro-, monochloro-, tribromo-, dibromo-, and monobromoacetic acid) in water was good enough. Minimum sample volume required was 2.5 ml and the assay time was 2 min.
4.1.3 Potentiometric sensors

A potentiometric sensor is a versatile, simple, rapid and inexpensive method for target determination. Potentiometric techniques are used for the electrochemical transduction of ion selective sensors utilizing MIP, which serves as a selective molecular recognition membrane or layer in the sensor system. There are relatively few reports dealing with potentiometric molecular sensors based on MIPs (Heng et al., 2000; Zhou et al., 2004; Kitade et al., 2004). Sadeghi et al. (2007) fabricated a potentiometric sensor based on MIPs for determination of levamisole hydrochloride. The preparation of MIPs was accomplished by using methacrylic acid as a functional monomer, p-divinylbenzene as the crosslinker and AIBN as initiator and the sensing membrane was prepared by mixing polyvinyl chloride powder and MIP particles with a plasticizer. Levamisole hydrochloride was measured in the activity range from 2.5 μmol L\(^{-1}\) to 100 mmol L\(^{-1}\) and the limit of detection was 1.0 μmol L\(^{-1}\). The response time was short (<15 s) and the membrane could be used for 4 months without any significant divergence in response. Liang et al. (2009) described a potentiometric sensor based on an MIP membrane ion-selective electrode for determination of melamine in milk, which was prepared using methacrylic acid and EDMA. The MIP membrane electrode showed a near-Nernstian response (54 mV/decade) to the protonated melamine over the concentration range of 5.0×10\(^{-6}\) to 1.0×10\(^{-2}\) mol L\(^{-1}\). The electrode exhibited a short response time of 16 s and was stable for more than 2 months.

4.1.4 Voltammetric sensors

Studies on amperometric and voltammetric sensors have also been reported. Metallic voltammetric electrodes are particularly interesting due to their high sensitivity and versatility, with a choice of potential range, waveform and electrode material. Yoshimi et al. (2001) investigated the change in structure and diffusive permeability of the MIP layer in the presence or absence of template and reported sensitive detection of template-theophylline by measuring the peak current of ferrocyanide oxidation. A thin layer of MIP composed of methacrylic acid as functional monomer and EDMA as cross-linking monomer was grafted onto the surface of conductive indium-tin oxide (ITO). The porosity and diffusive permeability of the MIP layer, the “gate effect”, is sensitive to template-analyte. The morphological change of the gate effect is still being investigated. Blanco-López et al. (2003) investigated the development of a voltammetric sensor for vanillylmandelic acid (VMA) based on acrylic MIP-modified electrodes. Their MIP-based sensors were able to give responses 5-10 times higher than those of non-imprinted electrodes in a non-excessive time lapse of 25 min. The peak current recorded with the imprinted sensor after rebinding of VMA was linear to its concentration in the range of 19-350 μg mL\(^{-1}\), whereas the response of the control electrode was independent of its concentration.

4.2 Electrochemical sensor chips

Towards practical use, our groups have developed voltammetric sensor chips for toxic compounds such as triazine herbicides and bisphenol A, which have recently attracted international attention as endocrine disrupting chemicals (Shoji et al., 2003; Fuchiwaki et al., 2008; Kubo et al., 2008; Yokota et al., 2008). These sensor devices are composed of a gold electrode chip, which delineate an electrochemical active area with a polyimide layer, and the MIP layer as the recognition element for atrazine, simazine and bisphenol A. In
principle, the analytes penetrate into the matrix of the MIP layer and bind to the imprinted pore and the analytes close to gold surface are detected by electrochemical reaction on the gold surface. The atrazine sensor chip was fabricated by directly polymerized MIP for atrazine (Atr-MIP) composed from methacrylic acid and EDMA onto a gold surface. By introducing LiCl as electrolyte into the MIP, electrochemical reduction of atrazine was facilitated and cathodic peak current depended on the concentration of 1-10 µM atrazine (Shoji et al., 2003). The obtained results were compared to the study of Atr-MIP composed from methacrylic acid and EDMA by other groups (Table 1). The response of simazine was only 28% to atrazine although simazine was reduced electrochemically at a higher level than triazine. The optimum preparation of a thinner Atr-MIP layer for sensitive determination was then studied and the detection of an environmental concentration 50 nM (11 ppb) of atrazine was achieved with a thinner layer of Atr-MIP (Kubo et al., 2008).

![Table 1](image.png)

Table 1. Comparison of the Selectivity of Atrazine-Imprinted Polymer (Shoji et al., 2003)

The simazine sensor chip was also fabricated by using methacrylic acid and EDMA (Fuchiwaki et al., 2008) (Fig. 5). The MIP preparation for simazine (Sim-MIP) and the electrochemical determination were investigated to establish a simazine sensor system because there were no reports for them (Fuchiwaki et al., 2007). Surprisingly, the simazine sensor chip was 29 times more sensitive to simazine than the bare gold electrode and the selective response to simazine compared to structural analogues such as atrazine. The bisphenol A sensor chip was fabricated by polymerizing the MIP for bisphenol A (BPA-MIP) composed from 4-vinylpyridine as a functional monomer and EDMA (Yokota et al., 2008) on a sputtered gold electrode. In order to obtain the BPA-MIP thin layer, BPA-MIP was polymerized by UV-light irradiation, and the thickness of the layer was examined by changing the time of its irradiation and observed with AFM. BPA-MIP layer prepared by 5 min irradiation could recognize BPA concentration at a 5 to 15 µM range. These sensor chips based on molecular imprinting technique allows inexpensive, stable, small devices, and in situ determination of analytes.
In order to improve the Membrane-based electrochemical sensor system in the future, it would be desirable to control its pore size and pore density at will because of the analyte diffusion towards the electrode surface. Analytes and substances such as electrolytes diffuse through its pore in the MIP matrix. Their size and density normally depend on the amount of polymerization solvent, which acts as a porogen in the preparation of MIP, and how the solvent interacts with template is important, too. Therefore, although the MIPs are expected to be biomimetic polymers capable of tailor-made synthesis for any analytes, detailed research to obtain selectivity, enrichment and proper permeability are still needed with respect to each template-analyte. Minimizing the thickness of the MIP membrane is very important. Controlling the thickness of MIP could be performed by a spin-coating of pre-polymer mixture. Recently, innovative approaches for the preparation of an MIP thin layer have been proposed. As a novel approach, nanotubular membranes with pores a few nm in diameter had been developed (Martin et al., 2001). Preparation was based on the controlled deposition of gold layers on the pore walls of membranes having pore sizes of about 10 nm. By combining a self-assembled functional monolayer with the obtained nano-tubules, a membrane selective to target analyte could be obtained. Therefore, such interesting approaches would allow a new way for prompting MIP-based membrane technology.

### 4.3 Electrochemical sensor utilizing MIP-based solid phase extraction

The application of MIPs to the field of affinity-based solid phase extraction is expected due to their strong affinity for template-analytes. So this feature is suitable for easy separation of template-analytes from a mixture containing impurities by loading several extraction solvents as commonly described in traditional chromatography. In this extraction process, the analytes are at first adsorbed to the MIP packed-column. After the undesired impurities are washed out, finally the bound analytes are recovered.

The sorbents with affinity are normally expensive and their preparation requires precious and time-consuming processes. So the application of SPE-based inexpensive MIPs (SPE-MIP) has been investigated for atrazine (herbicide), propranolol and pentamidine (medicine) (Martin et al., 1997; Matsui et al., 1997; Muldoon et al., 1997).

Our groups reported highly sensitive and selective electrochemical sensor systems by combining SPE-MIP for simazine and amperometric determination by a cyclic voltammetry method (Fuchiwaki et al., 2007; Fuchiwaki et al., 2009). As a working electrode, an amalgamated gold electrode, which was alloyed with mercury, was used for the optimum
determination of simazine. Fifteen nM of simazine, as legally regulated in Japan, was detected specifically in the mixture of other herbicides after washing nonspecifically adsorbed herbicides to the MIP column with dichloromethane. The reductive current of simazine could be detected at a negative potential around -1.0 V with a mercury electrode because there were few substances of electrochemical reaction around -1.0 V. The electrochemical method can potentially discriminate among electroactive substances by voltammetric determination. Therefore, it could be concluded that MIP-based electrochemical sensors are very promising elements for highly selective sensors.

5. Conclusion

Molecular imprinting is an attractive technique to mimic biological recognition sites. Electrochemical measurement enables a miniature, simple and inexpensive device in the development of a sensor system. Combination of MIP technology and electrochemical measurements would allow the development of such a useful sensor device. However, there are few reports of biomimetic electrochemical sensors. The speed of development of this device would depend on the progress of MIP technology. MIPs have an advantage to overcome drawbacks of biological receptors; on the other hand, the possibility development of MIP materials as biomimetic receptors is still under investigation. Studies on MIP merge technologies from various sciences such as supermolecular chemistry and nanotechnology are on the way.

6. References

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