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COMMUNICATION

An all-solid-state imprinted polymer-based potentiometric sensor for determination of bisphenol S †

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An all-solid-state polymeric membrane potentiometric sensor for determination of bisphenol S has been developed by using the imprinted polymer as the receptor and the nanoporous gold film as the solid contact. The sensor has a linear concentration range of 0.1 to 2 μM with a detection limit of 0.04 μM.

Bisphenol analogues have been widely used in the production of polycarbonate plastics and epoxy resins for several decades. Among these bisphenols, bisphenol A (BPA) was the predominant compound and one of the mostly highly produced chemicals (over 8 billion pounds produced annually in the world).[1] However, in recent years, BPA has gradually been banned in many countries because of its estrogenic effect.[2,3] Nowadays, BPA has been gradually replaced by a new bisphenol analogue, bisphenol S (BPS), in industrial applications, especially for production of baby bottles.[4] Unfortunately, recent studies have showed that BPS has a biological toxicity similar to that of BPA. BPS can also act as an estrogenic endocrine-disrupting chemical.[5,6] Therefore, it is highly desired to develop analytical methods for detection of BPS.

Several approaches have been reported for determination of BPS, such as ultraviolet (UV) spectroscopy,[7] high-performance liquid chromatography (HPLC) [8] and HPLC-tandem mass spectrometry (HPLC-MS/MS).[9] However, these methods require expensive apparatus and tedious procedure. Chemical sensors have attracted considerable attention owing to their low cost, simple operation and suitability for on-site monitoring.[10] As generic and highly successful chemical sensors, potentiometric ion-selective electrodes (ISEs)[11,12] which allow simple, rapid and selective detection of analytes would be a promising alternative for BPS detection. In particular, recent improvements in the detection limits of polymeric membrane based ISEs have yielded sensors for the direct measurement in the subnanomolar concentration range.[13] Currently, such sensors have evolved to be an attractive tool for environmental trace analysis and potentiometric biosensing.[14-16] Despite spectacular progresses over the past few years, none of these sensors has been reported for determination of BPS.

During the past decades, molecularly imprinted polymers (MIPs) have emerged as seemingly general materials for selective recognition of a wide range of analytes with high affinities and selectivities similar to their biological counterparts. At present, potentiometric sensors based on MIPs as receptors have been successfully developed for determination of various species,[17-21] especially for organic species, which makes these sensors particularly suitable for their use in BPS detection. However, it should be noted that almost all of the previously developed ISEs based on MIPs are in traditional liquid-contact mode in which lower detection limits have been restricted by zero-current transmembrane ion fluxes.[22] This poses serious limit to their use at trace levels as required for determining BPS in environmental samples.

Solid-contact ISEs which eliminate the internal solution are easily miniaturized. They have been recognized as the means by which the next ISE generation will be constructed.[23,24] It has been discovered that ISE membranes with a solid contact rather than a traditional liquid inner contact are anticipated to give lower detection limits because of diminished ion fluxes.[25] Herein, we present a novel all-solid-state potentiometric sensor for sensitive detection of BPS in environmental samples. A MIP is incorporated into the sensing membrane and employed as a receptor for the selective recognition of BPS. A nanoporous gold (NPG) film which was *in situ* formed on a gold electrode surface is used as the solid contact.[26] In contrast to the additionally coated intermediate layers, such film is reusable and cannot easily peel off from the electrode surface when the ISE membrane is removed by organic solvents after measurement. It will be shown that the proposed potentiometric sensor can offer remarkably improved sensitivity and selectivity for determination of BPS. To our knowledge, this paper reports for the first time the application of potentiometric sensors for BPS detection.

The BPS-imprinted polymers were synthesized by the classical precipitation polymerization method[27] using methacrylic acid (MAA) and 4-vinylpyridine (4-VP) as the functional monomers and ethylene glycol dimethacrylate (EGDMA) as the cross-linker. The

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schematic representation of the imprinting process is shown in Scheme 1. In this process, the carboxyl group of MAA can interact via strong hydrogen bonding with the hydroxyl group of BPS. In addition, 4-VP binds BPS via π-π interaction with the aromatic moiety of the template, thus improving the binding affinity and specificity of the MIP.[28] The micrographs of the obtained imprinted beads were investigated by scanning electron micrography (SEM). As shown in Fig. 1a, the BPS imprinted beads are uniform and spherical with a diameter of roughly 1 μm. These uniform-sized beads can be well dispersed in the polymeric ISE membrane, which could induce more binding sites available in the membrane and lower membrane impedance.[21] The SEM images also illustrate that the non-imprinted polymer (NIP) beads synthesized with the same recipe have the similar morphological structure and particle size distribution (Fig. 1b).

The solid-contact layer based on the NPG film was fabricated by the multicyclic electrochemical alloying/dealoying method.[26,29] Cyclic voltammetry were utilized to characterize the obtained NPG film based electrode (see Fig. S1 in the Supporting Information). As expected, a symmetrical cathodic peak of the electrochemical reduction of gold oxide appears around 0.93 V. In addition, the real surface of the Au/NPG electrode was calculated by integrating the charges from the reduction peaks. The results show that the Au/NPG electrode has a much higher surface area (1.767 cm^2) than the bare gold electrode （0.303 cm^2）. It has been well established that a high surface area can lead to a large electrochemical double layer capacitance which is a prerequisite for developing a stable solid-contact ISE.[30] Thus, it can be expected that the NPG film based electrode will exhibit excellent response performance.

After fabrication of the proposed sensor, BPS was firstly tested by using the classical potentiometric method. BPS is a weak acid with a pK_a range of 7.8-8.2 and is readily deprotonated in aqueous solution at pHs higher than 8.2. The deprotonated BPS can thus be detected potentiometrically by the ISE based on MIP. For this purpose, 30 mM $NaHCO_3/Na_2CO_3$ buffer of pH 10.2 was applied as the detection medium. Since the sensitivity and linearity for the membrane electrode depends on the amount of MIP in the membrane which determines the number of the recognition sites, the effect of the MIP amount was tested and the results are shown in Fig. S2. It can be seen that the detection sensitivity increases upon increasing the amount of MIP up to 6.0 wt%, which is owing to the increase in the number of the binding sites for BPS. However, further increase in the amount of MIP would not significantly improve the sensitivity. This is probably due to the fact that part of the MIP may become insoluble and cannot be dispersed uniformly in the plasticized membrane. Therefore, 6.0 wt% was chosen as the optimal MIP amount.

Under the optimized conditions, the potential response of the all-solid-state ISEs based on MIP to the deprotonated BPS was shown in Fig. 2. The calibration plot was recorded over a concentration range between 3.0×10^{-3} and 1.0×10^{-8} M. It can be seen that the proposed electrode shows a classical Nernstian response with a slope close to the theoretical value for dianion in the test solution (-28.8 mV $decade^{-1}$). The linear range is from 3.0×10^{-3} to 1.0×10^{-5} M with a detection limit of 3.0×10^{-6} M which is calculated as the intersection of the two slopes according to the classical definition of the detection limit for an ISE. As shown above, the proposed potentiometric sensor can be effectively used for the detection of BPS which occurs exclusively as its dissociated form at pH 10.2. However, according to the US Environmental Protection Agency (EPA) standard, the lowest concentration at which BPS can induce estrogen-dependent gene expression in vitro is 300 nM.[31] Hence, the obtained detection limit may not satisfy the requirement for trace-level measurement of BPS in biological and environmental samples.

In recent years, it has been revealed that electrically neutral phenols and their derivatives could generate strong anionic potential responses on quaternary ammonium salt-doped polymeric membranes under near-neutral pH conditions. These unexpected anionic responses can be explained by the net movement of hydrogen ions from the membrane phase to the aqueous phase stimulated by neutral phenols.[28,32,33] Inspired by these findings, we explored the application of the nonclassical response in the BPS determination. In order to guarantee that BPS exists mostly in its neutral form, 30 mM phosphate buffer solution (PBS) with a pH of 5.0 was used as the background solution. Fig. 3 shows the typical dynamic potential responses of the proposed solid-contact electrode to neutral BPS. As illustrated, the response behavior of the MIP-based membrane electrode at pH 5.0 is quite different from that at pH 10.2. Although the direction of the potential responses is the same (anionic responses) at both pH values, the response slope at pH 5.0 is much larger than the theoretical value for the divalent anions. In particular, in the concentration range of 3.0×10^{-3} to 1.0×10^{-5} M, the slope is -62.9 mV $decade^{-1}$. Here, the potential difference between the baseline potential values and those measured at a fixed time (i.e., 250 s) after BPS addition is used for quantification. The dynamic responses of the electrode in the low concentration range are shown in Fig .4. Detailed analysis of the experimental results indicates that the potential response is proportional to the concentration of neutral BPS in the range of 0.1 to 2 μM with a detection limit of 0.04 μM (3σ). Such detection limit is comparable or lower than those obtained by the fluorometric and spectrophotometric methods.[7,34] Above all, the proposed sensor yields a detection limit below the EPA defined limit (i.e., 300 nM) in samples. In addition, the membrane renewal was accomplished by washing the membrane with a mixture of ethanol and PBS (1/4, *v*/*v*) to remove BPS from the surface of the polymeric membrane. Effective removal of BPS from the proposed membrane is demonstrated in Fig. S3. As illustrated, the sensor's response is fully reversible with a relative standard deviation of 6.3 % (10 μM, n = 3).

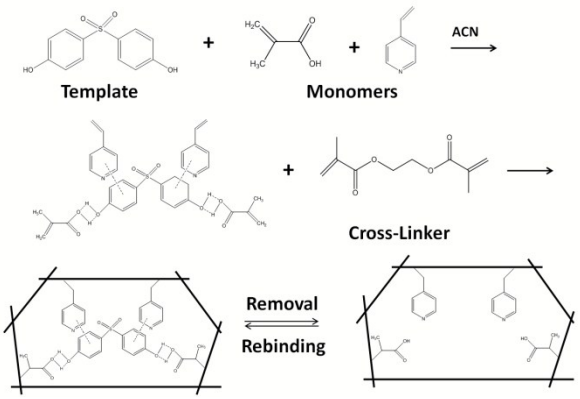
To confirm that the MIP particles in the sensing membrane is responsible for the excellent response performance of the MIP based potentiometric sensor, the responses of the NIP-based and the blank membrane electrodes were also investigated (Fig. S4). Clearly, both electrodes exhibit much smaller anionic responses than the MIP based electrode under the same conditions. These responses are probably due to the nonspecific interaction of neutral BPS with the ion-exchanger in the membrane. Evidently, it can be demonstrated that the observed potential responses are mainly induced by the specific interaction between BPS and its MIP in the membrane.

The selectivity of the proposed MIP-based sensor over other neutral phenols was characterized. As shown in Fig. 5, the sensor exhibits an excellent selectivity over other phenols such as phenol, 2-phenylphenol and 4,4'-dihydroxybiphenyl. Compared with the response to neutral BPS, no obvious potential changes with respect

to increasing the concentration from 0.2 to 2 μM are observed for these three neutral phenols (Fig. 5a), which suggests the specific recognition of BPS by its MIP. As a control, the potential response of the NIP-based membrane electrode was also evaluated. No significant changes in the potential responses can be observed as compared to that of the MIP-based ISE (Fig. 5b), which further confirms that the potential signals are mainly induced by the specific recognition interactions between the MIP and the target BPS.

The proposed MIP-based potentiometric sensor was finally applied to determination of BPS leached from the commercial BPA-free baby bottles. In order to illustrate its accuracy, the comparison between the proposed sensor and the HPLC method was performed. The extraction of BPS was done by soaking the bottle samples which was previously washed with de-ionized water and cut into very small pieces in de-oxygenated water and then heating the resultant mixture under reflux at 100°C for 24 h for release of BPS. The obtained extract solution was analyzed by the standard addition method after cooling to room temperature. The results are given in Table S1. It can be seen that the recoveries of baby bottle samples vary from 94% to 101% and the data obtained by the proposed electrode agree well with those obtained by the HPLC method, indicating that the proposed potentiometric sensor has a promising potential for real sample analysis.

Inserting Graphics



Scheme 1 Schematic illustration of the MIP synthesis.

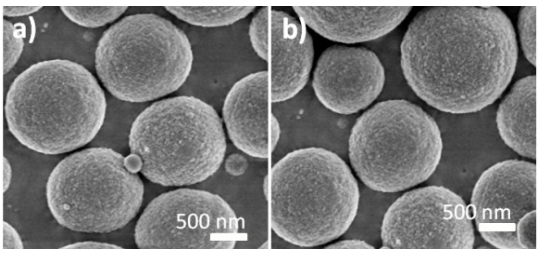


Fig. 1 SEM images of the obtained (**a**) MIP and (**b**) NIP beads.

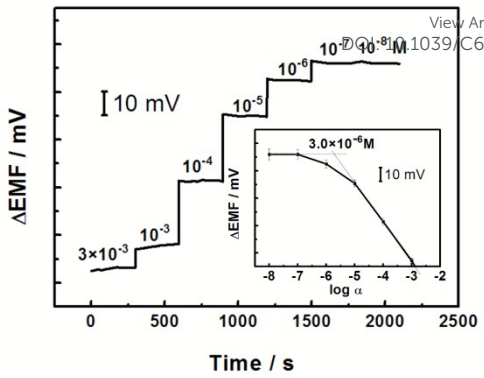


Fig. 2 Potentiometric responses of the proposed sensor based on MIP to deprotonated BPS. Experimental conditions: membrane composition (in wt%), 1.5 % TDMAC, 2.0 % ETH 500, 35.9 % PVC, 54.6 % DOP and 6.0 % MIP; detection background, 30 mM $NaHCO_3/Na_2CO_3$ buffer of pH 10.2; conditioning solution, 10^{-4} M BPS in 30 mM $NaHCO_3/Na_2CO_3$ buffer of pH 10.2. The inset shows calibration curve for detection of dissociated BPS. Error bars represent one standard deviation for three measurements.

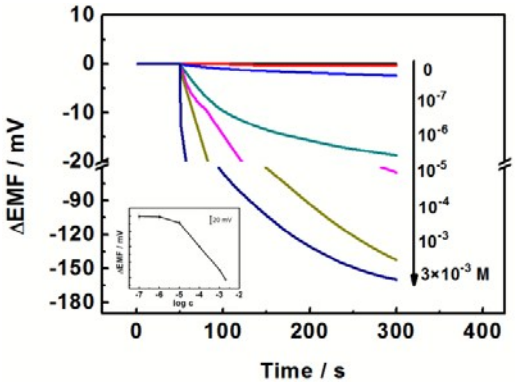


Fig. 3 Time-dependent potential response traces of the proposed MIP-based sensor for detection of neutral BPS in the concentration range of 1.0×10^{-7} to 3.0×10^{-3} M. Experimental conditions: detection background, 30 mM PBS with a pH of 5.0; conditioning solution, the same as the detection background. The inset shows the calibration curve for detection of neutral BPS. The potential difference between the baseline potential values and those measured at 250 s after BPS addition is used for quantification. Error bars represent one standard deviation for three measurements.

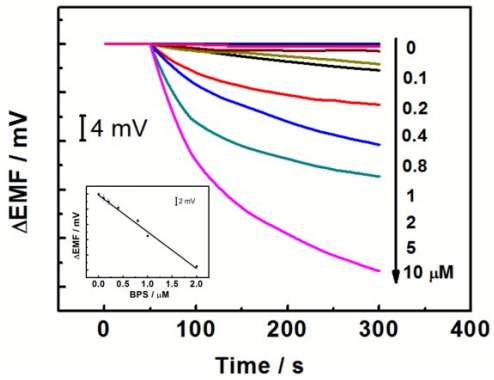


Fig. 4 Typical potential responses of the solid-contact electrode based on MIP to neutral BPS in the concentration range of 0.1 to 10 μM. The inset shows the calibration curve for neutral BPS detection. Other conditions are as given in Fig. 3. Error bars represent one standard deviation for three measurements.

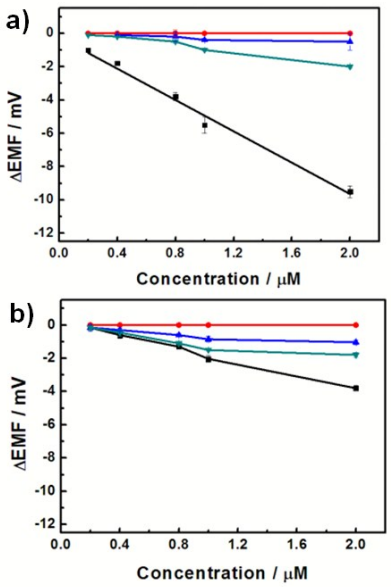


Fig. 5 Potentiometric selectivity of the MIP (a) and NIP (b) membrane-based sensors towards neutral phenols: (■), BPS; (▼), 2-phenylpheno; (▲), 4,4′-dihydroxybiphenyll; (●), phenol. Other conditions are as given in Fig. 3. Error bars represent one standard deviation for three measurements.

Conclusions

In summary, an all-solid-state potentiometric sensor for determination of BPS has been proposed. It is based on the MIP as the selective receptor and the NPG film as the solid contact. This is the first potentiometric sensor for BPS detection. Compared with the classical potentiometric method in which deprotonated BPS was detected, the proposed MIP-based sensor offers remarkably improved sensitivity for potentiometric detection of neutral BPS with a detection limit of 0.04 μM. Additionally, the proposed sensor shows an excellent selectivity, a good reproducibility and a satisfactory accuracy for real sample analysis.

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An all-solid-state polymeric membrane potentiometric sensor for sensitive and selective determination of bisphenol S is developed for the first time.