#### **RAPID COMMUNICATION**

# Potentiometric sensor for determination of neutral bisphenol A using a molecularly imprinted polymer as a receptor

Li-Juan Kou • Rong-Ning Liang • Xue-Wei Wang • Yan Chen • Wei Qin

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Abstract The aim of this paper is to develop a potentiometric sensing methodology for sensitive and selective determination of neutral phenols by using a molecularly imprinted polymer as a receptor. Bisphenol A (BPA), a significant environmental contaminant, is employed as the model target. The BPA-imprinted polymer is synthesized by the semi-covalent technique and incorporated into a plasticized poly(vinyl chloride) membrane doped with the tridodecylmethylammonium salt. The present electrode shows a linear anionic potential response over the concentration range from 0.1 to 1 µM with a detection limit of 0.02 µM, and exhibits an excellent selectivity over other phenols. The proposed approach has been successfully applied to the determination of BPA released from real plastic samples. It offers promising potential in development of potentiometric sensors for measuring neutral phenols at trace levels.

**Keywords** Molecularly imprinted polymers · Ion-selective electrodes · Bisphenol A · Phenols

L.-J. Kou · R.-N. Liang · X.-W. Wang · Y. Chen · W. Qin (⊠) Key Laboratory of Coastal Zone Environmental Processes and Ecological Remediation, Yantai Institute of Coastal Zone Research (YIC), Chinese Academy of Sciences (CAS), Yantai, Shandong 264003, China e-mail: wqin@yic.ac.cn

L.-J. Kou · X.-W. Wang Graduate University of the Chinese Academy of Sciences, Beijing 100049, China

L.-J. Kou · R.-N. Liang · X.-W. Wang · Y. Chen · W. Qin Shandong Provincial Key Laboratory of Coastal Zone Environmental Processes, YICCAS, Yantai, Shandong 264003, China

#### Introduction

Ion-selective electrodes (ISEs) have been routinely used for potentiometric detection of ion species in environmental and clinical applications [1]. However, very few ISEs have been developed for direct recognition of neutral species [2]. In recent years, it has been found that undissociated neutral phenols could generate anionic potential responses using poly(vinyl chloride) (PVC) liquid membranes doped with lipophilic nitrogen-containing compounds and metal porphyrins [3–5]. The net movement of hydrogen ions from the membrane interface to the aqueous phase stimulated by uncharged phenols is responsible for the anionic responses (Eq. 1) [3]. Unfortunately, the selectivity of such sensors is rather poor, which is governed mainly by the acidity and lipophilicity of each phenolic compound, rather than specific molecular recognition.

$$ArOH_{aq} + TDMA^{+}X_{mem}^{-} \rightleftharpoons TDMA^{+}ArO_{mem}^{-} + H_{aq}^{+} + X_{aq}^{-}$$
(1)

Molecularly imprinted polymers (MIPs) have gained wide acceptance as new molecular receptors for use in sensors since they have high affinities and excellent selectivities similar to those of antibodies, and are chemically stable and easy to prepare [6]. In recent years, potentiometric sensors based on MIPs have been successfully developed, while most of them are fabricated for ionic species [7, 8]. In this work, we utilize the specific binding properties of MIPs to develop a potentiometric sensing methodology for measuring neutral phenols with high sensitivity and excellent selectivity. Here, bisphenol A (BPA), a significant environmental contaminant commonly used in the production of polycarbonate plastics and epoxy resins, would be a particularly attractive model for neutral phenols [9]. It will be shown that the MIP-based membrane could offer remarkably improved sensitivity and selectivity for potentiometric detection of neutral phenols.

# Experimental

#### Reagents and materials

BPA, bisphenol A dimethacrylate, acetonitrile (ACN), methanol, methacrylic acid (MAA), ethylene glycol dimethacrylate (EGDMA), 4-vinylpyridine (4-VP), PVC, *o*-nitrophenyl octyl ether (*o*-NPOE), bis(2-ethylhexyl) sebacate (DOS), dioctylphthalate (DOP), tridodecylmethylammonium chloride (TDMAC), tetradodecylammonium tetrakis(4-chlorophenyl) borate (ETH 500) were purchased from Sigma Aldrich. 2,2-Azobis-isobutyronitrile (AIBN) and tetrahydrofuran (THF) were obtained from Sinopharm Chemical Reagent Co., Ltd (China). MAA and THF were distilled prior to use; 33 mM phosphate buffer solution (PBS) of pH7.5 was used for all the experiments to ensure that BPA is in its neutral form.

All other reagents were analytical grade and used as received. Aqueous solutions were prepared by dissolving the appropriate salts in the Pall Cascada ultrapure water.

### Synthesis and characterization of BPA-imprinted polymer

The BPA-imprinted polymer was synthesized by the semicovalent imprinting technique [10]. Bisphenol A dimethacrylate (1 mmol), 4-VP (4 mmol), EGDMA (10 mmol) and AIBN (50 mg) were mixed in ACN (25 mL) in a glass tube. The solution was degassed with nitrogen for 10 min, and then polymerized at 60 °C for 18 h. After polymerization, the polymer particles were added to a mixture of methanol/1 M NaOH (75:25  $\nu/\nu$ ), and heated in reflux with stirring for 20 h to remove the template. Here the mixture of methanol/1 M NaOH was used to readily open the ester bond in the compound of bisphenol A dimethacrylate. The non-imprinted polymer (NIP) was prepared following the same procedure except for omission of the template BPA. L.-J. Kou et al.

The obtained imprinted and non-imprinted polymers were characterized by scanning electron microscopy (SEM, JSM 5600 LV, operating at 15 kV).

To evaluate the adsorption capacity of the obtained polymers, batch binding experiments were performed. 20 mg of the imprinted polymer (MIP or NIP) was dispersed in 2 mL of acetonitrile solutions spiked with different concentrations of BPA, and then the mixtures were continuously oscillated for 24 h. The amounts of BPA in the supernatants were determined using HPLC at 230 nm.

## Membranes and electrodes

The membranes were prepared by pouring a 2 mL THF solution of 200 mg of membrane components into a glass ring (26 mm i.d.) fixed on a glass plate. After overnight evaporation of the solvent, 4-mm-diameter membrane disks were cut from the membrane and glued to plasticized PVC tubes with THF/PVC slurry. The MIP (NIP) membrane contained (in wt%) 6.0 % MIP (NIP), 1.0 % TDMAC, 2.0 % ETH 500, 36.4 % PVC and 54.6 % DOP; for comparison, the blank membrane contained 1.0 % TDMAC, 2.0 % ETH 500, 38.8 % PVC and 58.2 % DOP. 10 mM NaCl was used as the inner filling solution for each electrode. Before measurements, all the electrodes were conditioned overnight in 33 mM of pH7.5 PBS.

## Electromotive force measurements

Electromotive force measurements were carried out at 25 °C using a PXSJ-216L pH meter (Leici, Shanghai) in the galvanic cell: SCE/1 M LiOAC/sample solution/ISE membrane/inner filling solution/Ag, AgCl. Each membrane electrode was attached to an ATA-1B rotator (Model, Jiangfen Electroanalytical Instrument Co., Ltd, China) at a rotation speed of 3,000 rpm.





#### **Results and discussion**

## Synthesis and characterization of MIPs

The BPA-imprinted polymers could be synthesized by the non-covalent imprinting protocol for its simplicity and flexibility [11-13]. Unfortunately, this protocol suffers from problems of template leakage. In this work, the semicovalent protocol was employed for the MIP preparation to avoid template leakage and improve efficient rebinding, for which the template molecules are bound covalently to the functional monomer, but rebound based on the noncovalent interaction [14]. As shown in Fig. 1, the binding amounts for both MIP and NIP polymers increase with increasing the concentration of BPA. At the concentration of BPA of 1  $\mu$ M, the amount bound by the imprinted polymer is 15.1 µmol/g, while that bound by the control polymer is 4.2 µmol/g. These results indicate that the imprinted polymer shows much better binding properties with more specific recognition sites for BPA as compared to the control polymer. Figure 1 also shows the SEM images of MIP (A) and NIP (B). It can be seen that both of the particles have a spherical shape with a diameter range of  $0.5-1.0 \mu m$ .

Potentiometric responses of the MIP, NIP-based, and blank membrane electrodes

The responses of different polymeric membrane electrodes were measured to test the feasibility of using MIP as the sensing element for sensitive and selective detection of



**Fig. 2** Dynamic potential responses to 1  $\mu$ M BPA in 33 mM PBS of pH7.5 using a stir bar at 400 rpm (*a,b,c*) and a rotating electrode at 3000 rpm (*d*) for sample convection. Membrane ingredients: (*a*) bank membrane, 1.0 % TDMAC, 2.0 % ETH 500, 38.8 % PVC and 58.2 % DOP; (*b*) NIP membrane, 1.0 % TDMAC, 2.0 % ETH 500, 36.4 % PVC, 54.6 % DOP and 6.0 % NIP; (*c, d*) MIP membrane, 1.0 % TDMAC, 2.0 % ETH 500, 36.4 % PVC, 54.6 % DOP and 6.0 % MIP

neutral BPA. The results are shown in Fig. 2. It can be seen that the MIP-based membrane ISE (curve c) shows a much larger anionic response than the blank (curve a) and NIP-based (curve b) membrane electrodes, which suggests the specific interaction between BPA and its MIP in the polymeric membrane. Figure 2 also shows that the potential response can be largely increased by using a rotating disc electrode (curve d) as compared to a stir bar for



Fig. 3 Effects of the membrane components on the potential responses of the MIP-based membrane electrode: **a** imprinted polymer; **b** plasticizer; **c** quaternary ammonium salt. Unless indicated otherwise, the membrane composition was as follows: 1.0 % TDMAC, 2.0 % ETH 500, 36.4 % PVC, 54.6 % DOP and 6.0 % MIP; the rotation speed was 3,000 rpm



**Fig. 4 a** Typical dynamic potential responses of the MIP-based membrane electrode in PBS upon additions of different concentrations of BPA. The *inset* shows the calibration curve for BPA. Each *error bar* represents one standard deviation for three measurements. **b** Recycle potential response profiles for the blank 1  $\mu$ M BPA. Membrane composition: 1.0 % TDMAC, 2.0 % ETH 500, 36.4 % PVC, 54.6 % DOP and 6.0 % MIP; rotation speed: 3,000 rpm



 Table 1
 Application of the proposed sensor to determination of BPA released from the PC drinking bottles

Sample	Proposed sensor (µM) <sup>a</sup>	Recovery results			HPLC
		Added (µM)	Found (µM) <sup>a</sup>	Recovery (%)	(μινι)
Sample	$0.44 {\pm} 0.05$	0.30	$\begin{array}{c} 0.72\pm\ 0.06 \end{array}$	93	$\begin{array}{c} 0.47 \pm \\ 0.04 \end{array}$
Sample 2	$0.54 {\pm} 0.04$	0.30	$\begin{array}{c} 0.85 \pm \\ 0.06 \end{array}$	103	$\begin{array}{c} 0.49 \pm \\ 0.05 \end{array}$
Sample 3	$0.23 {\pm} 0.05$	0.30	$\begin{array}{c} 0.52 \pm \\ 0.05 \end{array}$	97	$\begin{array}{c} 0.25 \pm \\ 0.04 \end{array}$
Sample 4	$0.70 {\pm} 0.06$	0.30	$\begin{array}{c} 0.97 \pm \\ 0.10 \end{array}$	90	$\begin{array}{c} 0.65 \pm \\ 0.05 \end{array}$

<sup>a</sup> Average of three measurements±standard deviation

sample convection, which is due to the fact that the rotation mode could dramatically decrease the aqueous diffusion layer and thus enhance the mass transfer of the analyte to the membrane surface [15].

## Optimization of the membrane composition

The influence of the membrane composition was examined by testing the responses of the MIP-based polymeric membrane electrodes for BPA in the concentration range of  $0.01-1 \mu$ M. As shown in Fig. 3a, the electrode exhibits larger potential responses with increasing the amount of MIP in the membrane up to 6.0 %, which is probably due to the increase in the number of the binding sites for molecular recognition. However, further increase in the amount of MIP would not significantly improve the sensor's sensitivity. The effect of plasticizer on the potential response of the membrane is illustrated in Fig. 3b. It can be seen that higher responses can be obtained by using nonpolar plasticizers and DOP shows the best performance in sensitivity,



Fig. 5 a Potential responses to neutral phenols using the MIPbased membrane electrode: (*black filled square*) BPA; (*red filled circle*) phenol; (*blue filled upright triangle*) 2-phenylphenol; (*open inverse triangle*) 4,4'-dihydroxybiphenyl. **b** Potential responses to neutral phenols for control experiments: blank membrane, (*black* 

filled square) BPA; (red filled circle) phenol, (blue filled upright triangle) 2-phenylphenol and (open inverse triangle) 4,4'dihydroxybiphenyl; NIP-based membrane, (pink filled left-facing triangle) BPA. Rotation speed: 3,000 rpm; other conditions as in Fig. 2

which is probably due to the fact that BPA can be favorably extracted into the membrane with DOP as solvent. Figure 3b also shows that by decreasing the plasticizer content in the membrane higher anionic potential responses could be obtained. It is well known that lower amounts of plasticizer in the membrane induce the smaller diffusion coefficients, which can facilitate the accumulation of BPA molecules at the membrane interface thus causing higher potential responses [16]. Figure 3c indicates that the amount of the quaternary ammonium salt (i.e., TDMAC) incorporated in the membrane has a profound effect on the electrode response. Since the anionic potential responses of neutral phenols are based on proton dissociation induced by the quaternary ammonium salt in the membrane, negligible potential response was observed in the absence of TDMAC. However, a decrease in sensitivity can be caused by using the amounts of TDMAC higher than 1.0 %. This effect is consistent with the observations for polvion sensors (i.e. the increase in the ionic site concentration requires a higher sample concentration of polyion to reach the same phase boundary potential) [17].

Performance of the MIP-based polymeric membrane electrode

The typical dynamic potential responses to BPA using the proposed MIP-based membrane electrode under optimal conditions are shown in Fig. 4a. The potential difference between the baseline and the potential measured at 10 min after BPA addition is used for quantification. As shown in the inset of Fig. 4a, the anionic potential response is proportional to the concentration of BPA in the range of 0.1 to 1  $\mu$ M. The detection limit was calculated to be 0.02  $\mu$ M (3 $\sigma$ ), which is one order of magnitude lower than that of the NIP-based or the blank membrane electrode. Figure 4b shows the reversibility of the MIP-based membrane electrode. After each measurement, the membrane electrode was washed with a mixture of ethanol and PBS (1/4, v/v) to remove BPA from the membrane surface. As shown in Fig. 4b, the sensor's response can be fully reversible with a relative standard deviation of 3.9 % (1  $\mu$ M BPA, n=3).

The selectivity of the proposed MIP-based membrane electrode over other phenols such as phenol, 2-phenylphenol and 4,4'-dihydroxybiphenyl is shown in Fig. 5. Compared to the responses to BPA in the concentration range of  $0.1-1 \mu$ M, negligible potential changes can be observed for these three phenols using the MIP-based membrane electrode (Fig. 5a) and for all the phenols using the blank and NIP-based membranes (Fig. 5b). These results indicate that the measured potential responses are induced mainly by the specific recognition of the target BPA with the MIP as the receptor.

## Practical applications

To evaluate the feasibility of the proposed sensor, BPA released from the commercial polycarbonate (PC) drinking bottles was determined using the standard addition method. Each PC bottle was washed with water and cut into small pieces; 5 g of them was mixed with 20 mL de-oxygenated water which was then heated under reflux at 100°C for 12 h. After cooling to room temperature, the sample solution was tested by the present membrane electrode and the HPLC method, respectively. The results are shown in Table 1. As can be seen, BPA can be detected in real plastic samples with recoveries ranging from 90 % to 103 %, and the data obtained by the polymeric membrane electrode agree well with those obtained by the HPLC method. These results indicate that the proposed potentiometric sensor can be a promising and reliable tool for rapid detection of BPA.

## Conclusions

The selectivity of the conventional polymeric membrane electrodes for neutral phenols is rather poor. The potential response is governed mainly by the acidity and lipophilicity of each phenolic compound, rather than specific molecular recognition. By incorporation of MIP in the membrane, the selectivity and sensitivity of the electrode can be largely improved due to the high affinity binding of the imprinted polymer to the phenolic molecules. The proposed methodology offers promising potential in development of potentiometric sensors for measuring neutral phenols at trace levels.

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