ChemComm

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Journal:	*ChemComm*
Manuscript ID:	CC-COM-07-2014-005810.R1
Article Type:	Communication
Date Submitted by the Author:	12-Sep-2014

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Journal Name

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Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

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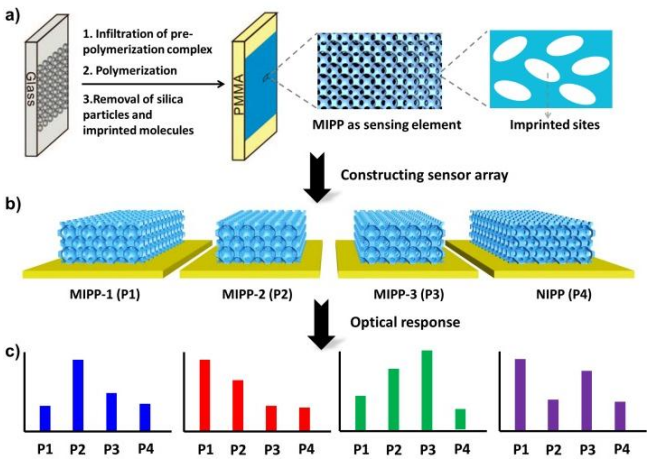
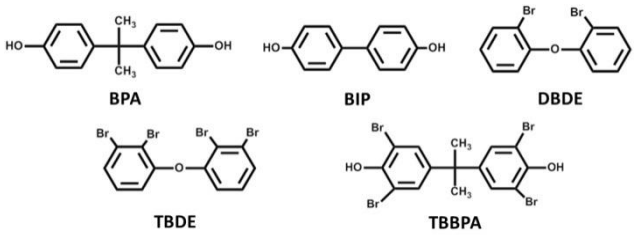
Molecularly imprinted photonic polymers can serve as ideal sensing elements for efficiently creating cross-reactive sensor array. Based on this concept, a new method for sensitive and label-free detection of the challenging PBDEs was developed, by which the direct detection and discrimination of trace levels of PBDEs against high-background of interferents were achieved with 100% accuracy.

Polybrominated diphenylethers (PBDEs) are the most commonly used brominated flame retardants and have been broadly applied as additives in consumer products and electronics in the past decades. However, due to the great potential impacts of PBDEs on human health and environment, monitoring of PBDEs is of great interest worldwide and has drawn considerable efforts.[1] In recent years, numerous analytical methods including gas chromatography, mass spectroscopy, and biosensors *et al* have been developed to detect the trace levels of the PBDEs pollutants in different matrices.[2] Nevertheless, still very few of the reported methods can truly realize the ability of highly sensitive and selective detection of PBDEs, particularly for the complex mixtures in real samples. The main challenge issue is the great variety of PBDEs (>200 kinds), and most of existing forms of PBDEs are commonly mixture of congeners with closely structural similarity. This feature of PBDEs samples makes the design and synthesis of proper receptors for chemical sensing very difficult. Moreover, brominated compounds are in general more readily debrominated and especially are easily subject to thermal decomposition. These additional and uncertain multiple interferences make the detected systems more complex and have a strong influence on the accuracy for discrimination. Thus, to overcome the problems mentioned above, the development of new sensing strategy for direct detection of the challenging PBDEs, in particular the PBDEs mixtures, is crucial and highly desirable.

Inspired by the mammalian olfactory system,[3] in this work, we present a novel sensory array strategy based on the molecularly imprinted photonic polymers (MIPPs) to meet the above PBDEs sensing challenges. MIPPs are the molecularly imprinted polymer matrices with integrated inverse opal (photonic) structure, which are first reported in our group in 2006 for chiral recognition.[4] They are produced by the combined use of colloidal-crystal templating and a molecular imprinting technique (Scheme 1a). Due to the unique hierarchical porous structure (3D-ordered macroporous arrays and imprinted binding nanocavities distributed in macroporous wall), MIPPs can serve as "ideal" sensing elements for the creation of cross-reactive sensory arrays. Remarkably, the molecular recognition events of imprinted binding cavities can be directly converted to a readable optical signal through a change of diffraction property of 3D-ordered macroporous arrays without the use of any labels (i.e. self-reporting signaling), and attractively accompanied by a visually perceptible color change. On the other hand, the interconnected macroporous structure with inherent high surface area greatly improves the mass transport and sensitivity of analytes in MIPPs, thus imparting MIPPs high sensing capability for ultra-trace level



Scheme 1 a) Schematic illustration of the preparation of molecularly imprinted photonic polymer as sensing element; b) construction of 4D MIPPs-based sensor array for sensing; c) schematic illustration of the optical response of the sensor array against analytes to produce recognition patterns.



Scheme 2 Chemical structures of the used analytes.

detection and fast response. More importantly, as molecular imprinting is a very general and well-established approach for creating molecular receptors, a large number of MIPPs with good selectivity is facilely accessible. Clearly, these unique features of MIPPs allow rapid fabrication of sensing elements with broad diversity and thus efficient construction of the corresponding cross-reactive sensor arrays with self-reporting signal transduction (Scheme 1b-c). Conceivably, the MIPPs-based cross-reactive sensor array should be suitable for directly detection and discrimination of PBDEs mixtures and even the trace PBDEs against high-background of other interferences.

As a demonstration, two PBDEs: 2,2'-dibromodiphenylether (DBDE), 2,2',3,3'-tetrabromodiphenylether (TBDE), one brominated flame retardant: tetrabromobiphenol (TBBPA), and two PBDEs mimics: bisphenol (BPA), 4,4'-biphenol (BIP) were selected as targeted analytes in this work (Scheme 2). The detection and discrimination of the given five analytes (down to $1x10^{-12}$ M) and even their mixtures in a wide range of concentrations, particular the trace analyte against a high-background of other interferences, could be efficiently and fast (~3 min) achieved with 100% accuracy, indicative of the powerful capability of MIPPs sensor array for complex PBDEs system. To the best of our knowledge, this is the first report on highly selective and sensitive detection of PBDEs and PBDEs mixtures based on cross-reactive sensor array.

Concretely, BPA-, TBBPA-, and BIP-imprinted as well as nonimprinted photonic polymers were separately fabricated and used as sensing elements to construct a 4D sensor array (Scheme 1b). Details of the fabrication and modestly optimized condition were provided in Figure S1-S2 in ESI. In our case, since PBDEs are always lack of interaction sites and have low solubility, which greatly limit their applications as templates, BPA, TBBPA and BIP instead of PBDE molecules were used as templates for molecularly imprinting process, respectively. Compared to PBDEs, the structural similar BPA, TBBPA or BIP has two hydroxyl groups to form hydrogen-bonding with functional monomer (acrylic acid) and thus the resulting imprinted binding sites with high binding affinity and good selectivity could be achieved.[5] Due to the structural similarity, the molecularly imprinted photonic films (MIPPs) still exhibited good selectivity to PBDEs. Figure 1A-B displays SEM images of the used SiO_2 colloidal crystal template and the resultant molecularly imprinted inverse opaline polymer film. The optical photography of the imprinted film in Figure S3 shows a uniform structure color, indicative of the well-organized photonic structure on macroscopic scale.

The hierarchical porous structure (3D-ordered macropores and the imprinted binding nanocavities distributed in macroporous wall) provides a prerequisite for the use of MIPPs as sensing elements and the construction of the cross-reactive sensor array. The differential

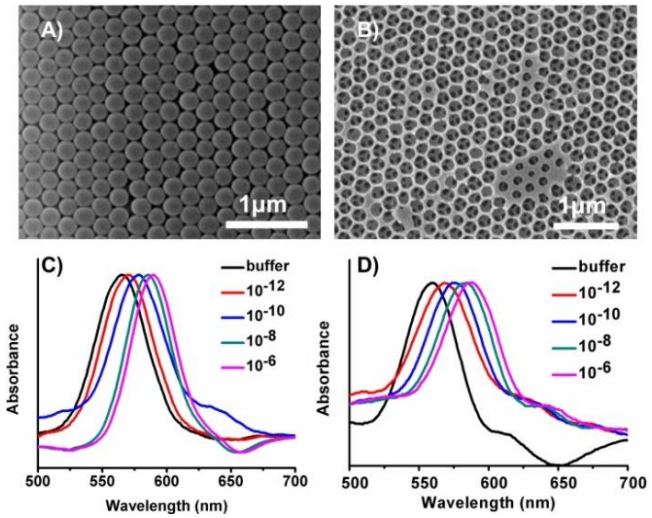


Fig.1 SEM images of the SiO_2 colloidal crystal template (A) and the resultant molecularly imprinted inverse opal photonic film (B); C) optical responses of the BIP-imprinted polymer film against DBDE; D) optical responses of TBBPA-imprinted polymer film against TBDE.

sensing capability of the MIPP-based cross-reactive array (P1, P2, P3 and P4 in Scheme 1b) for PBDEs was first examined toward the five analytes (see Scheme 2) of a series of concentrations in 5 mM phosphate buffer solution (pH 7.6). For all the analytes sensing, the incubation time was set to 3 minutes. The sensing behavior was detected by UV/Vis spectroscopy and all the measured optical response patterns are shown in Figure S4-S7 in ESI. For each analyte five parallel measurements were performed. As representative results, Figure 1C-D show the optical response of the BIP- and TBBPA-imprinted photonic films to DBDE and TBDE of different concentrations, respectively. In terms of the sensor sensitivity, clearly, even in an ultra-low concentration ($1x10^{-12}$ M), the prepared MIPPs still exhibited an observable optical shift to DBDE (ca. 6 nm) and TBDE (ca. 7 nm), indicating an ultra-sensitivity for PBDEs detection. To have a better illustration of the high levels of cross-reactivity in the MIPPs array, the line plots for five analytes at $1x10^{-10}$ M are displayed in Figure 2A. Obviously, BPA- and TBBPA-imprinted sensing elements demonstrated a preferred and maximum shift for imprinted molecule due to the complementary shape and size to the imprinted nanocavities. However, in the case of BIP-imprinted sensing element, due to the low solubility of BIP, a higher ratio of functional monomer (acrylic acid) was used in imprinting process, and as a result large amount of non-specific binding sites were generated in the resulting polymer and correspondingly the effect of molecular imprinting decreased to some extent. Nevertheless, originating from the cross-reactivity of molecular imprinting, differential response of sensing elements (P1, P2, P3 and P4) to each of the tested analytes was clearly observed (Figure 2A). The cross-reactivity in combination with the volume of sensing data (five measurements for each analyte) generates a distinctive but complex recognition pattern for each analyte.

To better understand the pattern recognition for PBDEs as well as their mimics (BPA, BIP and TBBPA), principal component analysis (PCA), a chemometric analytical method,[6] was used to reduce multi-dimensional data set into a two or three dimensionality. In our work, the data set (4 photonic polymers × 5 analytes × 5 times) was plotted in 3D principal component (PC) spaces which contain 98.8%

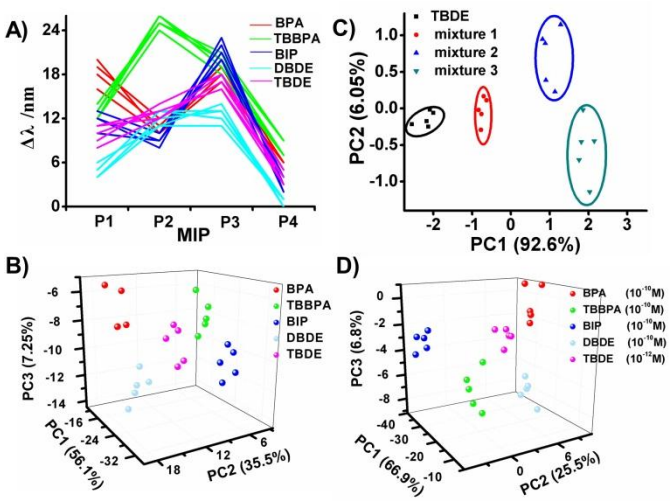


Fig.2 A) Response patterns of the MIPPs sensor array against each of the analytes ($1x10^{-10}$ M) for five times; B) 3D PCA plots for the identification of five analytes ($1x10^{-10}$ M) by MIPPs sensor array; C) 2D PCA plot for the identification of TBDE and three different mixtures by MIPPs sensor array: mixture 1 (TBDE and BPA); mixture 2 (TBDE, BPA, and TBBPA); mixture 3 (TBDE, BPA, TBBPA and BIP); D) 3D PCA plots for the identification of each analyte (TBDE: $1x\ 10^{-12}$ M, BPA: $1x10^{-10}$ M, TBBPA: $1x10^{-10}$ M, BIP: $1x10^{-10}$ M and DBDE: $1x10^{-10}$ M) by MIPPs sensor array.

Table 1 Comparison with other sensing analytical methods.

Method	GC[8]	LC[9]	Biosensors[2d]	Present
Cost	high	high	medium	low
Time	10 min	15 min		3 min
LOD	pg/ml	ng/g	ppt	pg/g

information, as shown in Figure 2B. Obviously, the PCA plots show a good discrimination of the five tested analytes in 3D PCA plots. The response for each analyte was clustered into five tight distinct groups, indicative of the good reproducibility of the response for each analyte. Based on jack-knife' analysis,[7] when all four roots were taken into consideration, all performed analysis allowed 100% correct classification of five analytes at the concentration of $1x10^{-10}$ M (Table S4-S6 in ESI). The similar sensing performance was also observed for the analytes at $1x10^{-8}$ M and even at the ultra-low concentration of $1x10^{-12}$ M (Figure S8-S10 and Table S1-S3, S7-S9). These results clearly indicate the good and direct detection and discrimination ability of the MIPPs-based array for trace levels of PBDEs and their mimics.

To further demonstrate the powerful discrimination ability of the MIPPs array for PBDEs, three complex PBDEs mixture solutions containing respectively two (TBDE and BPA), three (TBDE, BPA and TBBPA), and four (TBDE, BPA, TBBPA and BIP) analytes were used as targeted systems together with TBDE solution. In each test solution, the concentration of single analyte was set at $1x10^{-10}$ M. Figure 2C is a graphic representation of the principal component analysis (PCA) results. Obviously, the obtained response patterns were also well separated into four clusters (Figure 2C) with 100% accuracy based on 'jack-knife' analysis, indicating that the used MIPPs sensor array indeed has the detection and discrimination ability for the complex PBDEs mixtures (Table S10-11). More importantly, to check whether our sensor array has the ability for real samples sensing, five PBDEs mixture solutions containing respectively two (TBDE and BPA), three (TBDE, BPA and TBBPA), four (TBDE, BPA, TBBPA and BIP), five (TBDE, BPA, TBBPA, BIP and Octa-BDE) and six (TBDE, BPA, TBBPA, BIP, Octa-BDE and Deca-BDE) analytes dissolved in tap water and lake water (hard to know the components) were used as targeted analytes for sensing. In each test solution, the concentration of single analyte was set at $1x10^{-10}$ M (Table S12-15). Obviously, as shown in Figure S11-12, the 2D PCA plots also showed good discrimination for the six tested real samples and the detection accuracy was 100%, indicating the potential ability of our created MIPPs sensor arrays for real-world application. We believe the sensing element with good selectivity should be responsible for the excellent sensing performance. It is well-known that molecular imprinting is a generally applicable method for creating receptors. Thus, the obtained results also implicate the cross-reactive array based on the MIPPs sensing scheme should have great extended capability to sense other types of environmental pollutants.

Trace analyte identification against a high-background of other components is crucial for the real-world application of chemical sensors and commonly is quite a hard issue. In this respect, the high affinity and good selectivity of the sensing elements in our MIPPs sensor array also exhibited a good discrimination power. As shown in Figure 2D, even the concentration ($1x10^{-12}$ M) of TBDE is two orders of magnitude lower than that ($1x10^{-10}$ M) of other analytes, a clear discrimination of TBDE from high background of other components (BPA, TBBPA or BIP) was easily achieved in the 3D PCA plot, and the detection accuracy was up to 100%. These excellent detection results made our MIPPs-based array very promising for rapid PBDEs detection in real samples.

Besides signal self-reporting, high sensitivity and high selectivity, the strategy described above also shows other remarkable advantages such as response time and cost (Table 1), compared with other previous studies on PBDEs detection. Furthermore, we also performed quantitative study. Six complex PBDEs mixture solutions were used as targeted systems: mixture **1** (10^{-12} M TBDE, 10^{-10} M BPA, and 10^{-10} M TBBPA); mixture **2** (10^{-10} M TBDE, 10^{-10} M BPA, and 10^{-10} M TBBPA); mixture **3** (10^{-8} M TBDE, 10^{-10} M BPA, and 10^{-10} M TBBPA), mixture **4**: (10^{-12} TBDE, 10^{-10} M BPA, 10^{-10} M TBBPA and 10^{-10} M BIP), mixture **5** (10^{-10} TBDE, 10^{-10} M BPA, 10^{-10} M TBBPA and 10^{-10} M BIP) and mixture **6** (10^{-8} TBDE, 10^{-10} M BPA, 10^{-10} M TBBPA and 10^{-10} M BIP). Due to the unique features of the cross-reactive sensor array, not only qualitative identification of target analytes but also quantitative analysis can be realized. Indeed, as demonstrated in Figure S13, a good discrimination of the six complex PBDEs mixture solutions containing respectively three (TBDE, BPA and TBBPA), and four (TBDE, BPA, TBBPA and BIP) analytes at different concentration from 10^{-12} M to10^{-8} M could be achieved. Hence, the analytes with different concentration can be well identified. These preliminary results are encouraging. Although a few PBDEs were tested in this work, in principle, this cross-reactive based photonic sensing method is generally applicable for creating sensing elements of other types of PBDEs. Furthermore, by rationally optimizing the fabrication conditions of MIPPs, color change of sensing elements upon PBDEs

sensing should be visualized. By integrating the individual sensing elements into microchip, a 'pH-paper' like array with fast PBDEs detection and easy portability could be realizable. Now the related work is ongoing in our lab.

In summary, we developed a new method for convenient and sensitive detection of PBDEs based on molecularly imprinted photonic cross-reactive sensory array. The constructed photonic sensory array is characterized by excellent discrimination ability toward trace levels of PBDEs, PBDEs mixtures, and even the trace PBDEs against high-background of other components with 100% accuracy. Remarkably, due to the unique hierarchical porous structure such arrays exhibit quick response and direct generation of readable optical signals without use of any labels (i.e. self-reporting signaling), and thus expensive equipment and detectors could be omitted. It is expected that our work could not only provide a new detection method for PBDEs and but also be generally extended to develop the related sensory arrays for other environmental pollutants.

We gratefully acknowledge the financial support from the NSFC (21025311, 21121004, 21261130581 and 91027016), Ministry of Education (2011Z01014), MOST Program (2011CB808403, 2013CB834502) and the transregional project (TRR61).

Notes and references

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† Electronic Supplementary Information (ESI) available: [details of the performed experiments]. See DOI: 10.1039/c000000x/

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