ADVANCED FUNCTIONAL MATERIALS

FULL PAPER

DOI: 10.1002/adfm.200700498

# Stereoselective and Enantioselective Electrochemical Sensing of Monosaccharides Using Imprinted Boronic Acid-Functionalized Polyphenol Films**

By *Eran Granot, Ran Tel-Vered, Oleg Lioubashevski,* and *Itamar Willner**

Imprinted polymer films for the selective analysis of D-glucose and D-mannose are prepared by the co-electropolymerization of phenol with a 3-hydroxyphenyl boronic acid-monosaccharide complex containing D-glucose or D-mannose on a Au support. The analysis of the monosaccharides is based on a competitive electrochemical assay that employs the ferrocene-modified-monosaccharides as the redox labels. Similarly, enantioselectivity is demonstrated by the imprint of D-glucose recognition sites in the polymer and the application of the redox-active indicator.

## 1. Introduction

Electropolymerized films on electrodes are finding increasing interest as functional materials for sensing,[1,2] for the fabrication of solar cells[3] and light-emitting diodes (LEDs),[4] for the electrochemical activation of enzymes,[5] and for the mechanical actuation of microdevices by electrochemical stimuli.[6] Among the different functionally tailored polymers, imprinted polymers that include specific recognition sites are attracting growing interest.[7] Two general strategies to design imprinted polymers have been developed. One approach involves polymerization around molecular templates that include complementary recognition elements with the monomers, e.g., electrostatic interaction or H-bonds, followed by rinsing off the molecular template.[8,9] The second approach includes the copolymerization of monomers with polymerizable ligands that covalently link to the template molecule. The subsequent cleavage of the ligand–template bond enables the elimination of the molecular template, while forming structurally defined sites with appropriate ligands that bind the template substrate.[10] Different applications of molecularly imprinted polymers have been suggested, including their use for sensing,[11] material separation,[12] stimuli-triggered transport through membranes,[13] or slow release matrices.[14] Although the use of molecularly imprinted polymers (MIPs) as sensing materials seems obvious, several fundamental limitations are encountered. The density of imprinted sites is usually low, and hence, relatively thick MIP interfaces are needed, resulting in slow diffusion of the analyte and long time intervals for sensing. Furthermore, the thick sensing layer often prohibits communication between the bound analyte and the transducer on which the MIP is immobilized, e.g., electrodes, and thus, the readout signal of the sensing processes is perturbed. Albeit these difficulties notwithstanding, competitive optical assays for analyzing substrates in MIPs have been developed.[15] In recent studies, microgravimetric analyses of substrates were accomplished by the immobilization of MIPs on piezoelectric crystals.[16] For the electronic transduction of the recognition events of MIPs, it is essential to employ thin films in contact with the electronic transducers. Previously, different MIP films associated with electrodes[17] or field-effect transistors (FETs)[18] were used for electrochemical detection of different analytes. In the present study, we present a novel electrochemical method for the stereoselective and enantioselective detection of monosaccharides, using imprinted polymers. We describe the fabrication of thin polymer films composed of phenol and 3-hydroxyphenyl boronic acid linked to a specific monosaccharide on Au electrodes. We describe a competitive electrochemical assay for analyzing the specific monosaccharide and demonstrate stereoselective and chiroselective sensing.

## 2. Results and Discussion

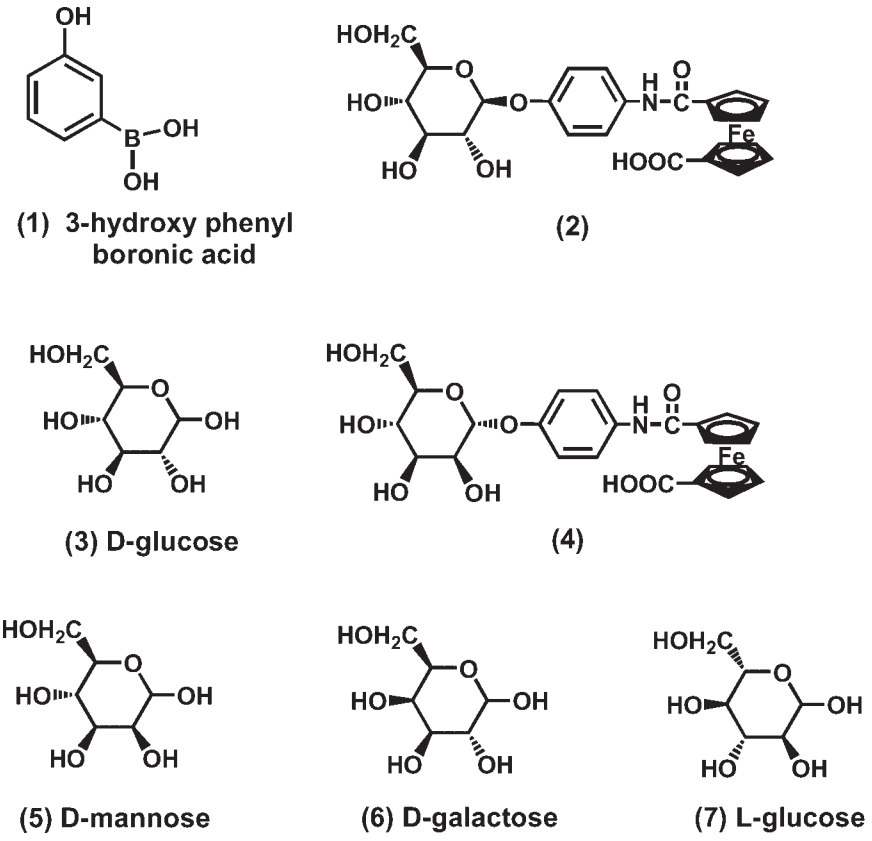
The compounds used in this study are shown in Scheme 1. The complexation of monosaccharides with the boronic acid ligand to form a boronic acid complex (Scheme 2A) is well established, and different monosaccharide sensors were developed based on this complex.[19] Previous studies have employed electropolymerization as a method to generate imprinted sites in polymers associated with electrodes.[20] Specifically, electropolymerized polyaniline containing the boronic acid ligand was used to imprint recognition sites for saccharides, and the effects of bound saccharides on the voltammetric response of the polymers were elucidated.

[*] Prof. I. Willner, E. Granot, Dr. R. Tel-Vered, O. Lioubashevski
Institute of Chemistry, The Hebrew University of Jerusalem
Jerusalem 91904 (Israel)
E-mail: willnea@vms.huji.ac.il

[**] This research was supported by the Israel Science Foundation.

ADVANCED FUNCTIONAL MATERIALS






**Scheme 1. Structure of compounds used in the study.**

Nonetheless, these polymer-functionalized electrodes did not yield electrochemical sensors. The present approach provides a competitive electrochemical assay for the analysis of saccharides in an imprinted electropolymerized polyphenol matrix. The method of generating the imprinted polymer film on the Au electrodes and the competitive electrochemical analysis of the monosaccharides are depicted, respectively, in Scheme 2B and C.

Phenol was electropolymerized on a Au electrode in the presence of 3-hydroxyphenyl boronic acid–monosaccharide complex under basic conditions (pH = 10.3), Figure 1A. The adsorbed monosaccharide was washed off from the film by immersing the electrode in 0.1 M HCl to yield the imprinted polymer. Figure 1B shows an atomic force microscopy (AFM) image of the resulting polymer on a Au support. The figure depicts a nonhomogenous polymer that yields ''bumps'' with a surface coverage of ca. 45% and heights of up to ca. 150 nm, and the average thickness of the film was evaluated to be 36 nm. X-ray photoelectron spectroscopy (XPS) analysis of the polymer film revealed an average atomic ratio of boron:carbon of ca. 0.01. This result suggests that the ratio of phenolic compounds used in the electropolymerization process is reflected with a similar ratio in the resulting polymer. The nonimprinted polymer film was prepared in a similar manner by the electropolymerization of phenol and 3-hydroxyphenyl boronic acid (in the absence of the monosaccharide). The method for analyzing the respective monosaccharides by electrochemical means is presented in Scheme 2C. This method employs a competitive assay between the association of the specific monosaccharide and the ferrocene-functionalized monosaccharide to the imprinted sites. For example, ferrocene-functionalized D-glucose (**2**), was used as a redox label for the analysis of D-glucose (**3**).

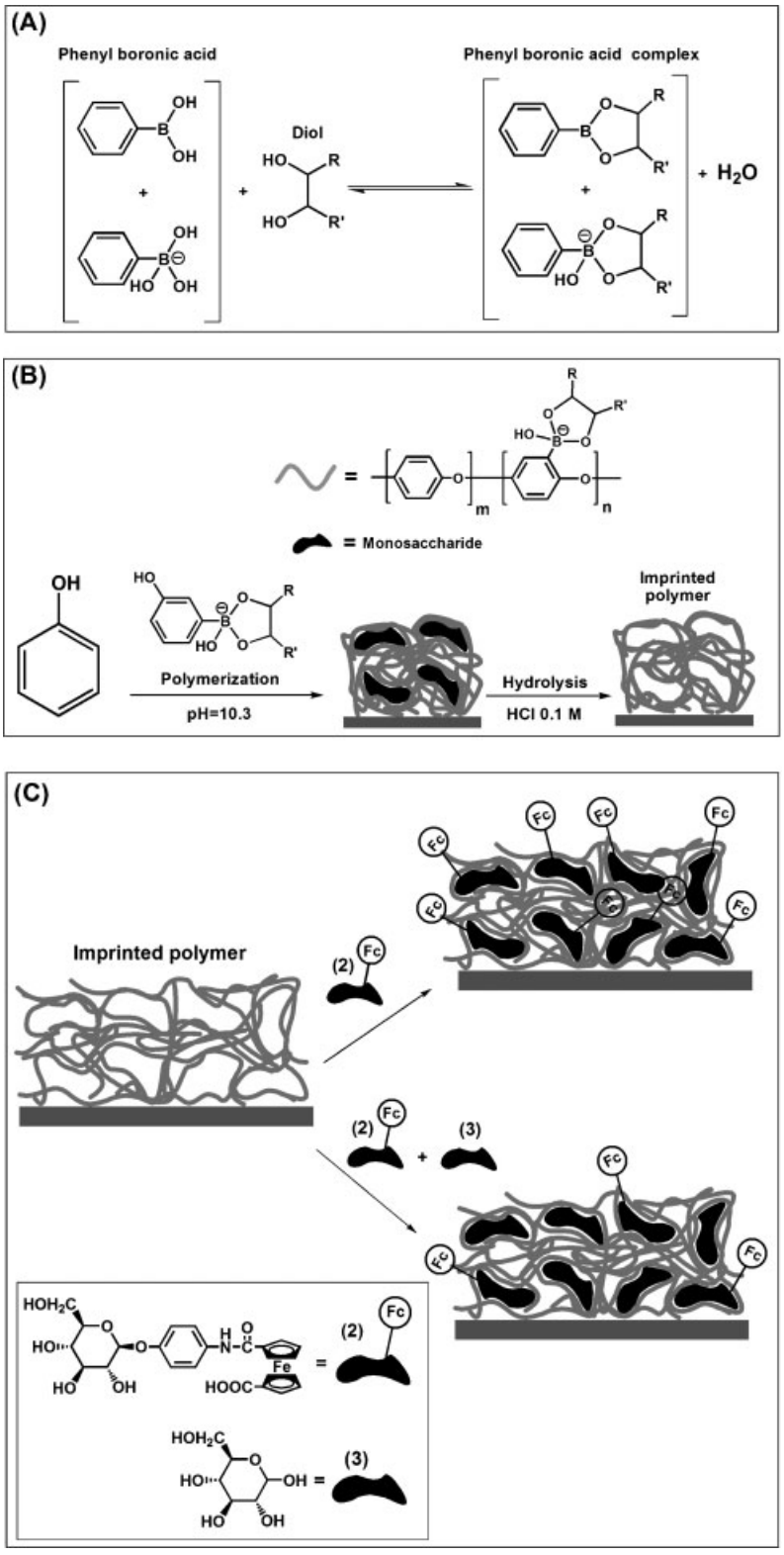
The analysis of **3** was performed by chronoamperometric measurements in the presence of the redox-active **2**. The redox response of **2** in the presence of D-glucose provides a quantitative measurement for D-glucose. The higher the amperometric response of the ferrocene-functionalized D-glucose **2**, the lower the concentration of D-glucose **3** in the analyzed samples. The redox wave of **2** is positively shifted by ca. 140 mV as compared to the quasi-reversible redox wave of ferrocene carboxylic acid. Figure 2 curves a–g show the time-dependent amperometric responses associated with the binding of the ferrocene-functionalized **2** at different bulk concentrations with the D-glucose-imprinted polymer. The current increases with time and levels off to a constant saturation value controlled by the equilibrium generated by the respective bulk concentration of **2** and the imprinted sites, as given by Equation 1

$$\text{Ferr.Sacch.} + \underset{(\alpha_p-\theta_p)}{\text{Polymer}} \overset{K_{ass.}}{\rightleftharpoons} \underset{(\theta_p)}{\text{Polymer-Ferr.Sacch.}} \quad (1)$$

$$\frac{1}{\theta_p} = \frac{1}{K_{ass.} \cdot [\text{Ferr.Sacch.}] \cdot \alpha_p} + \frac{1}{\theta_p} \quad \text{or} \quad K_{ass.} = \frac{\theta_p}{(\alpha_p - \theta_p) \cdot [\text{Ferr.Sacch.}]} \quad (2)$$

The association constant of **2** to the imprinted sites is given by Equation 2, where $\alpha_p$ is the total number of imprinted sites in the polymer film, and $\theta_p$ is the number of sites occupied by **2** at each bulk concentrations of **2**, i.e., $\theta_p$ is a fraction of $\alpha_p$. The coulometric analysis of the saturation values of the chronoamperometric response at each bulk concentration of **2** is proportional to $\theta_p$. Thus, the association constant, $K_{ass.}$, was found to be $(170 \pm 30)\ M^{-1}$, Figure 2, inset. The analysis of the data also allowed us to determine the charge associated with the total number of imprinted sites, which was found to be 3.41 mC, and therefore the total number of imprinted sites is $\alpha = 2.1 \times 10^{16}$. Knowing the thickness of the polymer film and the




**Scheme 2.** **A)** Preparation of the boronic acid complex. B) Preparation of the monosaccharide-imprinted polyphenol. (C) The competitive assay for the detection of D-glucose using the D-glucose-imprinted polymer.

electrode area, the density of imprinted sites was estimated to be $3.4 \times 10^{21}$ sites $cm^{-3}$.

The stereospecific binding affinity of the imprinted polymer to different monosaccharides was further investigated. Figure 3, curve a, shows the current responses of the D-glucose-imprinted polymer upon analyzing different concentrations of D-glucose **3** in the presence of ferrocene-functionalized D-glucose **2**, 2.5 mM. As the concentration of D-glucose increases, the amperometric response decreases. This is consistent with the fact that with competitive binding of the redox-active **2** and D-glucose **3** at the imprinted sites, less redox-label **2** can be associated with the imprinted sites as the concentration of D-glucose **3** increases. Figure 3, curve b, depicts the analysis of D-glucose by the competitive assay using the nonimprinted polymer. Clearly, only a residual amperometric response of ca. 50 μA is observed, regardless of the D-glucose concentration. Further selectivity studies related to the D-glucose-imprinted polymer were performed by employing **2** as redox indicator and analyzing other monosaccharides such as D-mannose (**5**), curve c, and D-galactose (**6**), curve d, by the competitive assay. Clearly, the nonimprinted monosaccharides **5** and **6** reveal a substantially lower affinity to the D-glucose-imprinted sites as compared to **3** (curve a). For example, at a D-glucose concentration of 2 mM, the current response of the redox label **2** drops from a value of 340 μA (at [D-glucose] = 0 mM) to 100 μA (at [D-glucose] = 2 mM). In the presence of **5** and **6**, under similar concentrations, the current decreases to 210 μA and 240 μA, respectively. It should be noted that the amperometric response of the ferrocene-tethered **2**, loaded on the D-glucose-imprinted polymer corresponds to 340 μA, Figure 3, while the saturated amperometric response of **2** upon dynamic loading of the polymer, Figure 2a, is only 120 μA. This apparent discrepancy is attributed to the fact that the loading of the polymer by **2**, Figure 3, is accompanied by equilibration of the electrode in the absence of an applied potential, whereas the dynamic binding of **2** to the imprinted polymer, Figure 2a, is examined under a constant potential, where the ferrocene units are oxidized. Presumably, the electrostatic repulsion between the ferrocene units leads to the lower loading of

ADVANCED FUNCTIONAL MATERIALS



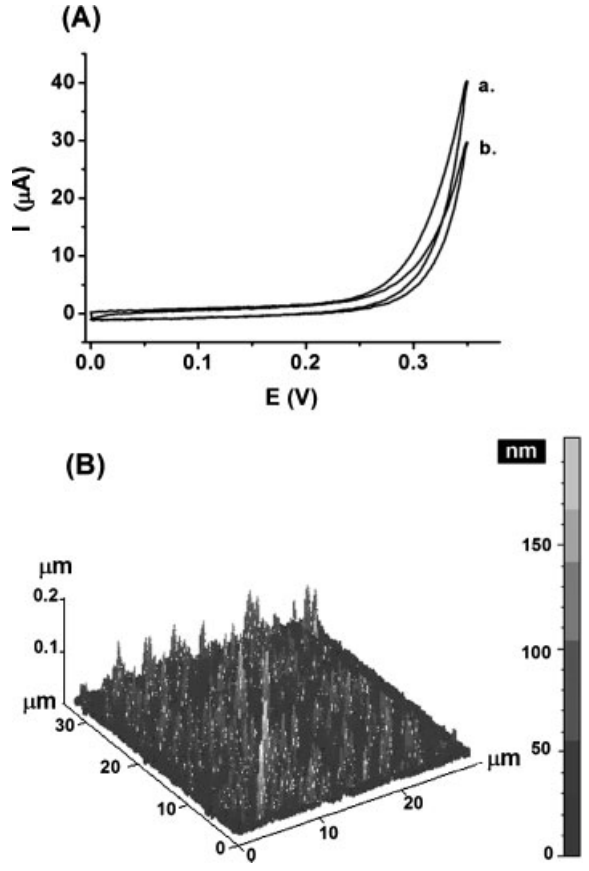



**Figure 1.** A) Electropolymerization of phenol in the presence of D-glucose-3-hydroxy phenyl boronic acid complex on a Au electrode, using two successive cyclic voltammetry scans, a) first scan, b) second scan. Electrolyte contains 5 mM phenol and 0.5 mM D-glucose-3-hydroxy phenyl boronic acid complex in PB, 0.1 M at pH = 10.3. The scan rate is 10 mV $s^{-1}$. B) An AFM image of a polyphenol electropolymerized Au electrode. Electropolymerization was performed according to the same experimental conditions as in Figure 1A. PB = phosphate buffer.

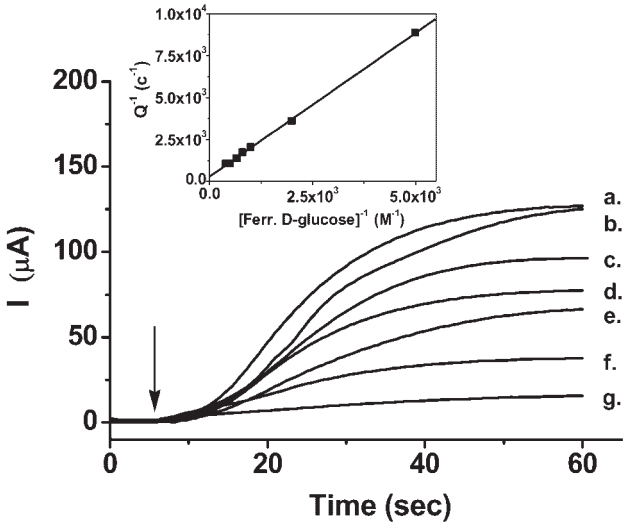



**Figure 2.** Time-dependent amperometric responses associated with the binding of the ferrocene-functionalized D-glucose (**2**) at different bulk concentrations: a) 2.50 mM; b) 2.00 mM; c) 1.50 mM; d) 1.25 mM; e) 1.00 mM; f) 0.50 mM, and g) 0.20 mM with the D-glucose-imprinted polymer film, measured in 0.05 M HEPES buffer at pH = 7.2. The measurements were initiated in a pure HEPES buffer solution and a concentrated volume of ferrocene-functionalized D-glucose was added at the time indicated by an arrow. The curves were recorded at E = 0.5 V vs. SCE. Inset: evaluation of the association constant, $K_{ass.}$, between ferrocene-functionalized D-glucose (**2**) and the D-glucose-imprinted polymer, according to Equation 2.

the imprinted polymer. We also note that the current response of **2** interacted with the nonimprinted polymer in the absence of D-glucose, Figure 3b is small compared to the maximal current response, 340 μA, of the **2**-loaded imprinted polymer in the absence of added D-glucose, Figure 3a. This is consistent with the fact that the nonimprinted polymer can be loaded by **2**, and the minute current response is due to non-specific association. These results indicate that the imprinted polymer reveals stereoselectivity towards the association of D-glucose compared to the other monosaccharides. The observed selectivity is particularly interesting since the other monosaccharides exhibit very similar molecular dimensions, and since the imprinted sites of D-glucose include the boronic acid ligands that may associate D-mannose as well as D-galactose. The observed selectivity is attributed, indeed, to the extremely delicate structural contours formed upon the process of imprinting the D-glucose. The boronic acid ligands in the D-glucose-imprinted sites are structurally oriented to bind the specifically oriented OH groups of the D-glucose. The association of the non-optimally oriented OH groups of D-mannose or D-galactose to the boronic acid ligand results in an incomplete structural fit with the imprinted sites, which leads to a lower binding affinity and, therefore, to the observed selectivity.

A comparative study was also performed on a D-mannose-imprinted polymer electrode that was fabricated in a similar manner to the D-glucose analogue, Scheme 2C. Similarly to the

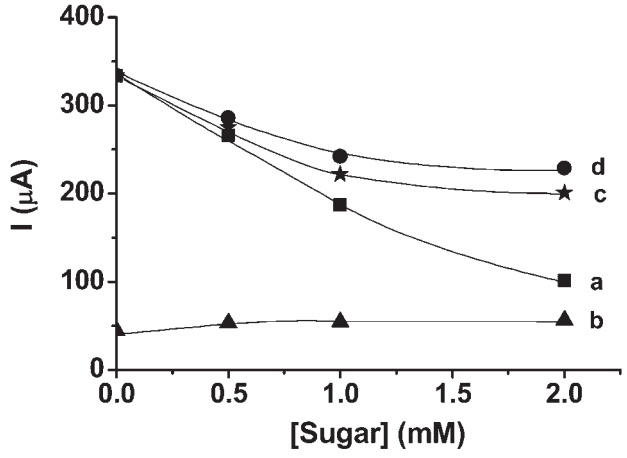



**Figure 3.** Current response upon the analysis of D-glucose by: a) The D-glucose-imprinted polymer film. b) The non-imprinted polymer film. Curves (c) and (d), correspond to the analysis of D-mannose and D-galactose, respectively. In all experiments a 2.5 mM of **2** is used as the redox label. The amperometric responses correspond to the steady-state currents measured at 0.5 V vs. SCE.

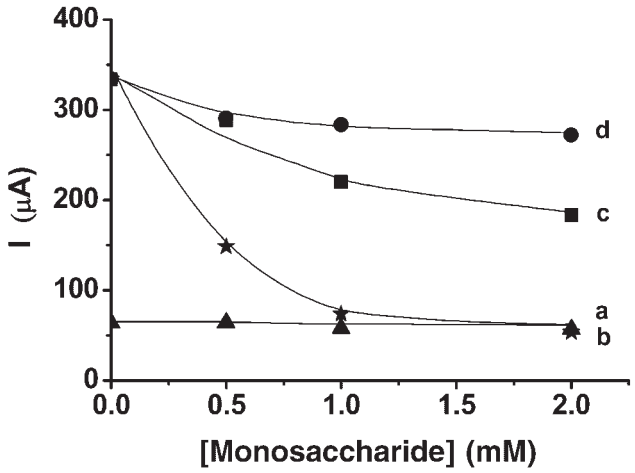



**Figure 4.** Current response upon the analysis of D-mannose by: a) The D-mannose-imprinted polymer film. b) The non-imprinted polymer film. Curves (c) and (d), correspond to the analysis of D-glucose and D-galactose, respectively, on the D-mannose-imprinted film. In all experiments a 2.5 mM of **2** is used as the redox label. The amperometric responses correspond to the steady-state currents at 0.5 V vs. SCE.

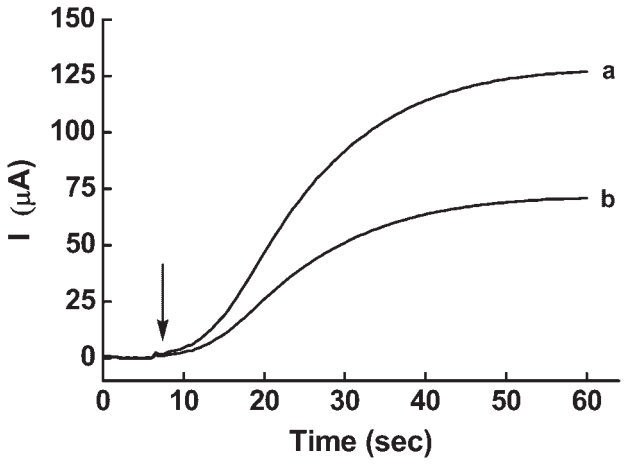



**Figure 5.** Time-dependent current responses upon the incorporation of 2.5 mM ferrocene-labeled-D-glucose (**2**) into a) D-glucose imprinted polymer film. b) L-glucose imprinted polymer film. The conditions of the experiments are detailed in the legend of Figure 8.

D-glucose-imprinted polymer, we studied the dynamics of association of the ferrocene functionalized mannose **4** to the D-mannose-imprinted polymer at different bulk concentrations of the ferrocene-modified saccharide. By analyzing the current responses of the redox-labeled D-mannose we were able to estimate the association constant of **4** with the D-mannose-imprinted sites to be $K_{ass.} = (870 \pm 40)\ M^{-1}$, and the density of sites in the polymer film was calculated to be $1.5 \times 10^{21}$ sites $cm^{-3}$.

Figure 4a, curve a, depicts the current responses of the Au electrode functionalized with the D-mannose-imprinted sites upon analysis with different concentrations of D-mannose (**5**) by the competitive assay, using a fixed concentration, 2.5 mM, of the ferrocene-functionalized D-mannose (**4**) as redox label. For comparison, curve b shows the control experiment, where the nonimprinted polymer is used. The resulting low, steady current, ca. 60 μA, implies that the nonimprinted polymer reveals a low binding affinity for the redox label **4**, and that the nonspecifically bound redox label is not affected by the presence of **5**. The selectivity of the imprinted sites for D-mannose was further demonstrated by applying the D-mannose-imprinted film-modified electrode to analyze D-glucose, **3**, curve c, and D-galactose, **6**, curve d. Compared to the significant decrease observed upon analyzing D-mannose, the currents associated with **4** upon analyzing D-glucose or D-galactose are substantially higher at similar concentrations as D-mannose. Thus, we realize that the affinity of **3** or **6** to the D-mannose-imprinted sites is substantially lower than that of D-mannose.

Our results suggest that polymer films that were produced by the electropolymerization of phenol with the phenol boronic acid complex, yield molecular contours with oriented boronic acid ligands that enable the accommodation of the respective monosaccharides and their coordination to the boronic acid ligands. These two effects act synergistically in the association of the specific monosaccharide with the imprinted sites, and lead to the observed stereoselectivity.

The stereoselectivity of the imprinted sites was further extended to demonstrate enantioselective recognition. Towards this goal, Au electrodes modified with imprinted polymer films for D-glucose and L-glucose were prepared. The time-dependent loading of the two polymer films by the ferrocene-functionalized D-glucose **2**, is depicted in Figure 5, curves a and b, respectively. Evidently, **2** yields a substantially higher saturation current in the D-glucose-imprinted film as compared to the L-glucose-imprinted film. That is, the

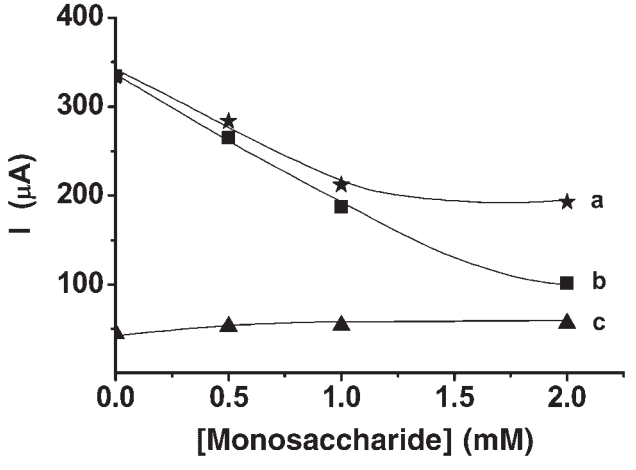



**Figure 6.** Amperometric responses upon the analysis of a) L-glucose and b) D-glucose by the D-glucose-imprinted polymer. c) The analysis of L-glucose by the non-imprinted polymer film (D-glucose yields a similar current response, Figure 3, curve b). In all experiments 2.5 mM of **2**, is used as the redox label. The amperometric response corresponds to the steady-state current measured at 0.5 V vs. SCE.

ADVANCED FUNCTIONAL MATERIALS



ferrocene-functionalized D-glucose (**2**) reveals higher affinity for the D-glucose-imprinted sites compared with the L-glucose imprinted sites. This enantioselectivity is further emphasized upon analyzing D-glucose (**3**) and L-glucose (**7**) with the D-glucose-imprinted polymer film. Figure 6 shows the current responses generated by the D-glucose-imprinted polymer-modified electrode upon analyzing different concentrations of L-glucose, curve a, and D-glucose, curve b, in the presence of **2**, 2.5 mM. The current associated with D-glucose is substantially lower than the current observed for the L-glucose. These results imply that enantioselectivity in the association of the L-glucose and D-glucose enantiomers to the D-glucose imprinted polymer was, indeed, achieved, and that L-glucose exhibits lower affinity for the D-glucose imprinted sites, as compared to the D-glucose.

## 3. Conclusions

The present study has introduced a new kind of electrogenerated molecularly imprinted polymer that is based on the electropolymerized poly(phenol/phenol-boronic acid) for the stereo-selective and enantio-selective recognition of monosaccharides. We have also developed a competitive assay for the electrochemical detection of the specific monosaccharides, using ferrocene-labeled monosaccharides as redox indicators. This method for generating molecular recognition sites by the electropolymerization of phenol and phenol boronic acid in the presence of other template molecules that include monosaccharide moieties, might be extended to other substrates, such as nucleotides or cofactors, e.g., FAD or $NAD(P)^+$.

## 4. Experimental

*Chemicals and Instrumentation*: 3-Hydroxyphenyl boronic acid (**1**), D-glucose (**3**), D-mannose (**5**), D-galactose (**6**), L-glucose (**7**), 4-aminophenyl $\beta$-D-glucopyranoside, 4-aminophenyl $\alpha$-D- mannopyranoside, 1,1′-ferrocenedicarboxylic acid, phenol, HEPES salt, and 1-(3-dimethylaminoproyl)-3-ethylcarbodiimide hydrochloride (EDC) were obtained from Sigma–Aldrich. Ultrapure water from Nanopure Diamond (Bornstead) source was used throughout all the experiments. Au-coated (50 nm gold layer) $2 \times 2$ cm glass plates (Analytical $\mu$-system, Germany) were used as working electrodes. Electrochemical measurements were performed in a standard three electrode electrochemical cell, consisting of a functionalized Au working electrode, a counter graphite rod ($d = 5$ mm) and a saturated calomel reference electrode (SCE). The electrochemical experiments were carried out using a PC-controlled (Autolab GPES software) electrochemical analyzer potentiostat/galvanostat ($\mu$Autolab, type III). AFM measurements were performed using a SMENA B (NT-MDT, Russia) atomic force microscope.

*Chemical Modification of the Electrodes*: Prior to the modification, the Au surfaces were treated with piranha solution (70% $H_2SO_4$ and 30% $H_2O_2$) for a period of 30 seconds and then extensively washed with ethanol and water and dried under a stream of $N_2$ (**CAUTION**: Piranha is a vigorous oxidant and should be used with extreme caution). The monosaccharide-3-hydroxyphenylboronic acid complex was prepared by reacting equimolar quantities of 3-hydroxyphenyl boronic acid (**1**) and D-glucose (**3**) or D-mannose (**5**), in phosphate buffer (PB), 0.1 M at pH = 10.3, for 24 h. The monosaccharide-imprinted polymer films were deposited on Au electrodes (exposed area 1.7 $cm^2$) by electropolymerizing 5 mM phenol and 0.5 mM of the specific monosaccharide-3-hydroxyphenylboronic acid complex in PB, 0.1 M at pH = 10.3. Electropolymerization was carried out using two successive cyclic voltammetry scans ranging between 0–0.35 V vs. SCE, at a scan rate of 10 $mV \cdot s^{-1}$, as shown in Figure 1. A similar procedure, excluding the presence of the monosaccharide-boronic acid complex, was employed in the fabrication of non-imprinted polymer-modified electrodes. The resulting modified electrodes were thoroughly rinsed with the PB solution to wash off remains of the reactants. Following electropolymerization, the monosaccharide was extracted from the imprinted polymer by immersing the electrode in 0.1 M HCl for 20 minutes at room temperature. Ferrocence-functionalized D-glucose (**2**) or D-mannose (**4**) were prepared by reacting 2.5 mM of 1,1′-ferrocenedicarboxylic acid with 2.5 mM of either 4-aminophenyl $\beta$-D-glucopyranoside or 4-aminophenyl $\alpha$-D-mannopyranoside in HEPES buffer, 0.05 M, pH = 7.2. The solution was stirred with 10 mM EDC for 2h at room temperature.

Received: May 3, 2007
Revised: August 7, 2007

[1] a) H. Gu, X. Su, K. P. Loh, *J. Phys. Chem. B* **2005**, *109*, 13611. b) T. Inoue, J. R. Kirchhoff, *Anal. Chem.* **2000**, *72*, 5755. c) C. Malitesta, F. Palmisano, L. Torsi, P. G. Zambonin, *Anal. Chem.* **1990**, *62*, 2735.

[2] a) M. Badea, A. Curulli, G. Palleschi, *Biosens. Bioelectron.* **2003**, *18*, 689. b) B. Lakard, G. Herlem, M. de Labachelerie, W. Daniau, G. Martin, J. C. Jeannot, L. Robert, B. Fahys, *Biosens. Bioelectron.* **2004**, *19*, 595. c) C. Malitesta, I. Losito, P. G. Zambonin, *Anal. Chem.* **1999**, *71*, 1366.

[3] a) L. M. Campos, A. Tontcheva, S. Guenes, G. Sonmez, H. Neugebauer, N. S. Sariciftci, F. Wudl, *Chem. Mater.* **2005**, *17*, 4031. b) R. Senadeera, N. Fukuri, Y. Saito, T. Kitamura, Y. Wada, S. Yanagida, *Chem. Commun.* **2005**, 2259. c) V. P. S. Perera, P. V. V. Jayaweera, P. K. Pitigala, P. K. Bandaranayake, G. Hastings, A. G. Perera, K. Tennakone, *Synth. Met.* **2004**, *143*, 283.

[4] a) M. Li, S. Tang, F. Shen, M. Liu, W. Xie, H. Xia, L. Liu, L. Tian, Z. Xie, P. Lu, M. Hanif, D. Lu, G. Cheng, Y. Ma, *Chem. Commun.* 2006, 3393. b) K. M. Maness, R. H. Terrill, T. J. Meyer, R. W. Murray, R. M. Wightman, *J. Am. Chem. Soc.* **1996**, *118*, 10609. c) S. Komaba, A. Amano, T. Osaka, *J. Electroanal. Chem.* **1997**, *430*, 97.

[5] a) E. Granot, E. Katz, B. Basnar, I. Willner, *Chem. Mater.* **2005**, *17*, 4600. b) O. A. Raitman, E. Katz, A. F. Bueckmann, I. Willner, *J. Am. Chem. Soc.* **2002**, *124*, 6487. c) S. V. Morozov, E. E. Karyakina, N. A. Zorin, S. D. Varfolomeyev, S. Cosnier, A. A. Karyakin, *Bioelectrochemistry* **2002**, *55*, 169. d) I. Willner, E. Katz, N. Lapidot, P. Baeuerle, *Bioelectrochem. Bioenerg.* **1992**, *29*, 29.

[6] a) E. Jager, O. Inganas, I. Lindstrom, *Science* **2000**, *288*, 2335. b) R. Baughman, *Synth. Met.* **1996**, *78*, 339. c) E. Jager, E. Smela, O. Inganas, *Science* **2000**, *290*, 1540. d) O. Inganas, I. Lindstrom, *Science* **1999**, *284*, 1281. e) E. Smela, O. Inganas, I. Lindstrom, *Science* **1995**, *268*, 1735. f) Y. Bar-Cohen, in *Biomimetics: Biologically Inspired Technologies* (Ed: Y. Bur Cohen ), CRC Press, Boca Raton, FL **2006**, Ch. 10, p. 267. g) M. Lahav, C. Durkan, R. Gabai, E. Katz, I. Willner, M. E. Welland, *Angew. Chem. Int. Ed.* **2001** *40*, 4095.

[7] a) A. Bossi, F. Bonini, A. P. F. Turner, S. A. Piletsky, *Biosens. Bioelectron.* **2007**, *22*, 1131. b) K. Haupt, *Chem. Commun.* **2003**, 171. c) A. Martin-Esteban, *Fresenius' J. Anal. Chem.* **2001**, *370*, 795.

[8] a) H. Huiqi, Y. Lei, K. Mosbach, *J. Mol. Recognit.* **2006**, *19*, 248. b) K. Haput, *Chem. Commun.* **2003**, *2*, 171.

[9] a) B. Sellergren, *Anal. Chem.* **1994**, *66*, 1578. b) B. Sellergren, *TrAC Trends Anal. Chem.* **1997**, *16*, 310.
[10] a) K. Haupt, K. Mosbach, *Chem. Rev.* **2000**, *100*, 2495. b) G. Wulff, *Chem. Rev.* **2002**, *102*, 1. c) A. G. Mayes, K. Mosbach, *Anal. Chem.* **1996**, *68*, 3769. d) A. G. Mayes, K. Mosbach, *TrAC Trends Anal. Chem.* **1997**, *16*, 321.
[11] a) A. Hillberg, K. Brain, C. Allender, *Adv. Drug Delivery Rev.* **2005**, *57*, 1875. b) S. Cosnier, *Anal. Bioanal. Chem.* **2003**, *377*, 507.
[12] a) M. Kempe, K. Mosbach, *J. Chromatogr. A* **1995**, *694*, 3. b) H. Huiqi, Y. Lei, K. Mosbach, *J. Mol. Recognit.* **2006**, *19*, 248. c) K. Haupt, P. A. G. Cormack, K. Mosbach, in *Biochromatography* (Ed: M. A. Vijayalakshami), Taylor and Francis, London **2002**, p. 419. d) V. T. Remcho, Z. J. Tan, *Anal. Chem.* **1999**, *71*, 248A. e) H. J. Wang, W. H. Zhou, X. F. Yin, Z. X. Zhuang, H. H. Yang, X. R. Wang, *J. Am. Chem. Soc.* **2006**, *128*, 15954.
[13] a) S. A. Piletsky, T. L. Panasyuk, E. V. Piletskaya, I. A. Nicholls, M. Ulbricht, *J. Membr. Sci.* **1999**, *157*, 263. b) J. M. Hong, P. E. Anderson, J. Qian, C. R. Martin, *Chem. Mater.* **1998**, *10*, 1029. c) J. Mathew- Krotz, K. J. Shea, *J. Am. Chem. Soc.* **1996**, *118*, 8154.
[14] a) C. Bodhibukkana, T. Srichana, S. Kaewnopparat, N. Tangthong, P. Bouking, G. P. Martin, R. Suedee, *J. Controlled Release* **2006**, *113*, 43. b) V. Bajpai, P. He, L. Dai, *Adv. Funct. Mater.* **2004**, *14*, 145.
[15] a) J. L. Suarez-Rodriguez, M. E. Diaz-Garcia, *Biosens. Bioelectron.* **2001**, *16*, 955. b) I. Surugiu, J. Svitel, L. Ye, K. Haupt, B. Danielsson, *Anal. Chem.* **2001**, *73*, 4388.
[16] a) S. P. Pogorelova, T. Bourenko, A. B. Kharitonov, I. Willner, *Analyst* **2002**, *127*, 1484. b) L. Cao, S. F. Y. Li, X. C. Zhou, *Analyst* **2001**, *126*, 184.
[17] S. Kroeger, A. P. F. Turner, K. Mosbach, K. Haupt, *Anal. Chem.* **1999**, *71*, 3698.
[18] a) M. Zayats, M. Lahav, A. B. Kharitonov, I. Willner, *Tetrahedron* **2002**, *58*, 815. b) S. P. Pogorelova, M. Zayats, T. Bourenko, A. B. Kharitonov, O. Lioubashevski, E. Katz, I. Willner, *Anal. Chem.* **2003**, *75*, 509.
[19] a) G. Wulff, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1812. b) S. Jiang, J. O. Escobedo, K. K. Kim, O. Alptuerk, G. K. Samoei, S. O. Fakayode, I. M. Warner, O. Rusin, R. M. Strongin, *J. Am. Chem. Soc.* **2006**, *128*, 12221. c) T. D. James, K. R. A. Sandanayake, R. Iguchi, S. Shinkai, *J. Am. Chem. Soc.* **1995**, *117*, 8982. d) N. Sallacan, M. Zayats, T. Bourenko, A. B. Kharitonov, I. Willner, *Anal. Chem.* **2002**, *74*, 702. e) W. Wang, X. Gao, B. Wang, *Curr. Org. Chem.* **2002**, *6*, 1285. f) T. D. James, K. R. A. Sandanayake, S. Shinkai, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1910.
[20] B. A. Deore, Z. Chen, T. Nagaoka, *Anal. Chem.* **2000**, *72*, 3989.
[21] a) B. A. Deore, S. Hachey, M. S. Freund, *Chem. Mater.* **2004**, *16*, 1427. b) B. A. Deore, M. S. Freund, *Analyst* **2003**, *128*, 803.