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Poly(aniline boronic acid)-based conductimetric sensor of dopamine

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Interdigitated microelectrodes derivatized with poly(aniline boronic acid) show a dopamine-sensitive response at pH 7.4.

The reversible complexation of boronic acids or esters with diols or hard base anions (*e.g.* F^-) to form anionic tetrahedral boronates has been used in numerous applications, including the selective transport of saccharides[1,2] and catecholamines,[3,4] molecular and anionic recognition,[5–7] and the racemic resolution of free sugars.[8] In the field of chemosensing, the optical (*i.e.* fluorescence, circular dichroism, absorption) or electrochemical (*i.e.* voltammetry, potentiometry) response of boron-containing receptors has been preferentially chosen as the signal transduction pathway of the binding event.[5–7,9] Recently, we[10–13] and others[14–16] have developed anion- and sugar-responsive chemically modified electrodes from the electropolymerization of different boronic acid- and boronate-substituted aromatic compounds.

In the pursuit of our investigations concerning the design of boronic acid-based sensory materials, we report herein a novel dopamine (DA) sensor consisting of an interdigitated microarray electrode coated with poly(aniline boronic acid) as the polyreceptor system. Under physiological conditions, the covalent anchoring of the aromatic diol to the immobilized boronic acid groups results in a decrease in the electrical conductivity of functionalized polyaniline. The conductivity changes were detected by the decrease in the drain current (I_d) between the two arrays at a constant offset potential. Dopamine is a biogenic amine acting as a neurotransmitter in the brain.[17] It has received considerable attention because of its known or suspected role in a variety of neuropsychiatric disorders such as Parkinson's disease and schizophrenia.[18] Consequently, the fabrication of implantable microelectronic devices which could operate in *in vivo* conditions with high sensitivity and selectivity is particularly challenging. Most of the pretreated or polymer-modified electrodes used for the electrochemical determination of DA did not contain binding centers capable of interacting specifically with the biologically relevant molecule.[19–24] For these systems, an ion-exchange membrane (*e.g.* Nafion) acting as an electrostatic barrier against potential interferents was often required to enhance their selectivity.[20,22,23] However, such electrodes showed serious drawbacks, such as non-uniform membrane thickness and accumulation or trapping of oppositely charged ions, giving poorly reproducible results.

In this study, the poly(aniline boronic acid **1**)-based conductimetric sensor can detect DA at physiological pH and in the presence of excess ascorbic acid. Moreover, it can be easily regenerated in acidic medium owing to the pH-sensitive boronic acid–DA complexation equilibrium.

An array of two platinum interdigitated microelectrodes (IMEs) having an interelectrode spacing of 10 μm is interconnected with a poly(aniline boronic acid) deposit potentiodynamically electrogenerated between −0.1 and 0.9 V *vs.* SCE at 0.1 V s^{-1} in 0.5 M H_2SO_4 containing 0.05 M **1** and 0.2 M KF.[25–27] The interconnection of IMEs requires the presence of fluoride in the electrolytic solution owing to the activation of the electropolymerization process caused by the complexation of this hard base with **1**.[10] A typical cyclic voltammogram of poly(**1**)-coated IMEs obtained in 0.5 M H_2SO_4 is shown in Fig. 1. It shows a first reversible redox process at *ca.* 0.17 V followed by a less well-resolved second one at 0.46 V.

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The electrochemistry of polyaniline in acidic aqueous solution has been largely described in the literature[28] and the two systems observed here correspond to the insulating protonated leucoemeraldine/conducting protonated emeraldine and conducting protonated emeraldine/insulating pernigraniline transitions. After a small potential difference (typically 50 mV) is applied between the two electrodes (source and drain), the flowing drain current I_d is recorded at a low scan rate (2–10 mV s^{-1}) as a function of gate voltage V_g controlled with respect to SCE.[27] Therefore, in this transistor configuration, the I_d–V_g curve shown in Fig. 1 reflects changes in relative polymer conductivity as a function of electrochemical potential. A finite potential window of high conductivity is observed from 0.15 to 0.50 V with conductivity changes coinciding with cyclic voltammetry peaks. Moreover, as already reported by Wrighton and co-workers for polyaniline,[26] a scan rate independent hysteresis is also visible. The conducting properties of poly(**1**) are not degraded for pH values < 2, as proved by the reproducibility of the I_d–V_g curve on subsequent scans.

Toward the goal to detect DA in physiological conditions, the poly(**1**)-coated IMEs are then analysed in a pH 7.4 phosphate buffer solution (PBS). The stability of their voltammetric and conductimetric characteristics is found to be reached in PBS after *ca.* 2 h. Once equilibrated, the modified IMEs exhibit a single reversible redox process at −0.12 V, as a result of the coalescence of the two systems observed in 0.5 M H_2SO_4 (Fig. 2). Moreover, the potential window where resistivity is low narrows with a resistivity minimum centered around 0 V at pH 7.4 (Fig. 3). Under these conditions, poly(**1**) is found to be much less electroactive and conducting. Indeed, the maximum drain current declines by a factor of ~14 in comparison with the value obtained in 0.5 M H_2SO_4. However, the fact that poly(**1**) is still conducting at pH ~7 is somewhat unexpected because the polyaniline films electrosynthesized in the absence of a stabilizing anionic polymer, such as Nafion or poly(vinylsulfonate), are usually electroinactive above pH 5. Therefore, this result demonstrates that the boronic acid moieties enable extension of the electrochemical activity and the conductivity of polyaniline towards higher pH. It can be explained by strong

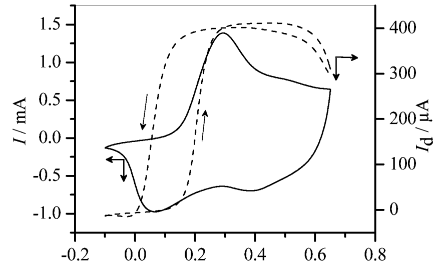

Fig. 1 (Solid line) Cyclic voltammogram at 0.05 V s^{-1} of poly(**1**)-coated IMEs in 0.5 M H_2SO_4 and (dashed line) corresponding I_d–V_g curve at 2 mV s^{-1} (50 mV offset potential). Electropolymerization charge: ~700 mC cm^{-2}.

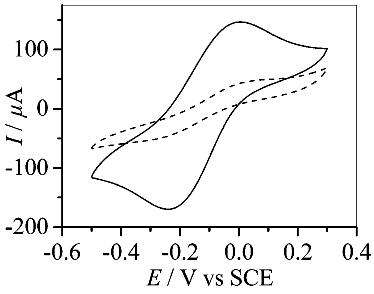

Fig. 2 Cyclic voltammograms at 0.05 V s^{-1} of poly(**1**) at pH 7.4 (solid line) in the absence and (dashed line) in the presence of 5×10^{-3} M dopamine.

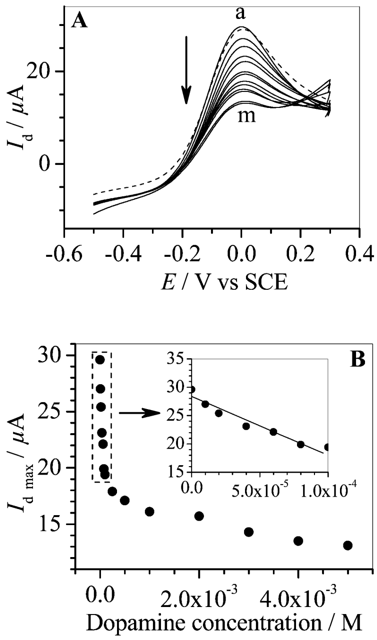

Fig. 3 (A) I_d–V_g curves at 10 mV s^{-1} (50 mV offset potential) of poly(**1**)-coated Pt IMEs (solid line), a) in the absence and in the presence of (b) 10^{-5}, (c) 2×10^{-5}, (d) 4×10^{-5}, (e) 6×10^{-5}, (f) 8×10^{-5}, (g) 10^{-4}, (h) 2.5 $\times 10^{-4}$, (i) 5×10^{-4}, (j) 10^{-3}, (k) 2×10^{-3}, (l) 4×10^{-3} and (m) 5×10^{-3} M dopamine; (dashed line) in the presence of 5 mM ascorbic acid. (B) Corresponding calibration curve for dopamine.

intra- or interchain tetrahedral boron–nitrogen interactions[29,30] which would stabilize the protonated emeraldine form to some extent at pH 7.4.

In the presence of DA, the device shows analyte-induced changes in resistance. A decrease in the film conductivity as measured by I_d–V_g experiments is observed with the addition of DA (Fig. 3A). For example, a 2 mM solution of DA leads to a *ca.* 2-fold decrease in the maximum I_d ($I_{d\ max}$). As can be seen in Fig. 2, this chemoresistive effect is commensurate with an electroactivity loss of poly(**1**). It must be pointed out that the conductimetric response of poly(**1**) is not changed in the presence of ascorbic acid up to a tested concentration of 10 mM. Moreover, the interaction with DA is specific for the boronic acid-containing polymer, as $I_{d\ max}$ of unfunctionalized polyaniline is not modified in the presence of DA when analysed at pH 2.1.[31] The decrease in the film resistance is expectedly due to steric effects caused by the binding of DA to the immobilized boronic acid moieties and leading to conformational perturbations of poly(**1**), as already observed with saccharides.[5,14] The $I_{d\ max}$ – (DA concentration) calibration curve displayed in Fig. 3B is characterized by an initial linear plot at low DA concentrations (< 0.1 mM) followed by a plateau for larger concentrations indicating that all the binding sites in the film are occupied. The detection limit is found to be below 10 μM. Another important feature is that the original state of this conductimetric sensor can be recovered after immersion of poly(**1**)-coated IMEs in 0.5 M H_2SO_4 for few min. After this relatively simple chemical treatment, the voltammetric and conductimetric responses are found to be similar to those shown in Fig. 1, indicating that the free form of the immobilized boronic acid moieties has been regenerated.

In conclusion, the poly(**1**)-based sensor shows a reversible chemoresistive response to dopamine without interference by ascorbic acid. The selectivity of this device is attributed to the DA binding to the immobilized boronic acid groups. Some parameters, such as the film thickness, must now be optimized in order to improve its sensitivity.

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