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Bioelectrochemistry 59 (2003) 11–19
Bioelectrochemistry
www.elsevier.com/locate/bioelechem

Simultaneous electroanalysis of dopamine and ascorbic acid using poly (*N*,*N*-dimethylaniline)-modified electrodes

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Received 25 February 2002; received in revised form 23 August 2002; accepted 28 August 2002

Abstract

Glassy carbon (GC) electrode is modified with an electropolymerized film of *N*,*N*-dimethylaniline (DMA). This polymer (PDMA) film-coated GC electrode is used to electrochemically detect dopamine (DA) in the presence of ascorbic acid (AA). Polymer film has the positive charge in its backbone, and in neutral solution DA exists as the positively charged species whereas AA exists as the negatively charged one. In cyclic voltammetric measurements, favorable ionic interaction (i.e., electrostatic attraction) between AA and PDMA film causes a large negative shift of the oxidation potential for AA compared to that at the bare electrode. Oxidation potential for DA is positively shifted due to the electrostatic repulsion. The PDMA film shows hydrophobicity by incorporating uncharged hydroquinone molecule within the film. DA is also incorporated into the film due to hydrophobic attraction even though DA has a positive charge. The responses of DA and AA at polymer-modified electrodes largely change with the concentration of the monomer (i.e., 0.2, 0.1 and 0.05 M DMA) used in electropolymerization and thus with the film thickness. Hydrophobicity of the polymer film shows great influence on the voltammetric responses of both DA and AA. In square wave voltammetric measurements, the PDMA film-coated electrode can separate the DA and AA oxidation potentials by about 300 mV and can detect DA at its low concentration (e.g., 0.2 μM) in the presence of 1000 times higher concentration of AA, which is close to the physiological level. AA oxidizes at more negative potential than DA. The electrode response is not affected by the oxidized product of AA. So unlike the bare electrode, the fouling effect as well as the catalytic oxidation of AA by the oxidized form of DA are eliminated at the PDMA film-coated GC electrode. The electrode exhibits the stable and sensitive response to DA.

Keywords: Electropolymerization; Poly (*N*,*N*-dimethyl aniline); Dopamine; Ascorbic acid; Hydrophobicity

1. Introduction

Neurotransmitters (NTs) are the chemical messengers that transmit a message from one neuron to the next. This transmission proceeds by the secretion of NTs from one neuron and then their binding to the specific receptor located on the membrane of the target cell [1]. This interaction between NT and the receptor is one of the major modes of communication between neurons [2]. Dopamine (DA), the most significant catecholamine, belongs to the family of excitatory chemical NT [3] and plays a very important role in the functioning of central nervous, renal, hormonal and cardiovascular system [2,4]. Dysfunction of dopaminergic system in central nervous system (CNS) is related to neurological disorders such as schizophrenia, Parkinson's disease and to HIV infection [5,6]. The postsynaptic dopamine receptors have been divided into two major subtypes, D_1 and D_2, based on their adenylate cyclase-related activity [7]. Many attempts were taken to discriminate the different selectivity of dopamine analogs in binding with specific receptor. Bone et al. [8] showed that hydrophobic factor is one of the important factors that are responsible for selective DA receptor–ligand binding (i.e., D_1 receptor selectivity). Dopamine was found to be a most potent neurotransmitter competitor for those ligands that selectively recognize D_1 receptor [9,10].

Electrochemical detection of DA has received much interest because of its importance in CNS and easy oxidation property. In the electroanalysis of NTs, carbon

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doi:10.1016/S1567-5394(02)00156-1

electrodes have been widely used compared to metal electrodes due to its biocompatibility with tissue, having low residual current over a wide potential range and having minimal propensity to show a deteriorated response as a result of electrode fouling [11–13]. A major interference is created by ascorbic acid (AA) which presents by 10^3 times at higher level than DA in human brain [14]. Although AA oxidizes by several hundred millivolts at more positive potential than DA at carbon electrodes, in the presence of DA, a homogeneous catalytic oxidation of AA occurs by oxidized DA [15]. This results in an incorrect measurement of DA. For selective detection of DA, many different strategies have been used to modify the electrode surface. These include modification by iodide [16], ascorbic acid oxidase [17], polymer film [18–22], and self-assembled monolayers of mercaptoalkanes [23–26], electrochemical pretreatment [27] and covalent modification [28].

Polymer-modified electrodes (PMEs) prepared by electropolymerization have received extensive interest in the detection of analytes because of its selectivity, sensitivity and homogeneity in electrochemical deposition, strong adherence to electrode surface and chemical stability of the film [29,30]. Selectivity of PMEs as a sensor can be attained by different mechanisms such as size exclusion [31], ion exchange [21] and hydrophobic interaction [32]. Information concerning the hydrophobicity of the coating films can help to better evaluate the sensitivity of the examined sensor to the desired analytes.

Electropolymerization of *N*,*N*-dialkyl aniline (DAA) on electrode surface has been studied by many groups [35–37]. The anion exchange property and electrode kinetics of metal complexes incorporated into the polymer films were also studied [34–36]. This polymer film is considered to be a promising material in modification of electrode surface due to having some advantageous properties (e.g., pH-independent anion exchange property, strong attachment to the electrode surface and high chemical stability in air). The present study is concerned with the simultaneous detection of dopamine in the presence of ascorbic acid by using poly (*N*,*N*-dimethyl aniline) (PDMA) film-coated electrode (Scheme 1). The PDMA film was prepared by electropolymerization of DMA on glassy carbon (GC) electrode surface. Also, its cationic and hydrophobic behavior was examined.

2. Experimental

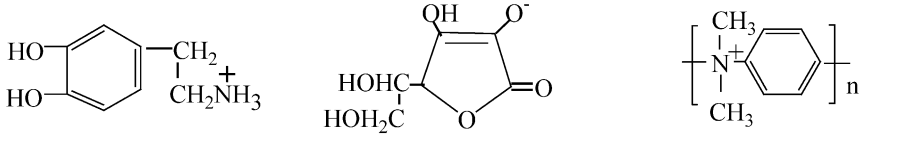
2.1. Materials

Monomer used in electropolymerization, i.e., *N*,*N*-dimethyl aniline (DMA), was purchased from Tokyo Kasei Chemical Industry and used without further purification. Dopamine hydrochloride (Kanto Chemical) and ascorbic acid (Aldrich) were used as received. Phosphate buffer solution (0.2 M, pH 7) was prepared by using $Na_2HPO_4{\cdot}12H_2O$ and $NaH_2PO_4{\cdot}2H_2O$ (Kanto). All other reagents were of analar grade and were used as received. All solutions were prepared with deionized water purified by Milli-Q system (Millipore, Japan).

2.2. Apparatus and procedures

Electrochemical measurements were performed at laboratory temperature (25 ± 1 °C) by using a standard three-electrode, two-compartment configuration with a glassy carbon (GC, diameter: 3 mm) electrode as working electrode, a Pt wire as counter electrode and a NaCl-saturated Ag|AgCl electrode as reference electrode which was used with salt bridge. All electrochemical experiments (i.e., electropolymerization, cyclic voltammetry and square wave voltammetry) were carried out using computer-controlled electrochemical analyzer (BAS 50 B/W). To record square wave voltammograms (SWVs), the following instrumental parameters were used: step potential, 4 mV; square wave amplitude, 25 mV; frequency, 15 Hz; quiet time, 2 s; and sensitivity, 10 μA. The thickness of the polymer film was measured by using Surface Profiler DEKTAK-3030 (VEECO Instruments Inc.).

The surface of electrode was polished first on fine emery paper and then with 1.0 and 0.06 μm alumina powder, and finally sonicated with Milli-Q water for 7–10 min. Before electropolymerization, the polished electrode was electrochemically pretreated in 0.2 M phosphate buffer solution (pH 7) by scanning repeatedly the electrode potential between -0.2 and $+2.0$ V vs. $Ag|AgCl|NaCl_{(sat)}$ at 10 V s^{-1} for 20 min. The PDMA film was deposited on the pretreated electrode surface by continuous electrooxidation of the corresponding monomer of 0.2, 0.1 or 0.05 M in 0.5 M Na_2SO_4–H_2SO_4 solution (pH 1) in the potential range -0.2 to $+1.5$ V at 50 mV s^{-1} for 1 h. The film-deposited



Dopamine (DA) (at pH 7) | Ascorbic acid (AA) (at pH 7) | Poly (*N*,*N*-dimethyl aniline) (PDMA)

Scheme 1. Structures of dopamine, ascorbic acid and poly (*N*,*N*-dimethyl aniline).

electrode was washed with 0.05 M H_2SO_4 solution and then with 0.2 M phosphate buffer solution (pH 7). All sample solutions were deoxygenated by bubbling N_2 gas before each experiment.

2.3. Measurement of the film thickness

The film thickness (ϕ) under dry state was measured using the previously reported procedure [38,39]. Measurement of the film thickness requires a sharp boundary between the clean portion of the electrode and a part covered by polymer film. Such type of boundary was created by covering the GC plate electrode (26×11 mm^2) with adhesive insulating tape, keeping a portion (6.35 mm^2) uncoated. This uncovered portion then acted as a working electrode and the polymer film was electrochemically deposited by the previously mentioned procedure. The electrode was washed with milli-Q water and then dried in silica gel for overnight. After that the adhesive tape was stripped from the GC plate. The average difference in the surface profile between the clean portion and polymerized portion of GC plate, measured by the surface profiler, was taken as the film thickness under dry state.

3. Results and discussion

3.1. Preparation of PDMA film

The typical cyclic voltammogram for continuous oxidation of DMA was obtained, and agreed closely with that in the previous reports [33–35]. Similar voltammograms were obtained throughout the experiments, reflecting the reproducibility of the polymerization process. The GC electrode surface was electrochemically pretreated prior to polymerization. Such a pretreatment causes the formation of some functional groups (e.g., –OH, –COOH) on the electrode surface as well as increasing the surface roughness [40]. Thus, well deposition of the positively charged film was achieved. This formed polymer film showed well cationic property: the positively charged sites of the polymer film strongly attract negative redox couple $[Fe(CN)_6]^{3-/4-}$ into the film and repel positive redox couple $[Ru(NH_3)_6]^{2+/3+}$ from the film, which was confirmed based on cyclic voltammograms demonstrating favorable [34,36] or unfavorable incorporation of the redox species into the film (data not shown). Note that the steady state incorporation reached was observed to depend on the ionic interaction between the polymer film and the analytes. As the positive charge of the film is independent of the solution pH, similar behavior was observed in acidic, neutral and alkaline solutions.

3.2. Oxidation of AA

Fig. 1 shows the cyclic voltammograms (CVs) of AA at bare and PDMA film-coated GC electrodes. The pK_a value

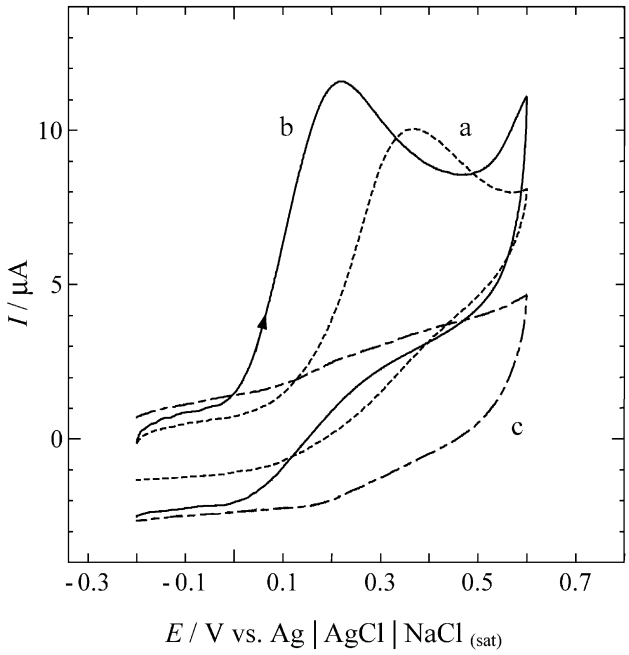


Fig. 1. Cyclic voltammograms (CVs) for 0.5 mM AA in 0.2 M phosphate buffer solution (pH 7) at (a) bare and (b) PDMA film-coated GC electrodes. Dotted-dashed line (c) shows the CV of the PDMA film-coated GC electrode in 0.2 M phosphate buffer solution (pH 7). Potential scan rate: 100 mV s^{-1}.

of AA is 4.17 [24], and thus it exists as a negatively charged species at neutral pH. Oxidation of AA at bare electrode is generally believed to be totally irreversible and requires high over potential. Also, no reproducible electrode response is obtained due to fouling of the electrode surface by the adsorption of the oxidized product of AA. At the bare GC electrode, AA oxidizes at 350 mV vs. Ag|AgCl|$NaCl_{(sat)}$, while at the cationic PDMA film-coated GC electrode a large negative shift (ca. 150 mV) of the oxidation potential as well as increase in peak current were observed. This negative shift of oxidation potential may be due to the favorable electrostatic attraction between the cationic film and anionic AA. Such an interaction would lead to the increase in concentration of AA within the film.

3.3. Oxidation of DA

Fig. 2A shows the CVs of DA at bare and PDMA film-coated GC electrodes. At pH 7, DA exists as a cation with a positively charged amino group (pK_a 8.9) [24]. In both cases, quasi-reversible responses were obtained. At the bare electrode the peak separation, ΔEp, is 65 mV at potential scan rate of 100 mV s^{-1}, while at the PDMA film-coated GC electrode, ΔEp is 97 mV. Thus, the reversibility of the electrode reaction decreased at the polymer-modified electrode. Also at the polymer-modified electrode the current response was decreased significantly. The peak potential for the oxidation of DA was shifted to the positive direction of potential at the polymer-modified electrode. These results

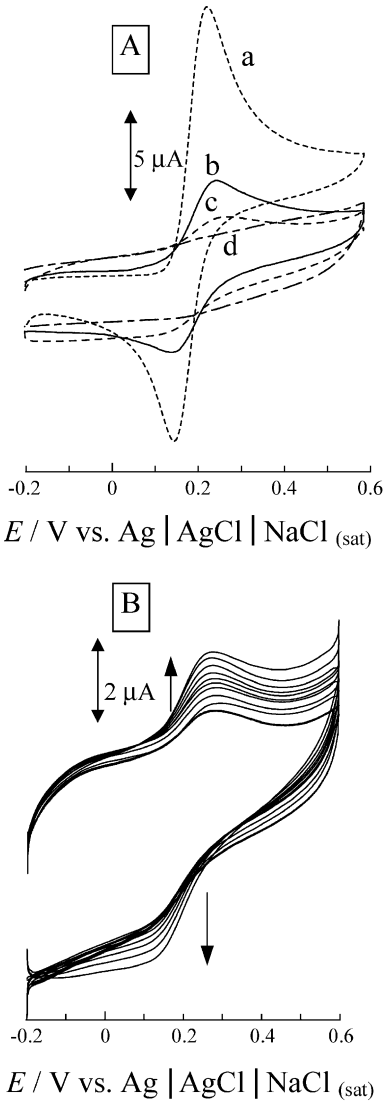


Fig. 2. (A) Cyclic voltammograms for 0.5 mM DA in 0.2 M phosphate buffer solution (pH 7) at (a) bare and (b) PDMA film-coated GC electrodes. Dotted-dashed line (d) shows the CV of the PDMA film-coated GC electrode in phosphate buffer solution (pH 7). (c) CV response for PDMA film-coated electrode obtained after continuous potential scanning in 0.5 mM DA solution and transfer to the fresh supporting electrolyte solution. (B) CV response obtained for PDMA-film coated electrode at every 10-min intervals during continuous potential scanning in 0.5 mM DA solution. Potential scan rate: 100 mV s^{-1}.

may be attributed to the electrostatic repulsion of cationic DA with the PDMA film. Fig. 2B shows the CV response obtained for the PDMA film-coated electrode at 10-min intervals during continuous potential scanning in DA solution. Both the oxidation and reduction peak currents were observed to increase with potential scanning and finally, well-defined steady-state redox response was obtained. After that, when the electrode was transferred to the fresh supporting electrolyte solution, a stable redox response was found (Fig. 2A, curve c). From this it can be stated that DA is confined stably in the PDMA film by stronger hydrophobic attraction than electrostatic repulsion between them.

3.4. Hydrophobic behavior of PDMA film

Fig. 3A shows the CV responses of neutral species, hydroquinone (HQ), at bare and PDMA film-coated GC

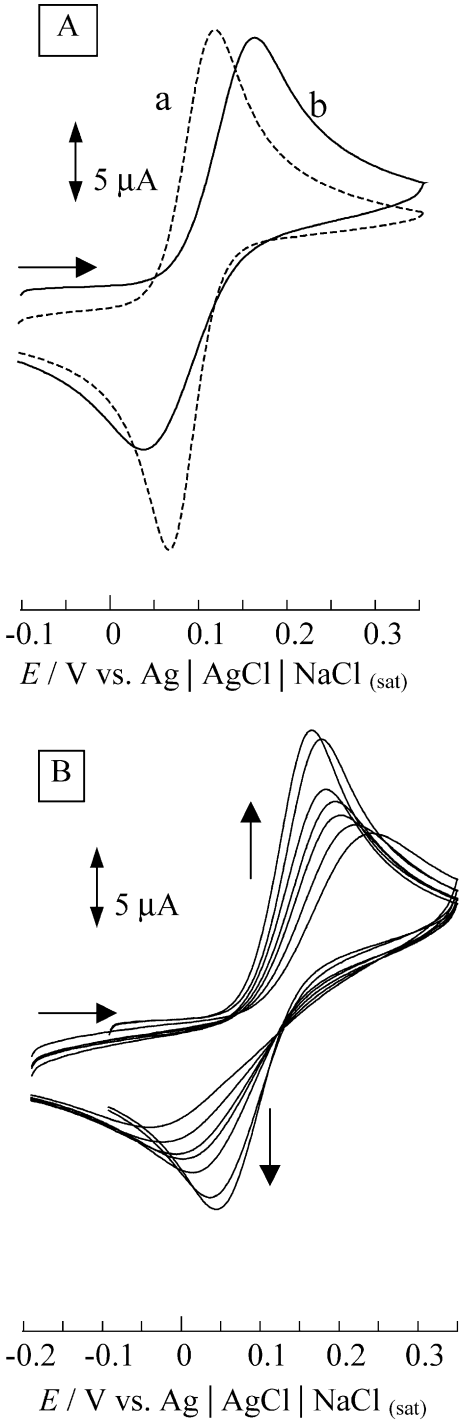


Fig. 3. (A) Curve a: cyclic voltammogram for 0.5 mM HQ in 0.2 M phosphate buffer solution (pH 7) at bare GC electrode; Curve b: cyclic voltammogram recorded after incorporation of HQ into PDMA film and then transfer of PDMA film-coated GC electrode into 0.2 M phosphate buffer solution (pH 7). (B) CV response obtained for PDMA film-coated electrode at 20-min intervals during continuous potential scanning in 0.5 mM HQ solution. Potential scan rate: 50 mV s^{-1}.

electrodes. HQ was observed to be gradually incorporated into the film with the increase in redox peak currents as well as the decrease in the separation between anodic and cathodic peak potentials (Fig. 3B). After reaching the steady state, the electrode was washed with buffer solution and then the CV response was measured in the solution containing only supporting electrolyte (Fig. 3A, curve b). Then the electrode gave a well-defined redox wave. So, HQ is well incorporated within the film as in the case of $[Fe(CN)_6]^{3-/4-}$. In the latter case, the incorporation occurred via anion exchange with SO_4^{2-}, the supporting electrolytic anion that was incorporated into the film during the electropolymerization process [35]. On the other hand, in the case of HQ, such an ionic exchange may not be involved. Instead, the incorporation of HQ into the film is considered to occur via a hydrophobic interaction between them. So, the PDMA film posses both ionic (anion exchange) and hydrophobic properties, which enable to favorably incorporate anionic and/or neutral hydrophobic species in its matrix.

In *in vivo* dopamine–dopamine receptor binding strategy, hydrophobic aromatic interaction is an important factor that is responsible for selective binding in comparison with other factors, (e.g., ionic interaction and hydrogen bond interaction) [9,41]. The PDMA film-coated electrode gave a redox response of DA even when it was used in DA solution and then transferred into the solution containing only supporting electrolyte (Fig. 2A, curve c). That is, DA was found to be confined stably in the PDMA film by stronger hydrophobic attraction than electrostatic repulsion between them. The aromatic ring moiety of DA may be involved in the hydrophobic interaction. On the other hand, in the case of AA, such a hydrophobic interaction was not observed. Thus, the electrochemical response of DA at the PDMA film-coated GC electrode is based on the net contribution of electrostatic repulsion and hydrophobic attraction.

3.5. Effect of DMA concentration used for electropolymerization on electrochemical behavior of DA and AA

Fig. 4 shows the CVs of DA and AA at the PDMA film-coated GC electrodes prepared by electropolymerization at different monomer concentrations, (i.e., 0.05, 0.1 and 0.2 M). In the case of DA, the current response was increased and the peak separation was slightly decreased (i.e., ΔEp's: 90, 97 and 107 mV for 0.2, 0.1 and 0.05 M DMA, respectively) with the increasing the monomer concentration. In the case of AA, both the peak current and potential were observed to change with the monomer concentration. The peak current response for AA is increased with the increasing the film thickness of such kind of anion exchange polymer [42]. Increasing the monomer concentration causes the increase in the thickness of the PDMA film on the electrode surface. The measured values of the film thickness were 0.3, 0.16 and 0.087 μm for 0.2, 0.1 and 0.05 M monomer concentrations, respectively. Thus, the surface coverage of DA on the electrode surface increases

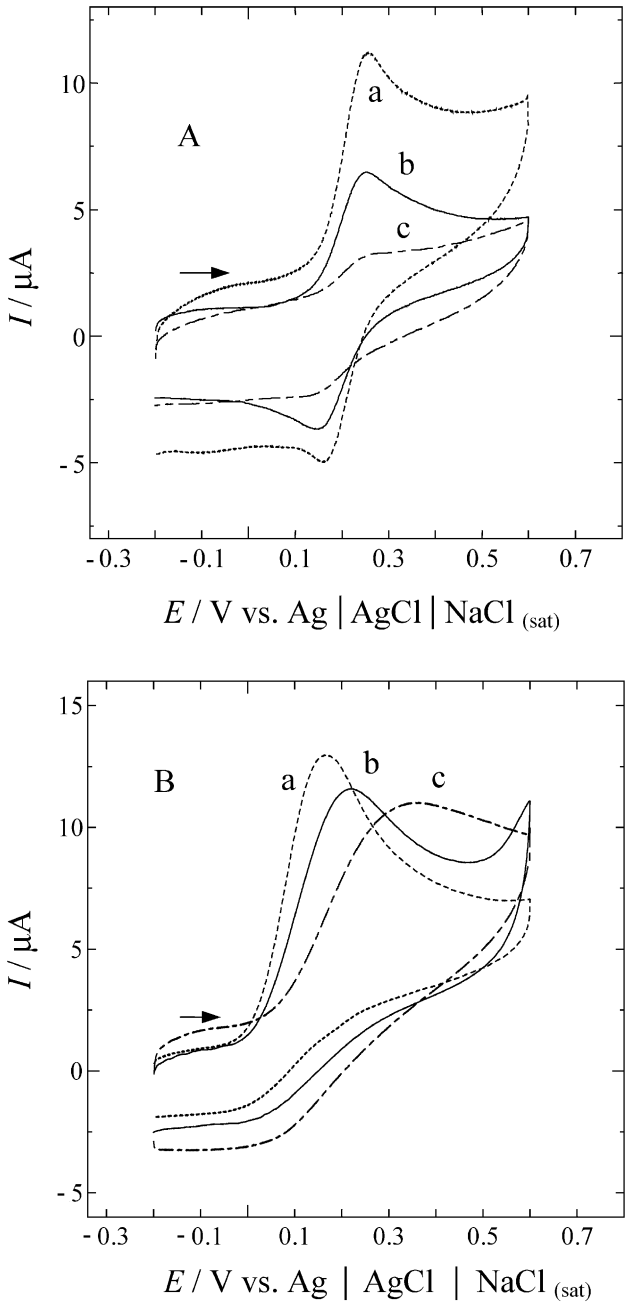


Fig. 4. Cyclic voltammograms for (A) 0.5 mM DA and (B) 0.5 mM AA in 0.2 M phosphate buffer solution (pH 7) at PDMA film-coated GC electrodes prepared from different monomer concentrations. Monomer concentrations: (a) 0.2, (b) 0.1 and (c) 0.05 M DMA. Potential scan rate: 100 mV s^{-1}.

with increasing thickness of the PDMA film. Electropolymerization at higher concentration of monomer may cause an increase in net positive charge within the resulting film and lead to enhanced electrostatic attraction between the cationic film and anionic AA. Thus, the peak current for AA is increased and the peak potential is shifted to less positive potential with an increase in monomer concentration.

3.6. Simultaneous detection of AA and DA

The above results indicate that both the cationic and hydrophobic behavior of PDMA film may mainly contribute to the response of DA and AA at this electrode. The next attempt was taken to detect AA and DA simultaneously by using the PDMA film-coated GC electrode. Fig. 5B shows the square wave voltammograms (SWVs) of AA and DA coexisting in a solution at bare and PDMA film-coated GC electrodes. The bare electrode cannot separate the responses of DA and AA and gave a large response due to homogeneous catalytic oxidation of AA by the oxidized DA (Fig. 5B, curve c). The PDMA film-coated electrode gave two peaks (Fig. 5B, curve d). One peak at +230 mV corresponds to the oxidation of DA. Then the current response at

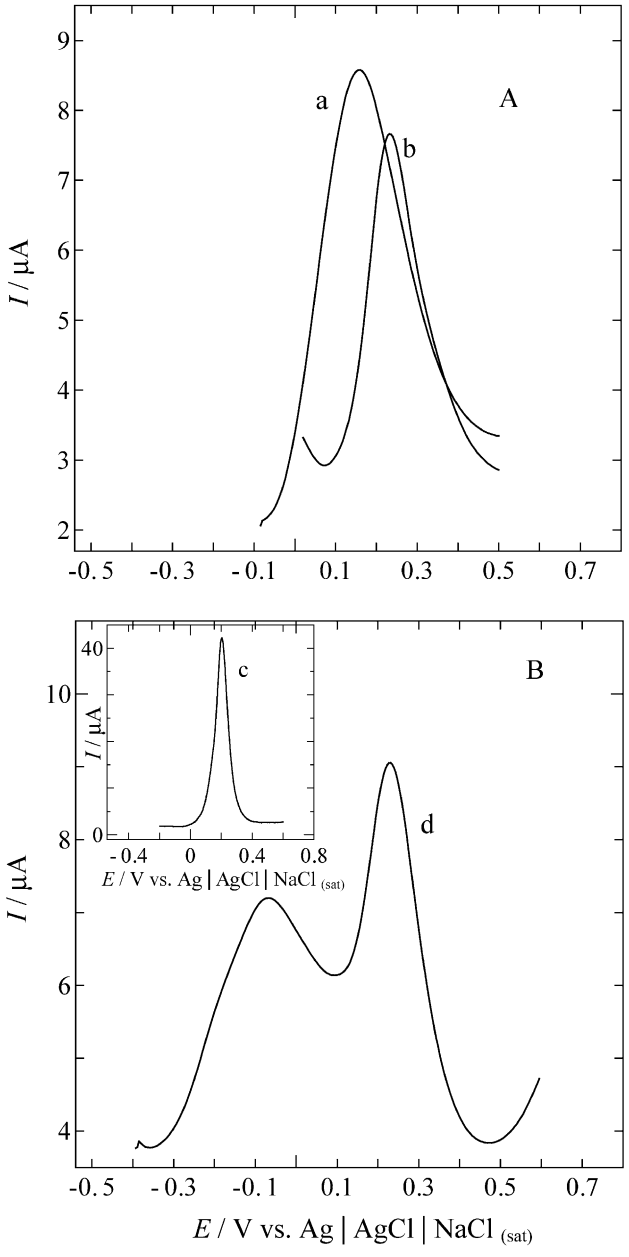


Fig. 5. (A) Square wave voltammograms (SWVs) for (a) 0.5 mM AA and (b) 0.5 mM DA at PDMA film-coated GC electrodes in 0.2 M phosphate buffer solution (pH 7.0). (B) SWVs for the homogeneous solution of 0.5 mM AA and 0.5 mM DA at (c) bare and (d) PDMA film-coated GC electrodes.

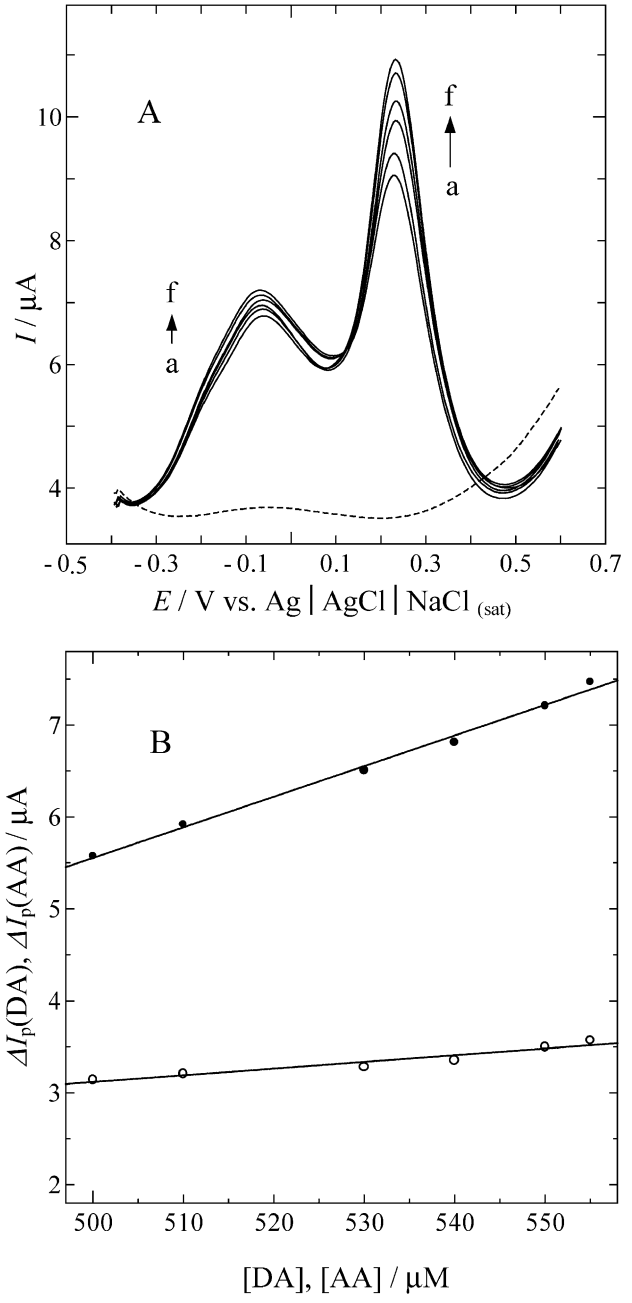


Fig. 6. (A) Square wave voltammograms of AA and DA at PDMA film-coated GC electrode in 0.2 M phosphate buffer solution (pH 7). [DA] and [AA] were simultaneously changed. [AA]=[DA]: (a) 500, (b) 510, (c) 530, (d) 540, (e) 550 and (f) 555 μM. Dotted line shows the SWV of the PDMA film-coated GC electrode in phosphate buffer solution (pH 7). (B) Relationship between the anodic peak currents and the concentrations of AA and DA. Data were taken from Fig. 6A. (●) is for DA and (○) is for AA.

this potential is approximately the same as that given by DA in the absence of AA (Fig. 5A, curve b). The peak current at +150 mV was not found though AA was oxidized at +150 mV in the absence of DA (Fig. 5A, curve a). Instead of this peak, another one was observed at ca. −68 mV. To confirm that these two peaks are for DA and AA, respectively, both concentrations of DA and AA are simultaneously increased at micromolar level. Fig. 6A represents the SWVs at different concentrations of DA and AA. Fig. 6B shows concentration dependences of peak current of DA, ΔI_p(DA), and of AA, ΔI_p(AA) (the data were taken from Fig. 6A). Both DA and AA were initially present at 0.5 mM and then both concentrations were simultaneously changed at micromolar level. Both of the peak currents were observed to increase linearly with the increase in concentration with the correlation coefficient and sensitivity of 0.998 and 0.041 μA μM^{-1}, respectively, for DA, and 0.996 and 0.018 μA μM^{-1} for AA (Fig. 6B). Interestingly the peak current for DA which was corrected by substracting the background current, ΔI_p(DA), was increased linearly with the increase in concentration of DA, while that for AA, ΔI_p(AA), was increased linearly but at much slower rate. This is probably due to the fact that the diffusion of DA through the polymer film is faster compared to that of AA. It was also observed that the electrode can sense the increase in low level of DA (0.2 μM) in the presence of high concentration of AA (0.2 mM). Fig. 7 represents the SWVs at different concentrations of DA where the concentration of AA was kept constant. Here also the peak current for DA was increased linearly with the increase in DA concentration with the correlation coefficient of 0.997 and sensitivity of 0.094 μA μM^{-1} (Fig. 7B). Thus, the peak at −68 mV was found to be the response for AA. DA was found to be hydrophobically incorporated within the film (Fig. 2A, curve c) and the number of moles of DA that is entrapped in the polymer was found to be ca. 16% of the total positive charge in the polymer film. The entrapping of DA into the polymer film causes an increase in net positive charge within it, because the aromatic part of DA is involved in hydrophobic interaction and its cationic amino part is protruded outward (Scheme 2). This may be the reason for the peak potential shift of AA to more negative potential in the presence of DA. Furthermore, the attachment of DA or incorporation into the film causes retardation of the permeation of AA through the film. Thus, the current level of AA at the PDMA film-coated GC electrode is lower in the presence of DA compared to that in its absence. AA was oxidized by 300 mV at less positive potential than DA and the peak currents for DA in the absence and presence of AA were found to be almost the same. This suggests that the oxidation of AA mediated by the oxidized DA cannot occur at the PDMA film-coated GC electrode. It can also be noted

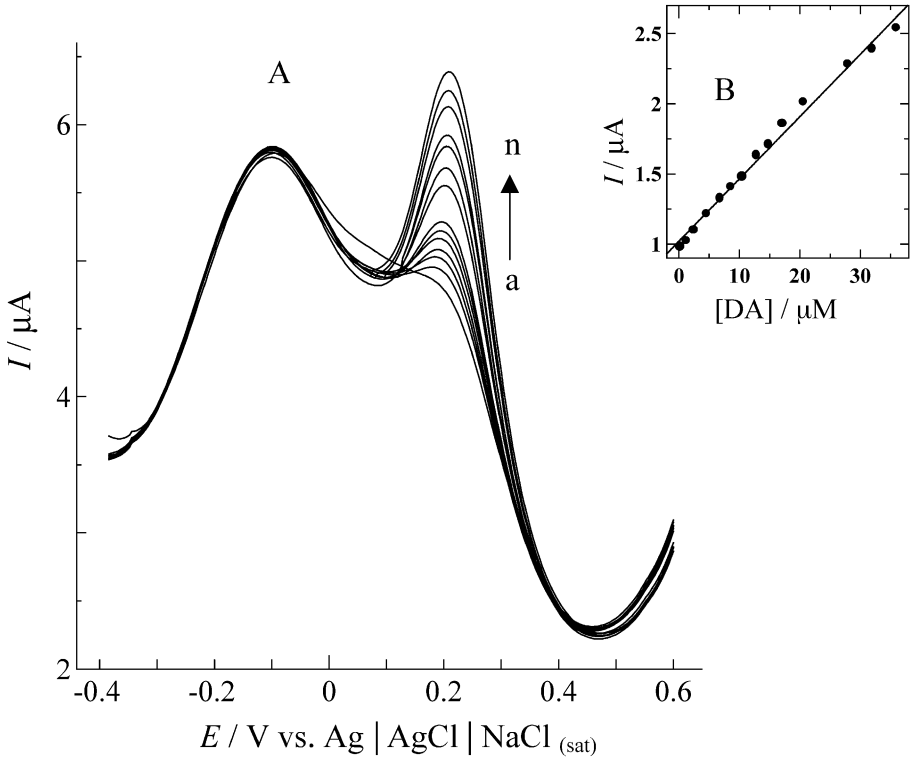
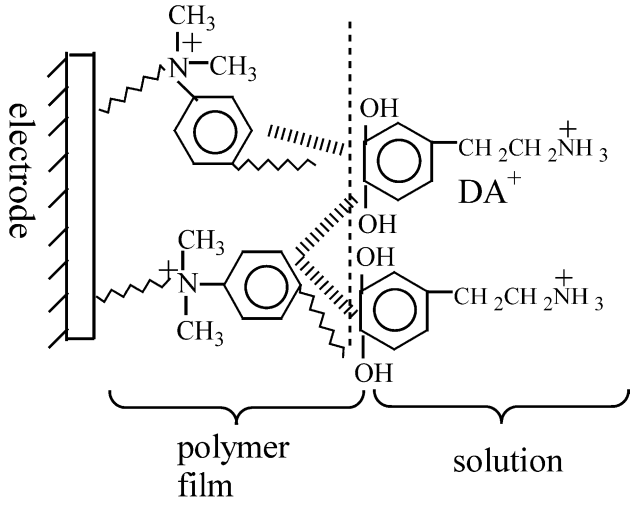


Fig. 7. (A) Square wave voltammograms of AA and DA at PDMA film-coated GC electrode in 0.2 M phosphate buffer solution (pH 7). [DA] was changed and [AA] was kept constant (i.e., [AA] = 0.2 mM, [DA]: (a) 0.2, (b) 1.2, (c) 2.4, (d) 4.6, (e) 6.8, (f) 8.6, (g) 10.4, (h) 12.8, (i) 14.8, (j) 17.2, (k) 20.6, (l) 28, (n) 32 and (o) 36 μM). (B) Relationship between the anodic peak current and the concentration of DA. Data were taken from Fig. 7A.



Scheme 2. Schematic drawing of hydrophobic interaction between DA and the PDMA film.

from this result that in the presence of AA at millimolar level, the electrode can sense the increase of DA at micromolar concentration which is close to the physiological condition. Thus, the selective and sensitive detection of DA in the presence of high concentration of AA was achieved at this electrode. The stability of the electrode was checked by dipping it in phosphate buffer solution for 24 h and then measuring its response to AA after 24 h. AA oxidized at the same potential and the current response was found to be same as that obtained by the freshly polymerized electrode, so the electrode showed a stable response.

In the case of the electrode modified with Nafion®, an anionic and hydrophobic polymer, selective detection of DA was achieved as the cationic DA is greatly attracted to the polymer film both by electrostatic and hydrophobic interactions [43]. Such an electrode that selectively detects DA as well as removes the interference of AA is more advantageous over those electrodes that only selectively detect DA or only separate the oxidation peaks of AA and DA. The PDMA film-coated GC electrode can be considered to be such an electrode that selectively senses DA and also removes the influence of AA at the same time.

4. Conclusions

The polymer (PDMA) film of *N*,*N*-dimethyl aniline has been electrochemically deposited on GC electrode surface by continuous electrooxidation of the corresponding monomer. The electroanalysis of AA and DA has been performed at this PDMA film-modified electrode. Favorable electrostatic interaction between positively charged film and negatively charged AA shifts its oxidation peak potential to less positive direction of potential, while that of DA shifts to positive direction due to electrostatic repulsion. DA also shows a hydrophobic attraction to the film. The PDMA film-coated GC electrode can simultaneously detect AA and DA which coexist in a homogeneous solution, and the separation of the oxidation peak potentials for AA and DA is about 300 mV. Also it can detect DA of low concentration (0.2 μM) in the presence of 1000 times higher concentration of AA which is close to the physiological level. The electrode shows a stable response without fouling of the electrode surface by the adsorption of the oxidized product of AA. The anionic interfering molecule AA is attracted by the positively charged film. However, its permeability through the polymer film to the electrode surface is retarded in the presence of DA. The selective detection of DA is achieved at the PDMA film-coated GC electrode in the presence of AA.

Acknowledgements

The present work was financially supported by Grant-in-Aids for Scientific Research on Priority Areas (no. 417), Scientific Research (no. 12875164) and Scientific Research (A) (no. 10305064) from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

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