An electrochemical sensor for 3,4-dihydroxyphenylacetic acid with carbon nanotubes as electronic transducer and synthetic cyclophane as recognition element†

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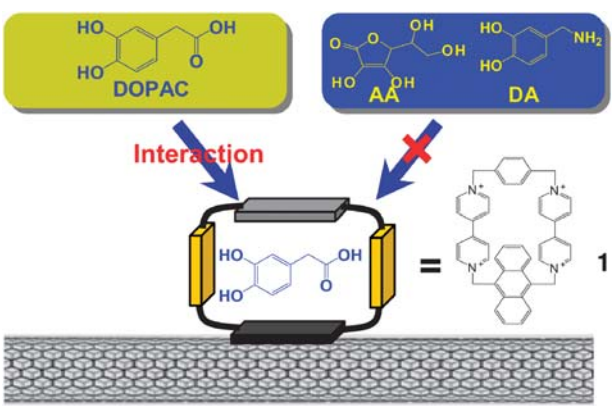
A new electrochemical sensor was demonstrated for selective sensing of 3,4-dihydroxyphenylacetic acid (DOPAC) through a non-oxidative mechanism by using single-walled carbon nanotubes (SWNTs) as the electronic transducer and a synthetic cyclophane electron acceptor as the recognition element.

Selective determination of dopamine (DA) has attracted increasing interest because of the great importance of DA in many physiological and pathological processes.[1] Although substantial efforts have been made towards the effective electrochemical measurement of DA, the low concentration of such species in the central nervous system (CNS) and the great interference from other kinds of electroactive species endogenously existing in the CNS, particularly its main metabolite, 3,4-dihydroxyphenylacetic acid (DOPAC), and ascorbic acid (AA), have made this goal a long-standing challenge.[2] In this context, alternative measurements of DOPAC could provide an indirect but effective approach to determination of the DA level because, on one hand, DOPAC is considered as one of the main products of DA degradation by the action of the enzyme monoamine oxidase,[3] and, on the other hand, DOPAC exists at a much higher level (micromolar range)[2f] than DA (nanomolar range) in the CNS. Nevertheless, the co-oxidation of DOPAC with other kinds of electroactive species, AA in particular, at almost all types of electrode makes this oxidative protocol difficult in practice for selective determination of DOPAC.[4]

In this communication, we wish to report a new electrochemical sensor for selective determination of DOPAC by using single-walled carbon nanotubes (SWNTs) as the electronic transducer and a synthetic cyclophane as the recognition element, as shown in Scheme 1. It is widely accepted that the unique features of carbon nanotubes have made them very promising in developing electrochemical devices, such as electrochemical biosensors and biofuel cells.[5] On the other hand, one type of cyclophane, tetracationic cyclobis(paraquat-*p*-phenylene) ($CBPQT^{4+}$), has been previously used as an electron acceptor for fundamental investigations of donor–acceptor (D–A) interactions with different kinds of electron donors and for the preparation of a large variety of rotaxanes and catenanes.[6] The method demonstrated here for the selective sensing of DOPAC with a non-oxidative mechanism is essentially based on the rational functionalization of a SWNT transducer with a cyclophane recognition element that exhibits a stronger binding affinity for DOPAC over AA and DA, which eventually enables effective recognition of DOPAC to be achieved virtually interference-free from AA and DA at the SWNT–solution interface. The use of SWNTs as electronic transducer is essentially based on their good conductivity and strong interaction with the synthetic recognition unit employed in this study, as well as the enhancement of the electrochemical properties of the adsorbed electroactive compounds, as reported previously.[7] To the best of our knowledge, the electrochemical sensor demonstrated here has not been reported so far and may find some interesting applications in physiological and pathological investigations.

In order to functionalize the SWNT transducer with the tetracationic cyclophane recognition element, we substituted one of the aromatic subunits in $CBPQT^{4+}$ with anthracene to give compound **1** (ESI†), in the expectation that compound **1** would be stably adsorbed onto the SWNT transducer through π–π stacking interaction between SWNTs and the anthracene moiety of compound **1**. The functionalization of the SWNT



Scheme 1 Schematic illustration of the strategy for selective sensing of DOPAC with an electrochemical sensor by using SWNTs as the electronic transducer and the synthetic cyclophane as the recognition element.

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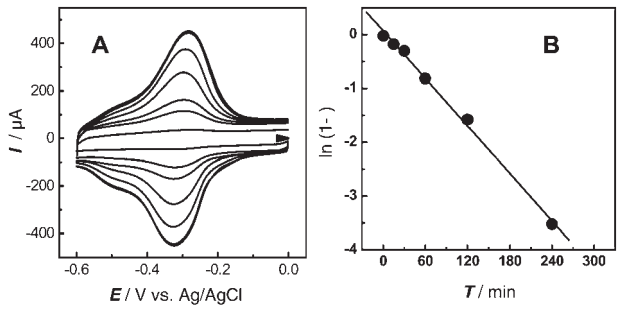

Fig. 1 (A) CVs obtained at the SWNT-modified GC electrode in phosphate buffer (pH 7.0) containing 1.0×10^{-4} M of compound **1** after the electrode was immersed in the solution for different times of (from the centre outwards) 30 s, 15 min, 30 min, 1 h, 2 h, 4 h and 6.5 h. Scan rate, 50 mV s^{-1}. (B) Kinetic plot of $\ln(1 - \theta)$ *versus* time.

transducer with a recognition element from compound **1** to form an electrochemically functional **1**–SWNT nanocomposite was characterized by cyclic voltammetry (CV) with the SWNT-modified glassy carbon (GC) electrode in the aqueous solution of compound **1**, as displayed in Fig. 1. The peak currents of the redox wave at −0.35 V clearly increase with increasing the immersion time, suggesting the adsorption and the continuous growth of compound **1** onto SWNTs. The adsorption kinetics were calculated from the kinetic plot shown in Fig. 1(B), according to the following equation:[8]

$$\ln(1 - \theta) = -kct$$

where k is the adsorption rate constant, t is the time the electrode spent in the solution of compound **1**, and c is the concentration of compound **1**. θ is the fractional coverage of compound **1** and is equal to $\Gamma_{0'}/\Gamma_0$, where $\Gamma_{0'}$ and Γ_0 are the surface coverage at any time and at the saturation plateau, respectively. The surface coverage of compound **1** was determined by integrating the peak area displayed in Fig. 1(A). The k value was calculated from the slope of the kinetic plot and was estimated to be 2.45×10^3 cm^3 $mol^{-1}s^{-1}$.

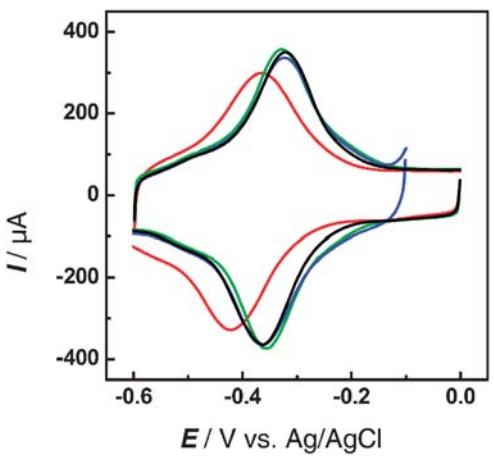

Fig. 2 CVs at **1**–SWNT-modified GC electrode in 0.10 M phosphate buffer (pH 7.0) in the absence (black curve) and presence of AA (blue curve), DA (green curve), or DOPAC (red curve). The concentration of each species was 2.9 mM. Scan rate, 50 mV s^{-1}.

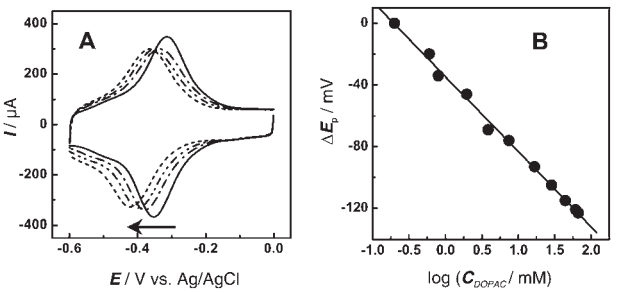

Fig. 3 (A) CVs at a **1**–SWNT-modified GC electrode in 0.10 M phosphate buffer (pH 7.0) containing DOPAC with different concentrations of (from right to left) 0.0, 0.9, 1.7, to 2.9 mM. Scan rate, 50 mV s^{-1}. (B) Plot of the shift in the reduction peak potential (ΔE_p) of a **1**–SWNT-modified GC electrode in 0.10 M phosphate buffer solution *versus* the logarithm of DOPAC concentration ($\log(C_{DOPAC})$).

The stable adsorption of compound **1** onto SWNTs was further supported by the appearance of the redox wave with almost unchanged peak currents upon consecutive potential cycling at the electrode first immersed in the aqueous solution of compound **1** and then transferred into pure phosphate buffer without compound **1**. These results convincingly demonstrate that the strategy of substitution of one aromatic subunit in $CBPQT^{4+}$ enables the stable adsorption of the recognition elements onto the SWNT transducer, forming a stable SWNT electrochemical sensor for selective sensing of DOPAC, as described below.

The prepared **1**–SWNT nanocomposite confined on a GC electrode exhibits two pairs of redox waves at −0.35 V and −0.80 V (Fig. S1†), characteristic of the consecutive two-electron redox processes of two paraquat subunits (*i.e.*, 1,1′-dimethyl-4,4′-bipyridinediium) in compound **1**.[6c] The small separation between the cathodic and anodic potentials and the linear relationship between the peak currents and potential scan rate (Fig. S2, inset†) are indicative of a fast surface-confined electron transfer process in the **1**–SWNT nanocomposite confined on a GC electrode in the phosphate buffer.

Fig. 2 compares CVs obtained at the **1**–SWNT-modified GC electrodes before and after the addition of DOPAC, AA or DA into solution. The CV of the electrode (black curve) remains essentially unchanged with the addition of AA (blue curve) or DA (green curve). In contrast, the addition of DOPAC clearly results in a negative shift of the redox potential of the electrode (red curve).

The observed negative shift of the redox potential could be presumably understood by the stronger binding affinity of the synthetic cyclophane recognition element (*i.e.*, compound **1**) towards DOPAC over AA and DA. It is known that DOPAC exists mainly in the anionic form while DA mainly exhibits the cationic form at pH = 7. The electrostatic interaction between compound **1** and DOPAC is thus expected to be stronger compared with that between compound **1** and DA. On the other hand, the weaker binding of compound **1** with AA may be due to the relatively weak π–π interaction between them. In short, the stronger binding affinity of compound **1** towards DOPAC could be due to the synergic electrostatic, π–π and D–A interactions. Such interactions could lead to an increase

in the electron density of compound **1** and may eventually be responsible for the observed negative shift in the peak potential in the presence of DOPAC, as depicted in Fig. 2. This unique feature of compound **1** enables the prepared **1**-functionalized SWNT electrochemical sensors to function as a new kind of electrochemical sensor for the non-oxidative and selective sensing of DOPAC.

Fig. 3(A) depicts CVs obtained at the **1**–SWNT-modified GC electrode in phosphate buffer containing different concentrations of DOPAC. The reduction peak potential was clearly shifted negatively with increasing DOPAC concentration in solution. The shift in the peak potential (ΔE_p) was linear with the logarithm of DOPAC concentration within the concentration range from 0.9 mM to 66 mM with a linear coefficiency of 0.998 (Fig. 3(B)). In addition, we have found that, on reducing the surface coverage of **1**–SWNTs and, as such, the number of recognition elements of compound **1** on the GC electrode, the dynamic range of DOPAC could be lowered to the μM level (Fig. S3†), which is close to the physiological level of DOPAC in the CNS.[2f] Such a high selectivity and sensitivity of the electrochemical sensor convincingly suggests could have potential applications for effective determination of DOPAC in biological systems.

In conclusion, we have developed a new kind of electrochemical sensor for selective sensing of DOPAC through a non-oxidative mechanism by functionalizing the synthetic cyclophane recognition element onto the SWNT electronic transducer. The stronger binding affinity of the synthetic cyclophane towards DOPAC over AA and DA endows the as-prepared electrochemical sensor with a high selectivity for DOPAC sensing. This property of the electrochemical sensor combined with its tunable sensitivity suggests it has potential applications in physiological and pathological investigations.

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