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Preparation of N-doped carbon quantum dots for highly sensitive detection of dopamine by an electrochemical method[†]

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A simple electrochemical biosensor was developed based on an N-doped carbon quantum dot (NCQD) modified glass carbon electrode (NCQD/GCE). The modified electrode displayed a good linear and broad response for the detection of dopamine (DA). The as-prepared biosensor also exhibited satisfactory selectivity even with interference of ascorbic acid (AA) and uric acid (UA). Inorganic ions also had no effect on detecting DA.

Dopamine (DA) is a catecholamine in the brain that acts as a neurotransmitter and chemical messenger.¹ In biological systems, the normal concentration range of DA is from 10^{-8} to 10^{-6} M.² It is reported that abnormal production of DA in the brain is related to the severity and progression of neurological and neurodegenerative disorders such as Parkinson's disease, attention-deficit hyperactivity disorder (ADHD) and Huntington's disease.³ So the sensitive detection of DA concentration is very important for not only clinical diagnostics but also for pathological research.

Different methods have been developed for the determination of DA, such as high performance liquid chromatography,⁴ fluorescence method,⁵ spectrophotometry⁶ and electrochemical method.⁷ Among these analytical methods, electrochemical method has a number of advantages, including simple operation, low cost effect and high sensitivity. Because DA is an electroactive compound that can be easily oxidized on the electrode, electroanalysis of DA based on its electro-oxidation has been received much attention due to its considerably high sensitivity, rapid response, low cost and ease of operation.⁸ Based on the inherent redox activity of DA and excellent characteristics of electrochemical methods, many materials including metal oxide nanoparticles,⁹ conducting polymer,¹⁰ carbon based materials,¹¹ nanocomposites,¹² *etc.*, have been developed for the direct electrochemical determination of DA. However, the analytical performance (such as detection limit, stability and selectivity) of these modified electrodes are not entirely satisfactory to the practical application in biological samples due to the presence of ascorbic acid (AA), former DA and its metabolites in the body.

As a new type of the nanocarbon family, carbon quantum dots (CQDs) exhibit many advantages, such as low cytoxicity, high chemical stability, easy preparation, and environmental friendliness.¹³ More and more attentions have been paid to these emerging carbon nanomaterials, including their syntheses, property studies, and applications.¹⁴ In our previous work,¹⁵ N-doped carbon quantum dots (NCQDs) can efficiently induce charge delocalization and tune the work function of carbon because the doping of N atoms. In this work, NCQDs were firstly prepared from a carbohydrate polymer by a hydrothermal approach as described previously. Then, NCQDs were loaded on the bare glassy carbon electrode by Nafion solution to form NCQDs modified glass carbon electrode (NCQDs/GCE). The as-prepared modified electrode has been used as a biosensor to detect DA by electrochemical method.

Fig. 1A shows the typical TEM image of NCQDs. It can be found that the NCQDs are relatively uniform with diameters of *ca.* 5–10 nm. The average diameter of original NCQDs measured by DLS is 7.4 nm, which agree with that observed by TEM measurement, as shown in Fig. 1B. Using Rhodamine B as standard (see Table S1 in ESI†), NCQDs exhibit excellent monodispersity with polydispersity index (PDI) at 18.97%. The zeta potential of NCQDs is -20.9 mV (Fig. 1C). It indicates the negative charge nature for the surface of NCQDs. Confirmed by infrared spectroscopy analysis (see Fig. S1 in ESI†), there is a

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⁴Qixin Honours School, Zhejiang Sci-Tech University, Hangzhou 310018, P. R. China ⁴School of Life Science, Zhejiang Sci-Tech University, Hangzhou 310018, P. R. China [†] Electronic supplementary information (ESI) available: Details of materials, synthesis of NCQDs, characterization, quantum yields of NCQDs, FTIR spectrum of NCQDs, DPV curve NCQDs/GCE in 0.1 M PBS at various pH values, calculation of limit of detection (LOD) and comparison of some characteristics of different novel electrodes for the determination of DA. See DOI: 10.1039/c4ra16773b



Fig. 1 The TEM image (A), DLS distribution (B), zeta potential (C) and XRD pattern of NCQDs (D).

broad peak in the range of 2500–3750 cm⁻¹ which reveals abundant of hydroxyl, carbonyl and carboxylic acid groups distributed on the surface of NCQDs. The typical X-ray diffraction (XRD) pattern of the as-prepared NCQDs is shown in Fig. 1D. The two broad peaks centered at $2\theta = 10.27^{\circ}$, 26.7° can be observed, which are contributed to the graphene oxide and graphene structure, respectively.¹⁶ A weak broad peak centered at $2\theta = 43.3^{\circ}$ is assigned to (101) diffraction patterns of graphitic carbon.

X-ray photoelectron spectrum (XPS) was utilized to confirm the effective incorporation of nitrogen and surface chemical properties of the obtained NCQDs. As shown in Fig. 2A, XPS spectrum for NCQDs contains three prominent peaks with C, N and O at percentage of 59.81%, 19.45% and 20.73%, respectively. The C^{1s} spectrum of NCQDs contains three components and the main peak at 284.7 eV corresponds to graphitic sp² C. It



Fig. 2 XPS spectrum of NCQDs (A) and high-resolution XPS spectra of C (B) and N (C) and O (D) over NCQDs.

indicates that most of the carbon atoms are arranged in a conjugated lattice. The peak at 285.2 eV represents the N-sp² C bonds in the N-containing carbon dots and the 287.2 eV peak corresponds to N-sp³ C bonds (Fig. 2B).¹⁷ The N^{1s} peak has three components, indicating that N is present in three different bonding characters, as shown in Fig. 2C. The peaks at 398.8 and 399.2 eV can be assigned as the presence of "pyrridinic" and "pyrrolic" N, respectively. Therefore, N is present in a π -conjugated system where two p-electrons are present in the system. A peak at 399.6 eV corresponds to graphitic N, indicating an N atom is replacing the C atom inside the carbon dots.17 The highresolution O spectrum of the NCQDs display three peaks at 530.2, 530.6 and 531.1 eV, which are attributed to the C=O, C-O-H and C-O bonds (Fig. 2D). It implies the as-prepared NCODs are rich in hydroxyl, carbonyl and carboxylic acid groups on their surfaces.18-23

The NCODs/GCE electrode was prepared using a simple drop casting method by casting a NCQD-Nafion solution onto the surface of a glassy carbon electrode and dried under room temperature in the air. Fig. 3A shows the typical cyclic voltammograms (CV) curves in 0.1 M PBS solution with the potential range from -1.0 to 0.6 V. As expected, the CV curves exhibit well-defined redox peaks with the scan rate range from 20 to 350 mV s⁻¹. The peak currents are increased gradually with increasing of scan rate. Fig. 3B shows the relationship between the peak current and scan rate obtained from the experimental data in Fig. 3A. The anodic and catholic peak currents show a linear dependence on the square root of the scan rate as following: $I_{\rm PC} = 0.4311 + 0.1572 V^{1/2}$, $R_2 = 0.9967$; $I_{\rm PA} = 0.1742 - 0.1742 - 0.1742 - 0.1742$ $0.1908V^{1/2}$, $R_2 = 0.9924$. This deviation from a linear relationship suggests that the redox reaction of NCQDs is a surfacecontrolled process, not a diffusion-controlled process.²⁴

Electrochemical impedance spectroscopy (EIS) is an effective method to characterize the interfacial electrical property of modified electrode. In EIS, the semicircle diameter of the impedance is equal to the electron transfer resistance, which controls the electron transfer kinetics of the redox probe at the electrode surface.²⁵ Fig. 4A shows the results of impedance spectroscopy of bare glassy carbon electrode (curve a) and NCQDs/GCE in 0.5 M KNO₃ and 5.0 mM Fe(CN)₆^{3-/4-} (curve b). The bare GCE shows a small semicircle with a charge transfer resistance (R_{ct}) of about 300 Ω at high frequencies. However, after casting NCQDs onto the surface of GCE, the Nyquist plot consists of a semicircle at high frequency and a straight line at



Fig. 3 CV curves of NCQDs in 0.1 M PBS obtained at different scan rates (A), linear relation between peak current and the square root of the scan rate (B).



Fig. 4 Nyquist plots of bare glassy carbon electrode (a), and NCQDs/GCE (b) in 0.5 M KNO₃ and 5.0 mM $Fe(CN)_6^{3-/4-}$ (A), cyclic voltammetry curves of NCQDs/GCE at a scan rate of 50 mV s⁻¹ in 0.1 M PBS (pH = 7.4) with or without of DA (B), DPV responses of NCQDs/GCE with the different concentrations of DA (C), the related linear relationship between currents and the concentrations of DA using NCQDs/GCE as electrode (D).

low frequency, with $R_{\rm ct}$ value around at 8023 Ω . It is attributed to the formation of NCQDs layer that embracing the electron transfer. The middle frequency semicircle is attributed to charge transfer. It implies that the NCQDs/GCE is an excellent electrical conducting material.

On the basis of the excellent electrochemical properties of NCQDs, it would be applied to detect electroactive molecules. To verify the recognition capabilities of NCQDs, an electroactive molecule-dopamine (DA) has been chosen as the guest molecule. Fig. 4B shows the CV curves obtained with the scan rate at 50 mV s⁻¹ in 0.1 M PBS (pH = 7.4) and the concentration of DA at 0.5 mM. Compared with the oxidation peak with absence of DA, higher electrochemical response toward DA molecules can be observed. And the potential of oxidation peak increased from 0.15 V to 0.20 V, and current intensity increasing about 40% as well.

NCQDs/GCE is applied to detect DA by different pulse voltammetry (DPV). As shown in Fig. 4C, upon increasing the concentration of DA in PBS, the oxidation peak current improves significantly which suggests that NCQDs/GCE could be applied to the quantitative determination of DA. The anodic peak current of DA shows a good linear relationship with DA concentration in the range from 0 to 1.0 mM (Fig. 4D). The linear regression equation is defined as $I_p = 3.67 + 42.85c$ with $R_2 = 0.9977$ (Fig. 4D). Since the normal concentration range of DA in human body is from 10^{-8} to 10^{-6} M,² it is evident that the NCQDs/GCE has excellent electrochemical activity, which can be a promising sensor for DA clinical determination. The lowest detection limit is evaluated to be 1×10^{-9} M (signal-to-noise (S/N) = 3) (see in ESI†), which is better than that of some previous reports (see Table S2 in ESI†).²⁶

The pH of the electrolyte can affect the stability of NCQDs/GCE, as reported previously.²⁷ The DPV curves of

NCQDs/GCE in 0.1 M PBS obtained at various pH values are shown in Fig. S2.[†] No significant difference is founded, which indicates the excellent stability of NCQDs/GCE against different pH environments. DPV curves for detection of DA using NCQDs/GCE electrode under different pH conditions are shown in Fig. 5A. The oxidation peak currents of DA on the NCQDs/GCE are decreased from pH = 6.0 to 8.4. The optimal pH value is 7.4 that close to the normal physiological environment, which has been selected for evaluating the detection performance of DA on NCQDs/GCE. The potentials of oxidation peaks versus the value of pH are shown in Fig. 5B. A linear relationship with potentials and pH can be obtained with the correlation coefficient at 0.9981. It indicates that protons participate in the oxidation of DA. According to the Nernst equation, the relation between E_p and pH is $E_p = (-0.0592m/n)$ pH + b (where *n* is the electron transfer number and *m* is the number of protons participating in the electrochemical oxidation reaction, respectively). The equation can be defined as: $E_{\rm p} = 0.44 - 0.055$ pH. The slope of this equation is 55 pH mV⁻¹. It close to the theoretical value of equal electronic and proton transfer process at 58.0 pH mV $^{-1}$. It is demonstrated that the ratio between protons transferred from DA to NCQDs/GCE and electronics participating in the reaction is close to 1:1, which proves that the redox process of DA on NCQDs/GCE is a two-step process with two electrons and two protons.28 When the pH < 7.0, most of the amino group on DA are in cationic form for the protonation reaction in acidic environment. Firstly, the protonated DA molecules lose two electrons to form dopaquinones. Then, dopaquinones further lose electrons to completion of intramolecular cyclization.28 Since acidity promotes the intramolecular cyclization, the oxidation peak currents of DA on the NCQDs/GCE are decreased from pH = 6.0 to 8.4.

Uric acid (UA) and ascorbic acid (AA) always exist in biological environment along with DA,²⁹ it is significantly important to simultaneous determine of DA in the presence of UA and AA. The effect of UA or/and AA on the determination of 0.1 mM DA is conducted by DPV measurement, as shown in Fig. 6A. An oxidation peak centered at 0.2 V assigned to DA can be observed with only presence of DA. Upon the addition of UA or AA, new oxidation peak that assigned to UA (around -0.56 V) or AA (around -0.22 V) can be founded. The position of oxidation peak of DA has not been moved even both of UA and AA involved for the electrochemical detection of DA. It implies that UA



Fig. 5 Effect of pH on the differential pulse voltammograms of NCQDs/GCE in 0.5 mM DA and 0.1 M PBS (A), relation between peak current and different pH (D).



Fig. 6 DPV curves of 0.1 mM DA and/or other interference (0.1 mM UA and/or 0.1 mM AA) on NCQDs/GCE (A), the changes of NCQDs/GCE activity as it preserved in PBS (pH = 7.4) solution (D).

or/and AA have no influence the sensitivity for detection of DA. The as-prepared NCQDs/GCE has excellent selectivity for DA determination.

The stability and reproducibility are the important considerations for the practical application of electrochemical sensors. To evaluate the working stability of NCQDs/GCE, the sensor without renewing the electrode surface subjected to determine of 0.5 mM DA in 0.1 M PBS (pH = 7.0) with 30 min intervals. After 360 min, the modified electrodes retained 95.0% of their initial activity (Fig. 6B). When the measurements are completed, the modified electrode is stored in the PBS. After 15 days, the current response on the NCQDs/GCE still remained about 87.0% (Fig. 6B), indicating excellent stability and reproducibility.

The effect of ions on the NCQDs/GCE electrochemical activity is also investigated. When the relative error is lower 5%, substances are considered as no interference for DA detection. As shown in Fig. 7, it is found that 300-fold concentration of Na⁺, Cl⁻, NO³⁻, SO⁴⁻, 100-fold concentration of Mg²⁺ and Ca²⁺ caused negligible influence for peak current of DA. The results demonstrated that these ions have no interference for DA detecting using NCQDs/GCE. From the results above, we believe that N-doping is a simple but useful process for CQDs because N-doping easily manipulates local electronic structure.³⁰ By using N doping, the Fermi potential is changed, this kind of dopant would increase the density of electronic states at its Fermi level and open the band gap of CQDs. The electron transfer efficiency of NCQDs and the binding with electro-active molecules in the solution would be improved as well. Herein, NCQDs show their robust ability for electron transfer from DA to electrode surface and high electrochemical sensitivity to DA molecules.



Fig. 7 The changes of NCQDs/GCE activity as different ions added into the solution when detected DA.

Conclusions

The N-doped carbon quantum dots (NCQDs) have been prepared by simple hydrothermal synthesis of carbohydrates. The prepared NCQDs were utilized for modification of glassy carbon electrode to detect DA selectively. CV and EIS measurements confirmed that NCQDs/GCE has been effectively absorbed onto the surface of bare glassy carbon electrode. The NCQDs modified electrode displayed higher electrochemical response to DA. Especially, NCQDs exhibited an excellent electrochemical performance for DA with broad linear range (0 to 1×10^{-3} M) and low detection limit (1.0×10^{-9} M) at a signalto-noise ratio of 3. This NCODs modified electrode has excellent anti-interference to DA determination with presence of UA or/and AA. The inorganic ions had no effect on detecting of DA as well. The decreasing of electrochemical activity was only about 10% after exposure in PBS solution for 15 days which showed excellent stability and reproducibility.

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