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Modulating Electrode Kinetics for Discrimination of Dopamine by PEDOT:COOH Interface Doped with Negatively-charged Tri-carboxylate

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Abstract:

The rapidly developing field of conducting polymers in organic electronics has many implications for bioelectronics. For biosensing applications, tailoring the functionalities of the conducting polymer's surface is an efficient approach to improve both sensitivity and selectivity. Here, we demonstrated a facile and economic approach for the fabrication of a high-density, negatively-charged carboxylic acid group-functionalized PEDOT (PEDOT:COOH) using an inexpensive ternary carboxylic acid, citrate, as a dopant. The polymerization efficiency was significantly improved by addition of LiClO₄ as a supporting electrolyte yielding a dense PEDOT:COOH sensing interface. The resulting PEDOT:COOH interface had a high surface density of carboxylic acid groups of 0.129 $\mu\text{mol}/\text{cm}^2$ as quantified by the toluidine blue O

(TBO) staining technique. The dopamine response measured with the PEDOT:COOH sensing interface was characterized by cyclic voltammetry with a significantly reduced ΔE_p of 90 mV and a 3 fold increase in the I_{pa} value compared with the non-functionalized PEDOT sensing interface. Moreover, the cyclic voltammetry and electrochemical impedance spectroscopy results demonstrated the increased electrode kinetics and highly selective discrimination of dopamine (DA) in the presence of the interferents ascorbic acid (AA) and uric acid (UA) resulted from the introduction of negatively-charged carboxylic acid groups. The negatively-charged carboxylic acid groups could favor the transfer, preconcentration and permeation of positively charged DA to deliver improved sensing performance, while repelling the negatively-charged AA and UA interferents. The PEDOT:COOH interface facilitate measurement of dopamine over the range of 1 - 85 μM , with a sensitivity of 0.228 $\mu\text{A } \mu\text{M}^{-1}$, which is 4.1 times higher than that of a non-functionalized PEDOT electrode (0.055 $\mu\text{A } \mu\text{M}^{-1}$). Our results demonstrate the feasibility of a simple and economic fabrication of a high density PEDOT:COOH interface for chemical sensing, which also has the potential for coupling with other bio-recognition molecules via the carboxylic acid moieties for the development of a range of advanced PEDOT-based biosensors.

Keywords: PEDOT, citrate doping, carboxylic acid groups, dopamine discrimination, electrode kinetics

Introduction

Poly(3,4-ethylenedioxythiophene) (PEDOT) has emerged as the preferred active component in studies of a number of fundamental and applied organic electronic and optoelectronic

devices, including organic photovoltaic cells (OPVs)¹, organic light-emitting diodes (OLEDs)², organic field-effect transistors (OFETs)³ etc. The employment of PEDOT in organic electronics is attractive due to its reversible doping state, good electronic and ionic conductivity, excellent stability, and interesting optical and electrochemical properties. In addition to organic electronics, PEDOT has also been widely applied in bio-interfaces and bio-materials for biomedical applications in recent years⁴⁻⁵. Further fine-tailoring of the conducting polymer interfaces to improve conductivity, functionality, morphology and compatibility is required to meet the demands of specific applications such as specific recognition⁶⁻⁷, cell capture⁸⁻⁹, chronic neural interfaces¹⁰ and enhanced electrochemical performance¹¹⁻¹⁴.

In recent years, efforts have been devoted to develop functionalized PEDOT interfaces with active chemical groups, such as carboxylic acid¹⁵, azidomethyl¹⁶, hydroxymethyl¹⁷, chloromethyl¹⁸, bromoisobutyric acid⁸ and sialic acid⁶. Among them, the introduction of a carboxylic acid group-functionalized PEDOT interface endows a wide range of advanced sensing features such as recognition functional groups, anchoring sites for conjugation, a negatively-charged interface and enhanced biocompatibility. A common strategy to fabricate carboxylic acid group-functionalized PEDOT interface relies on co-polymerization with a mixture of EDOT monomers and functional carboxyl EDOT (EDOT-COOH) monomer with a confined ratio¹⁹. However, the polymerization reactivity of functional EDOT-COOH is difficult to optimize and has a low polymerization efficiency, thus yielding a relatively low density PEDOT:COOH interface¹⁹. In addition, the availability of commercial EDOT-COOH monomer is limited, expensive, or requires a complicated synthesis. Alternatively, other strategies involve the incorporation of carboxylic acid groups containing active materials or large biomolecules into the cationic PEDOT as dopants, such as graphene oxide²⁰, hemin²¹ or polysaccharides²². The incorporation of large molecular weight dopants affects the surface and bulk properties and disrupts the electrical properties of the PEDOT interface⁶. Moreover, due to the relatively low-

density of carboxylic acid group moieties within the above mentioned large molecular weight dopants, it remains difficult to create a high-density carboxylic acid group-functionalized PEDOT interface for sensing applications.

As one of the crucial neurotransmitters in cardiovascular, renal, hormonal and central nervous systems, the physiological level of dopamine (DA) in extracellular fluid is of great importance in clinical diagnosis of the DA-correlated neurological disorders of Parkinson's and Alzheimer's diseases²³. Various techniques have been investigated and developed for DA determination, among which electrochemical methods have received much attention on account of their simple operation, ease of miniaturization, rapid response and high sensitivity. However, the discrimination of DA from co-existing ascorbic acid (AA) and uric acid (UA) in physiological samples is challenging due to the closely similar oxidation potential for these three molecules. In order to diminish this problem, many modified electrodes have been constructed to separate the oxidation peaks of DA, AA and UA, such as carbon nanomaterials²⁴⁻²⁵, metal complexes²⁶⁻²⁷, polymers²⁸⁻²⁹, redox mediators³⁰⁻³¹ and their composites³². In addition, the different protonated/deprotonated forms of DA (pKa 8.9), AA (pKa 4.2) and UA (pKa 5.4) under physiological conditions (pH 7.4) provides a charge effect to circumvent this issue by attracting the cationic DA to a negatively-charged electrode interface while repelling the anionic AA and UA³³. Various kinds of negatively-charged electrode interfaces have been constructed to increase the discrimination of dopamine from the interferents, such as surfactants^{28, 34}, polymers^{29, 35}, carbonaceous materials³⁶ and metal-based materials³³ etc.

Herein, we demonstrated a facile and economic approach to fabricate a high-density, negatively-charged carboxylic acid group-functionalized PEDOT using an inexpensive ternary carboxylic acid, citrate, as dopant. The polymerization efficiency was significantly improved by addition of LiClO₄ as a supporting electrolyte, yielding a dense PEDOT:COOH film. The PEDOT:COOH electrode kinetics for DA, AA and UA were modulated via the introduction of

a negatively-charged carboxylic acid group. The rich and negatively-charged tri-carboxylate doped PEDOT:COOH interface favors the transfer, preconcentration and permeation of positively charged DA to deliver improved sensing performance, while repelling the negatively-charged AA and UA interferences, resulting in highly sensitive and highly selective determination of dopamine.

Experimental section

Materials. 3, 4-ethylenedioxythiophene (EDOT), sodium citrate dihydrate, lithium perchlorate (LiClO_4), Toluidine Blue O (TBO), Dopamine hydrochloride (DA), L-ascorbic acid (AA) and uric acid (UA) were bought from Sigma-Aldrich (USA). Potassium hydroxide (KOH), acetic acid ($\text{CH}_3\text{CO}_2\text{H}$), disodium hydrogen phosphate monohydrate ($\text{Na}_2\text{HPO}_4 \cdot \text{H}_2\text{O}$) and sodium dihydrogen phosphate (NaH_2PO_4) were purchased from Merck (Darmstadt, Germany). 0.1 M Phosphate buffer solutions (PBS 7.4) were prepared by mixing Na_2HPO_4 and NaH_2PO_4 stock solution. All chemicals were of analytical grade and used without any further treatment. Deionized water from Milli-Q System was used throughout.

Electropolymerization of carboxylic acid group-containing PEDOT interface. The 3-mm glassy carbon electrode (GCE, surface area 0.0707 cm^2) was carefully polished with 0.3 and $0.05 \text{ }\mu\text{m}$ aluminum slurries and rinsed by deionized water under sonication. The monomer solutions containing 10 mM EDOT with different dopant concentrations were sonicated for 30 mins prior to use. Different PEDOT interfaces were electropolymerized in the monomer solution using a constant potential of 1.1 V for 300 s. For the preparation of PEDOT: citrate (denoted as PEDOT:C), GCE was immersed and electropolymerized in 10 mM EDOT and 20 mM sodium citrate (which acts as both electrolyte and dopant) solution. For comparison, PEDOT doped with perchlorate (denoted as PEDOT:P) was electropolymerized in 10 mM EDOT with 20 mM LiClO_4 solution. In order to increase the electropolymerization efficiency

and evaluate the doping effect of citrate, a series of PEDOT:P_xC_y (P_xC_y represents different concentration ratio between perchlorate and sodium citrate) interfaces were prepared in the solution containing 10 mM EDOT, 20 mM LiClO₄ and different concentrations of sodium citrate ranging from 5 mM to 80 mM. The resulting carboxylic acid groups containing PEDOT interfaces were denoted as PEDOT:P₄C₁, PEDOT:P₂C₁, PEDOT:P₁C₁, PEDOT:P₁C₂ and PEDOT:P₁C₄, respectively, according to the concentration ratio between LiClO₄ and citrate. Indium tin oxide coated glass (ITO) was used as an alternative working electrode during electropolymerization for the characterization experiments.

Characterization and electrochemical measurements. Scanning electron microscopy (SEM) images were recorded using a LEO 155 Gemini (Zeiss, Germany). The wettability of the PEDOT interfaces with different dopants was evaluated by static contact angle measured by applying 5 μ L deionized water on the PEDOT interface through a KSV CAM200 semi-automatic drop-shape analysis system (KSV Instrument, Helsinki, Finland). X-ray photoelectron spectroscopy (XPS) was acquired with Axis Ultra DLD instrument (Kratos Analytical, UK) equipped with a monochromatic Al(K α) X-ray radiation ($h\nu = 1486.6$ eV) source. Fourier transform infrared (FTIR) spectroscopy was performed using a VERTEX spectrometer (Bruker, USA) equipped with an attenuated total reflection (ATR) measuring cell. Thickness and roughness measurements were performed on a Dektak 6 M surface profilometer (Veeco Inc. USA) with scanning range of 2000 μ m. The surface density of carboxylic acid groups on the PEDOT surface was determined by the widely used toluidine blue O (TBO) staining technique³⁷⁻³⁸. Briefly, PEDOT electrodes (1×0.6 cm²) were incubated in 0.1 mM KOH solution containing 2 mM TBO for 2 h. Under the alkaline solution, the carboxylic acid groups deprotonate and bind to the positively charged TBO molecules with a ratio of 1:1. Then the PEDOT electrodes were thoroughly rinsed with 0.1 mM KOH solution to remove the

nonspecifically bound TBO molecules. Finally, the TBO molecules were desorbed by immersing in 5 mL 50% acetic acid for 30 min and used for absorbance spectroscopy measurement with a UV-vis spectrophotometer (UV-2450, Shimadzu, Japan) at 631 nm.

All electrochemical measurements were performed with a CompactStat potentiostat (Ivium, Netherlands) at room temperature with a conventional three-electrode system comprising a platinum wire as the counter electrode, a glassy carbon working electrode, and a silver/silver chloride (Ag/AgCl) electrode as the reference. Electrolyte solutions were purged with high-purity nitrogen for 10 minutes prior to each electrochemical experiment. PEDOT electrodes were equilibrated by running CVs in PBS (0.1 M, pH 7.4) for 20 cycles before each electrochemical experiment. Electrochemical impedance spectroscopy (EIS) measurements were made at PEDOT electrodes in 0.1 M PBS (pH=7.4) in the presence/absence of different analytes (DA, AA or UA, 0.5 mM) with a frequency range of 0.01 Hz to 100 kHz, 5 mV amplitude, and corresponding oxidation peak potential for different analytes. The impedance spectra were then fitted to an equivalent electrical circuit via ZSimpWin Software (AMETEK Scientific instruments). Differential pulse voltammetry (DPV) measurements were carried out in 0.1 M PBS solution at potential of 0.0 - 0.4 V, with a pulse time of 50 ms, pulse amplitude of 50 mV and scan rate of 5 mV/s.

Results and discussion

Optimization and characterization of PEDOT:P_xC_y electrode interfaces

In order to introduce a high density of carboxylic acid groups into the PEDOT interface, citrate containing ternary carboxylic acid groups was chosen as the co-dopant. However, the polymerization efficiency of PEDOT in the presence of citrate is relatively low (Figure S1), which may be caused by the low doping efficiency of PEDOT with the relatively large molecular weight citrate. To improve the polymerization efficiency, LiClO₄ was utilized as a

supporting electrolyte in the presence of citrate to assist the electropolymerization process, due to its high electropolymerisation efficiency with increase of electroactivity and crystallinity of the polymer³⁹, with different concentration ratios of LiClO₄ and citrate being examined. The PEDOT layers formed with different ratios of LiClO₄ and citrate were annotated as PEDOT:P_xC_y, while control samples were annotated as PEDOT:citrate (PEDOT:C) and PEDOT:perchlorate (PEDOT:P), respectively.

As can be seen in Figure 1a, PEDOT:C showed a light blue color on the electrode surface (inset image No.1) with a thickness of only $0.18 \pm 0.02 \mu\text{m}$, due to the relatively poor electrochemical polymerization process, while the PEDOT:P electrode was significantly thicker ($6.68 \pm 0.26 \mu\text{m}$) and appeared dark blue in color (inset image No.2), indicating that an effective electrochemical polymerization reaction had occurred. These results are in good agreement with the electropolymerization kinetics and CV curves in Figure S1. For PEDOT electrodes prepared in the presence of LiClO₄ and citrate, the thickness and roughness of the resulting of PEDOT:P_xC_y films decreased gradually from 3.38 to 1.46 μm (thickness) and from 1.62 to 0.39 μm (roughness) with decreases of the LiClO₄/citrate ratio from PEDOT:P₄C₁ to PEDOT:P₁C₄, compared to that of pure PEDOT:P. In addition, digital images of all PEDOT:P_xC_y electrodes appeared dark blue in color, indicating the formation of relatively dense PEDOT:P_xC_y films (insert of Figure 1a).

The corresponding electropolymerized PEDOT:P_xC_y electrodes were examined by CV in 0.1 M PBS (pH 7.4) with scan rate of 50 mV s^{-1} , and the interfacial capacitance was calculated from the voltammetric curves by summing the charge current density in the forward and reverse scans and dividing the sum by twice the scan rate⁴⁰⁻⁴¹. As shown in Figure 1b, the interfacial capacitance of the PEDOT:P_xC_y electrodes decreases from 6.22 to 2.44 mF cm^{-2} as the amount of citrate increases (perchlorate/citrate ratio decrease from 4:1 to 1:4), while the PEDOT:C showed the smallest value of 0.13 mF cm^{-2} and PEDOT:P had the largest value of 7.81 mF cm^{-2} .

², respectively. The results from the electrochemical capacitance of the PEDOT:P_xC_y electrodes is in good agreement with the measured thickness of the corresponding films. These results demonstrated the possibility of introducing citrate (ternary carboxylic acid molecules) assisted by LiClO₄ to prepare carboxylic acid group-functionalized PEDOT interfaces.

Figure 1. (a) Thickness and roughness of different PEDOT interfaces; inset is the digital image of different PEDOT interfaces on ITO, numbers 1-7 represent: PEDOT:C, PEDOT:P,

PEDOT:P₄C₁, PEDOT:P₂C₁, PEDOT:P₁C₁, PEDOT:P₁C₂ and PEDOT:P₁C₄, respectively; (b) Calculated capacitance of different PEDOT interfaces in 0.1 M PBS, Scan rate 50 mV s⁻¹, n=3.

DA electrocatalysis at different PEDOT:P_xC_y electrode interfaces

The electrochemical reaction of DA at different PEDOT:P_xC_y electrodes was assessed by CV in 0.1 M PBS (pH 7.4) containing 0.5 mM DA, at a scan rate of 50 mV s⁻¹. The corresponding CV curves are shown in Figure S2, and Table 1 compared the key parameters of DA electrocatalysis with different PEDOT:P_xC_y electrode interfaces. For all electrodes, a pair of redox peaks (I_{pa} and I_{pc}) with different peak separations (ΔE_p) and peak height currents were observed, as shown in Figure S2. PEDOT:C (without LiClO₄) showed small redox peaks ($I_{pa} = 0.06 \text{ mA cm}^{-2}$ and $I_{pc} = -0.04 \text{ mA cm}^{-2}$) and a large ΔE_p of 190 mV, indicating a poor electron and mass transfer process at the PEDOT:C electrode interface, presumably due to the low polymerization efficiency. For PEDOT:P (without citrate), the I_{pa} value (0.22 mA cm^{-2}) increased by about 4 fold and the ΔE_p value dramatically decreased to 90 mV compared to PEDOT:C, demonstrating the improved DA electrocatalysis accommodated by the high polymerization efficiency of PEDOT:P. By optimizing the polymerization efficiency and introducing the negatively-charged citrate co-dopant, the electrocatalysis of DA using the PEDOT:P_xC_y electrodes was further enhanced. The I_{pa} values of all PEDOT:P_xC_y interfaces were significantly higher than that of the pure PEDOT:P, which can be ascribed to the high density of negatively-charged ternary carboxylic acid groups from the citrate co-dopant on the PEDOT:P_xC_y interface, which facilitated the electrostatic attraction and permeation of positively charged DA. It was clear that the PEDOT:P₂C₁ electrode had the largest I_{pa} value of 0.66 mA cm^{-2} , which is approximately 10 and 3 times higher than that of the pure PEDOT:C and PEDOT:P, respectively. Importantly, the PEDOT:P₂C₁ interface showed significant

increase in I_{pa} , while retaining a small ΔE_p . This significant improvement can be assigned to the synergetic effect of citrate and LiClO_4 in the doping system, in which citrate acts as a dopant to introduce negatively-charged carboxylic acid groups, and LiClO_4 assists the electropolymerization efficiency of PEDOT. Therefore, the PEDOT:P₂C₁ electrode was chosen as the optimized electrode interface for DA electrocatalytic analysis hereafter.

Table 1. Comparison of DA electrocatalysis with different PEDOT electrodes (EDOT 10 mM).

Electrodes	I_{pa} (mA cm ⁻²)	I_{pc} (mA cm ⁻²)	E_{pa} (mV)	E_{pc} (mV)	ΔE_p (mV)
PEDOT:C	0.06	-0.04	0.300	0.110	190
PEDOT:P	0.22	-0.11	0.230	0.140	90
PEDOT:P ₄ C ₁	0.32	-0.19	0.235	0.145	90
PEDOT:P ₂ C ₁	0.66	-0.29	0.235	0.145	90
PEDOT:P ₁ C ₁	0.46	-0.22	0.260	0.130	130
PEDOT:P ₁ C ₂	0.40	-0.21	0.265	0.130	135
PEDOT:P ₁ C ₄	0.35	-0.17	0.265	0.120	145

Spectroscopy characterization and quantification of the carboxylic acid groups in the PEDOT:P₂C₁ interfaces

XPS and FTIR were used to investigate the chemical characteristics of the PEDOT interface. From the wide survey spectra in Figure 2a, characteristic sharp bands at 164, 286 and 533 eV can be seen for these PEDOT interfaces, which were assigned to S2p, C1s and O1s, respectively. The new appearance of Cl2p and Cl2s peaks in PEDOT:P₂C₁ and PEDOT:P at 164 and 207 eV indicated the doping of ClO_4^- in the PEDOT structures during the electropolymerization process. For PEDOT:P, the ratio between the characteristic element Cl from dopant ClO_4^- and characteristic element S from PEDOT moiety is 1:3 (Cl/S), as shown in

Table 2. This reveals the doping level of PEDOT:P is on average one dopant per three monomer residues, which is in agreement with the previously reported doping level for PEDOT with one dopant per three or four monomer residues⁴². Compared with PEDOT:P, the ratio of Cl/S for PEDOT:P₂C₁ decreased to 1:4 in Table 1. The decrease in the amount of ClO₄⁻ is likely associated to the co-doping of citrate within the PEDOT:P₂C₁ structure. Moreover, the incorporation of citrate as co-dopant in the PEDOT:P₂C₁ interfaces was further validated by the existence of C=O stretching bands of the -COOH groups at 1733 and 1678 cm⁻¹ via FTIR analysis (Figure S3)⁴³⁻⁴⁴.

High resolution scans of C1s, O1s, S2p and Cl2p core-level were performed, and the corresponding results with band deconvolution are shown in Figure 2b-d and Figure S4. As shown in Figure 2b, the deconvoluted C1s of PEDOT:C showed three typical bands originating from the PEDOT moiety at 285.0, 285.3 and 286.6 eV, which can be assigned to C-C/C-H, C-S and C-O, respectively. The apparent appearance of the shoulder at high binding energy for C=O (288.1 eV) and O=C-O (289.3 eV) in PEDOT:C spectrum indicate the doping of citrate into PEDOT structure. For PEDOT:P (Figure 2c), the main C/C-H, C-S and C-O bands showed an obvious decrease of binding energy to 284.3, 284.9 and 285.8 eV. The asymmetric tail at high binding energy is ascribed to the π - π^* shake-up transition^{42, 45-46}. Compared to the PEDOT:C and PEDOT:P spectra, the main bands of PEDOT:P₂C₁ (Figure 2d) corresponding to C/C-H, C-S and C-O are located at 284.5, 285.0 and 285.8 eV, which are in between the corresponding PEDOT:P and PEDOT:C. Besides that, the PEDOT:P₂C₁ demonstrates the same shoulder bands raised from C=O and O=C-O as PEDOT:C with shifting to lower bonding energy at 287.5 and 288.7 eV. The bands shifting and the COO⁻ shoulder evidenced the co-doping effect of citrate and ClO₄⁻ into the PEDOT:P₂C₁. The relative contents of these C states were calculated and listed in Table 1. Based on the atomic ratio of S/Cl and C-S/C=O, the amount of ClO₄⁻ and -COOH on the PEDOT:P₂C₁ interface were calculated to be 4.03

(PEDOT/LiClO₄) and 1.03 (PEDOT/-COOH), respectively. The co-dopants ratio between ClO₄⁻ and citrate (tri-carboxylic acid) on the PEDOT:P₂C₁ interface was then estimated to be 0.76:1. What's more, the detailed deconvolution of O1s, S2p and Cl2p core-level bands for all PEDOT interfaces are shown in Figure S4.

The total surface density of carboxylic acid groups on the PEDOT surfaces was quantified by following the previously reported toluidine blue O (TBO) staining technique (Figure S5), which uses the cationic dye to bond to negatively-charged carboxylic acid groups with a ratio of 1:1³⁷⁻³⁸. The PEDOT:P₂C₁ desorbed solution had a deep blue color and high absorbance resulting in a calculated surface carboxylic acid groups density of 0.129 $\mu\text{mol}/\text{cm}^2$, suggesting the appearance of carboxylic acid groups on PEDOT:P₂C₁ surface, while control PEDOT:P without carboxylic acid groups showed insignificant color change.

Figure 2. XPS survey (a) and C1s spectra of PEDOT:C (b), PEDOT:P (c) and PEDOT:P₂C₁ (d).

Table 2. The contents of the carbon-containing functional groups, the amount of ClO_4^- and -COOH dopant in PEDOT:C, PEDOT:P and PEDOT:P₂C₁.

Electrodes	Carbon containing groups (at%)						PEDOT /LiClO ₄ S/Cl (at/at)	PEDOT/- COOH C-S/C=O (at/at)	LiClO ₄ /c itrate (at/at)
	C-C/C- H	C-S	C-O	C=O	O=C-O	π - π^*			
PEDOT: C	13.26	12.63	57.13	8.37	8.61	-	-	1.51	-
PEDOT: P	11.44	12.67	49.63	-	-	26.27	2.96	-	-
PEDOT: P ₂ C ₁	9.11	11.31	58.37	10.98	10.23	-	4.03	1.03	0.76

Surface characterization of PEDOT:P₂C₁ interfaces

The surface morphology of the PEDOT:P₂C₁ interface was investigated by SEM and compared with the control PEDOT:C and PEDOT:P, as shown in Figure 3a-c. The PEDOT:P₂C₁ interface (Figure 3a) had a dense compact film with well distinguished and homogeneously distributed globular structure all over the surface, indicating a good electropolymerization efficiency, which is similar to the positive control PEDOT:P film (Figure 3c). In contrast, the morphology of the PEDOT:C interface was only covered with a small amount of granulated PEDOT, indicating a poor electropolymerization process caused by the citrate dopant interrupting the nucleation and subsequent growth process of PEDOT (Figure 3b). The SEM results suggest the synergetic effect of LiClO₄ and citrate on the interface morphology, in which LiClO₄ leads to highly efficient electropolymerization of PEDOT as reported before³⁹, and citrate acts as co-dopant in the PEDOT:P₂C₁ film. The increased electropolymerization efficiency of the PEDOT:P₂C₁ electrode is expected to provide not only sufficient carboxylic acid groups via the ternary citrate, but an increased thickness and roughness of the electropolymerized film. According to Wenzel's model described for the homogeneous wetting regime, the increase of roughness leads to an increase in hydrophilicity

for a hydrophilic substrate⁴⁷. The wettability of different PEDOT electrodes was evaluated by static water contact angle measurements as recorded in Figure 3d-f. The PEDOT:P₂C₁ exhibited the smallest contact angle of 14.7° compared to that of PEDOT:C (18.5°) and PEDOT:P (31.9°). The decreased contact angle of the PEDOT:P₂C₁ interface is likely due to the incorporation of sufficient carboxylic acid groups via citrate dopant, as well as the increased polymerization efficiency induced by LiClO₄ with increased surface roughness.

In addition, the stability of the PEDOT:P₂C₁ electrodes was studied by repeated CV scanning in the range of 0-0.4 V for 80 cycles (0.1 M, pH 7.4 PBS). (Figure S5). The capacitance values were calculated through the CVs to evaluate the stability of the PEDOT:P₂C₁ interface. The PEDOT:P₂C₁ showed a fairly good stability and retained 91.0% of its initial capacitance after 80 cycles. The good cycling stability may arise from the relatively larger molecular weight of citrate (compared with perchlorate), and the trip-carboxylate property (i.e. multiple negatively-charged groups) of the citrate that minimized the leakage of the citrate dopant.

Figure 3. SEM images of interface structure at different PEDOT electrodes of PEDOT:P₂C₁ (a), PEDOT:C (b) and PEDOT:P (c), insets are the corresponding high magnification images; digital images of wettability for PEDOT:P₂C₁ (d), PEDOT:C (e) and PEDOT:P (f).

Surface charge and pH dependent electrochemical characterization.

The electrochemical behaviors of the PEDOT:P₂C₁ and PEDOT:P electrodes were investigated by using two different charged redox probes (i.e. negatively-charged Fe(CN)₆^{3-/4-} and positively-charged [Ru(NH₃)₆]^{2+/3+}) to prove the surface charge effect of the PEDOT. As shown in Figure 4, both the PEDOT electrodes show quasi-reversible peaks with slightly different peak current densities and peak separations (ΔE_p) in these two redox probes. The voltammogram obtained from PEDOT:P electrode (Figure 4a) exhibited an anodic peak current density of 0.167 mA cm⁻² with a ΔE_p of 100 mV. For the PEDOT:P₂C₁ electrode, the anodic peak current density showed a slight decrease to 0.134 mA cm⁻² and the ΔE_p increased to 100 mV compared to that of the PEDOT:P electrode, demonstrating the negative effect of PEDOT:P₂C₁ due to the negatively-charged carboxylic acid groups at the interface. When the measurement was performed with the positively-charged probe [Ru(NH₃)₆]^{2+/3+} (Figure 4b), the electrochemical behaviors of the PEDOT electrodes were reversible. The anodic peak current density and ΔE_p for PEDOT:P electrode were 0.097 mA cm⁻² and 75 mV. The PEDOT:P₂C₁ showed 2.1 times higher anodic peak current density (0.201 mA cm⁻²) and 15 mV decreased ΔE_p to 60 mV. The improved electrochemical performance of PEDOT:P₂C₁ towards positively-charged probe can be ascribed to the surface charge effect by the high density of carboxylic acid groups at the interface.

The effect of pH on the peak potential and peak current density of DA at the PEDOT interface.

Since the electrochemical behaviour of the analyte is pH dependent, the peak potential and peak current density versus pH were examined.⁴⁸ Figure 4c and d show the CVs of PEDOT:P₂C₁ in the presence of 0.5 mM DA, and the corresponding plot of peak potential and peak current density with changing pH (3.4-9.4) of the supporting electrolyte. It is clear that the peak potential shifted negatively with pH increase, indicating that the electroactivity of DA is pH dependent. As shown in Figure 4d, the oxidation peak potentials of DA at PEDOT:P₂C₁ were linearly proportional to pH according to the equation $E_{pa} = 0.632 - 0.052 \text{ pH}$ ($R^2 = 0.986$). The slope of -0.052 V/pH is close to the theoretical value of -0.059 V/pH for equal proton and electron (2 H⁺/2 e⁻) transfer during the DA oxidation. Besides that, the oxidation current density (Figure 4d) increased gradually in the range of 3.4-7.4, reaching the highest peak current density at 7.4, and decreased after 7.4 in the alkaline solution. pH 7.4 was chosen as the optimized condition for DA electrochemical detection, which is also the physiological pH for human body.

What is more, the PEDOT:P electrode exhibited a similar trend for peak potential and peak current density (Figure S6).

Figure 4. CVs of PEDOT:P₂C₁ (a) and PEDOT:P interfaces in 0.1 M PBS (pH 7.4) containing 1 mM Fe(CN)₆^{3-/4-} (a), [Ru(NH₃)₆]^{2+/3+} (b); (c) CVs response of 0.5 mM DA at PEDOT:P₂C₁ interface in 0.1 M PBS with various pH ranging from 3.4 to 9.4; (d) the corresponding plots of peak potential and current density vs pH. Scan rate 50 mV s⁻¹.

Surface dependent discrimination of DA from AA and UA

The discrimination of DA at the PEDOT interfaces was evaluated using CVs. PEDOT:C is not shown because of the poor electrochemical properties resulting from an insufficient electropolymerization process. Figure 5 shows the CVs of PEDOT:P₂C₁ (a) and PEDOT:P (b) in 0.1 M PBS (pH 7.4) containing 0.5 mM AA, DA and UA, and their mixture, respectively. It is clear to see that the PEDOT:P₂C₁, comprising negatively-charged carboxylic acid dopant, delivered a dramatic improvement to the discrimination of DA in the presence of the two interferents (AA and UA) compared with the pure PEDOT:P. The PEDOT:P₂C₁ electrode showed a sharp oxidation peak for DA at 0.23 V, and significantly smaller responses for AA

and UA, with the oxidation peaks at around 0.10 V and 0.35 V, respectively. The ratio of oxidation peak height for DA, AA and UA is 19.2 : 1 : 3.3 (AA was denoted as 1). In contrast, the PEDOT:P interface showed a reverse effect with a broad and small oxidation peak for DA at 0.23 V, together with a strong response to the interferents, AA and UA, with larger oxidation peaks at 0.05 V and 0.35 V, respectively. The ratio of oxidation peak height for DA, AA and UA is 1.8 : 1 : 2.1 (AA was denoted as 1).

The relationship between the interfacial properties of the PEDOT:P₂C₁ and the PEDOT:P and their discriminative electrode kinetics toward DA, AA and UA was investigated using electrochemical impedance spectroscopy (EIS). The equivalent Randles model circuit (inset of Figure 5c) composed of mixed kinetic and charge-transfer control was applied to fit the impedance data with good matches between the experimental and fitted data. This is shown in Figure 5c and 5d, where R_s is the solution resistance, R_{ct} is the charge transfer resistance, CPE is the constant phase element for rough interface ($n = 0$ is pure resistor, $n = 1$ is pure capacitor), and W is Warburg impedance by diffusion contribution. For both PEDOT:P₂C₁ and PEDOT:P, the R_{ct} values showed an apparent decrease after the addition of analytes (DA, AA and UA) due to electrochemical polarization by the reaction of analytes at the PEDOT electrodes. Table S1 summarizes the R_{ct} change of the PEDOT:P₂C₁ and the PEDOT:P electrodes before and after addition of DA, AA and UA, respectively. The PEDOT:P₂C₁ interface showed a 66.7% change in R_{ct} after addition of DA, while showing a significantly smaller 26.7% and 29.3% change in R_{ct} after addition of AA and UA, respectively, suggesting that the PEDOT:P₂C₁ interface had much faster electrode reaction kinetics towards DA compared with AA and UA. In contrast, the PEDOT:P interface showed a 46.4% change in R_{ct} for DA, while having a much larger 76.1% and 66.2% change in R_{ct} in response to AA and UA, respectively. Furthermore, the Warburg coefficient (inversely proportional to the square root of the diffusion coefficient) of the PEDOT:P₂C₁ interface showed a 142.2% increase in the presence of DA, compared with

the PEDOT:P, which showed only a 61.6% increase. These EIS results are in good agreement with the CV measurements. Under physiological conditions (pH 7.4), dopamine is positively charged (pKa 8.9), while ascorbic acid (pKa 4.2) and uric acid (pKa 5.7) are negatively-charged³³. The PEDOT:P₂C₁ possesses a relatively high amount of negatively-charged carboxylic acid groups at the PEDOT interface which facilitates the transfer and preconcentration of the positively charged DA at the PEDOT:P₂C₁ interface by the electrostatic attraction and hydrogen-bonding interactions³³. The difference in electrode reaction kinetics in conjunction with the negatively-charged citrate co-dopant in the PEDOT:P₂C₁ interface facilitated the highly selective detection of DA and its discrimination from AA and UA interference.

Figure 5. CVs of PEDOT:P₂C₁ (a) and PEDOT:P (b) in 0.1 M PBS (pH 7.4) containing 0.5 mM DA, 0.5 mM AA and 0.5 mM UA and their mixture with scan rate of 50 mV s⁻¹; EIS spectra of PEDOT:P₂C₁ (c) and PEDOT:P (d) in 0.1 M PBS (pH 7.4) containing 0.5 mM DA, 0.5 mM AA and 0.5 mM UA at their corresponding oxidation peak potentials.

Electrochemical sensing of DA

The developed PEDOT:P₂C₁ electrodes were employed for electrochemical sensing of DA. As shown in Figure 6a and b, DPV measurements were performed with the PEDOT:P₂C₁ and PEDOT:P electrode. The anodic peak currents increased with successive additions of DA. As can be seen in the calibration curves in Figure 6c, the anodic peak current of the PEDOT:P₂C₁ electrode was linearly proportional to DA concentration over the range of 1-85 μ M, while the PEDOT:P electrode range was 5-85 μ M, due to the indistinguishable signal obtained in the 1-5 μ M range. The sensitivity of the PEDOT:P₂C₁ electrode for DA was calculated to be 3.24 μ A cm⁻² μ M⁻¹, which is 4.1 times higher than that of the PEDOT:P electrode (0.778 μ A cm⁻² μ M⁻¹). Besides that, the limits of detection (LOD) at PEDOT:P₂C₁ electrode for DA was 0.15 μ M by using equation $LOD = 3s/b$ (s is the standard deviation of the 10 blank, b is the slope of the calibration curve), which shows improved LOD compared to PEDOT:P electrode (1.25 μ M). The improved analytical performance for detection of DA by the PEDOT:P₂C₁ electrode, together with the wider linear range and higher sensitivity compared to that of PEDOT:P, can be attributed to the incorporation of a high-density of negatively charged carboxylic acid groups at the PEDOT interface, which contributes to the electrostatic accumulation of DA and enhances the electrode kinetics of DA at the PEDOT:P₂C₁ interface. The analytical performance of the PEDOT:P₂C₁ electrodes towards DA was also compared with other literature based on PEDOT modified electrodes (summarized in Table S2). Our PEDOT:P₂C₁ electrode showed good performance with respect to both the sensitivity and linear response compared with other PEDOT-based electrodes. Figure 6d shows the DPV measurement of DA (50 μ M) in the presence of AA (50 μ M) and UA (50 μ M) interferents, and their corresponding individual DPV responses. For PEDOT:P₂C₁, the AA and UA interference resulted in an insignificant increase of background current and a small shoulder peak in the high potential region. The anodic peak

height of the DPV response in pure DA is similar to that of mixed solution (DA, AA and UA), suggesting the satisfactory discrimination of DA from these common interferences. Compared to that, the PEDOT:P electrode showed the same phenomenon as CVs response to the mixture with a small oxidation peak for DA and UA, and a strong response to UA.

Figure 6. DPV spectra of PEDOT:P₂C₁ (a) and PEDOT:P (b) in 0.1 M PBS (pH 7.4) containing different concentration of DA (1 to 85 μ M); (c) corresponding calibration curves, $n=3$; (d) DPV curves of PEDOT:P₂C₁ and PEDOT:P in 50 μ M DA, 50 μ M AA, 50 μ M UA separately and their mixture.

Conclusions

We have demonstrated the development and utility of a novel PEDOT interface containing a high density of negatively-charged carboxylic acid groups. By using an inexpensive organic acid, citrate, together with perchlorate in a specific ratio, we succeeded in electropolymerizing a dense tri-carboxylate doped PEDOT interface. The optimized PEDOT:P₂C₁ interface with a high surface carboxylic acid groups density resulted in improved electrode kinetics and

facilitated the detection and discrimination of DA from the major interferents in physiological solutions, i.e. AA and UA. DA sensing with the PEDOT:P₂:C₁ electrode interface was performed by DPV, delivering a wider linear range and higher sensitivity compared to that of PEDOT without carboxylic acid groups. Our results demonstrated a facile and economic approach to fabricate functionalized PEDOT with carboxylic acid group-rich moieties for interfacial recognition, modulation of molecule diffusion and potentially for further chemical coupling and bio-conjugation, thus accelerate the potential development of new PEDOT based organic electronics for applications in sensing, biosensing, energy storage and catalysis.

Associated content

Supporting information

The supporting information is available xxx

CVs electropolymerization of PEDOT, CVs of PEDOT in DA, FTIR and XPS spectra of PEDOT, TBO staining absorbance spectra, fitted parameters obtained by EIS spectra of PEDOT.

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