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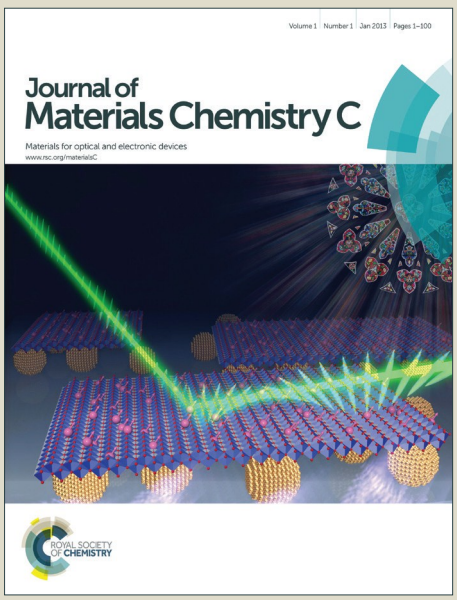

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ARTICLE

Highly-sensitive epinephrine sensors based on organic electrochemical transistors with carbon nanomaterials modified gate electrodes

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Organic electrochemical transistors (OECTs) have been found to be excellent transducers for various types of biosensors. Here, we report highly sensitive epinephrine sensors based on OECTs prepared on glass substrates by solution process. The device performance is optimized by immobilizing Nafion and carbon-based nano-materials, including carbon nanotube, graphene and graphene oxide, on the gate electrodes of the OECTs. The detection limit of the sensors is down to 0.1nM, which can cover the concentration level of epinephrine in medical detections. Considering that the devices can be prepared by facile solution process with low cost, the highly sensitive epinephrine sensors will be ideal transducers for disposal applications in the future.

1. Introduction

The metabolism of epinephrine, a neurotransmitter and hormone, can lead to glycogenolysis in liver and skeletal muscle, the mobilization of free fatty acid, the increase of plasma lactate and the improved force and rate of heart contraction.[1-2] Because of such physiological effects, it is prohibited to use in games by world anti-doping agency and has medical uses for patients with diseases such as cardiac arrest in emergency.[3-4] Therefore, highly sensitive epinephrine sensors have numerous important medical applications.

Many approaches, including liquid chromatography (HPLC),[5-6] polarography,[7] and electrochemical methods,[8-12] have been successfully used in the analysis of epinephrine.[13] Compared with many techniques based on expensive and unportable instruments, electrochemical methods are convenient, cost effective and suitable for miniaturization. For example, Tsai et al. employed Pd-Au nano-particles modified glassy carbon electrode to sense epinephrine with a detection limit of 50μM;[14] Valentini et al. used single-wall carbon nanotubes modified glass carbon and stainless steel microelectrode to determine the epinephrine concentration by cyclic voltammetry (CV) method with a detection limit of 2μM.[15] Copped è et al. used a cotton-fiber based organic electrochemical transistor (OECT) with a Pt gate electrode to detect epinephrine in NaCl solution and showed obvious responses when the concentrations of epinephrine were above 1 μM.[16] However, the normal concentration of epinephrine in human plasma is very low (~0.2 nM),[17] so the sensitivity of the above electrochemical methods should be dramatically improved before using them in practical applications.

OECTs, a type of organic thin film transistors (OTFTs) with solution gate, were firstly reported in 1984 and have been used in many applications.[18-21] OECTs can be operated in electrolytes for chemical and biological sensing applications and show many advantages, including high sensitivity, low working voltage, easy fabrication and feasibility of miniaturization.[21] OECTs have been successfully used in various types of sensors for detecting ions,[22] bacteria,[23] glucose,[24-26] neurotransmitters,[27-29] DNA[30], cells,[31] and so on,[32-35] which normally show very low detection limits due to the inherent amplification function of the transistors.[36] Therefore, highly sensitive epinephrine sensors are expected to be realized based on OECTs.

In this paper, OECTs with poly(3,4-ethylene dioxythiophene): poly(styrene sulfonate) (PEDOT:PSS) as the active layers were prepared by solution process. Then epinephrine sensors were fabricated based on the devices with Nafion/nanomaterial modified Pt gate electrodes. Different potentially low-cost carbon-based nanomaterials, including graphene flakes (Gr), graphene oxide (GO) and single walled carbon nanotubes (SWNTs), were used in the gate modification to improve the sensitivity. The device with Nafion and SWNTs modified on the gate electrode shows a detection limit down to 0.1nM, which is sensitive enough for practical uses. Considering that OECTs can be easily prepared with solution process, the OECT-based epinephrine sensors are promising for disposal clinical applications or medical safety checking.[37]

Fig. 1

2. Experimental

Materials

Phosphate buffered saline (10xPBS) solution (pH=7.4), epinephrine and Nafion (weight percentage is ~5% in a mixture of lower aliphatic alcohols and water), were purchased from Sigma

Aldrich Co. and stored at 4 ℃ for future use. PEDOT:PSS aqueous solution was purchased from Heraeus Ltd and stored at 4 ℃. Dimethyl sulfoxide (DMSO) was added into the PEDOT:PSS solution with the volume ratio of 5% to improve the conductivity and stability of PEDOT:PSS films. SWNT powder was purchased from Sigma Aldrich and diluted in DI water to 0.1mg/ml. GO water dispersion (2mg/ml) was purchased from Jining LeaderNano Tech L.L.C. and diluted to 0.1mg/ml for future use. Graphene flake powder was purchased from Jining LeaderNano Tech L.L.C. and dissolved in DI water to 0.1mg/ml.

Device fabrication

As shown in **Fig. 1**, OECTs were fabricated on cleaned glass substrates (size: 1cm × 1cm) in the following steps. First, the Ti/Pt source, drain and gate electrodes were deposited on the glass substrates by magnetron sputtering through a shadow mask. The channel length and width of the devices were 0.2 mm and 6.0 mm, respectively. Then the surface of the samples was treated by oxygen plasma, followed by spin coating (spin rate: 3400rpm) and patterning of PEDOT:PSS layers on the channel areas. The metal lines connected to the source, drain and gate electrodes are protected by a silicone layer (green layer in **Fig. 1a**) on the surface to avoid the direct contact with electrolyte during device characterization. Finally, the devices were annealed at 185 ℃ for 1 hour in a glove box filled with high purity Nitrogen gas.

SWNT, GO and Gr solutions (concentration: 0.1mg/ml) were mixed with Nafion (5 wt.%) solution in a volume ratio of 1:1. Then 5μl of each mixture solution was drop-coated on the 3mm × 3mm Pt gate electrodes of the OECT-based sensors. The modified devices were stored in a 4 ºC refrigerator before testing.

Device characterization

Before electrical measurements, the channel and modified gate electrodes were rinsed with PBS solution thoroughly to remove the undesired residue left on the OECTs. In the measurement of channel current (I_{DS}) as a function of time (t), each epinephrine sensor was immersed in 10mL PBS solution that was slowly stirred in a beaker. The source, drain and gate electrodes of the device were connected to two Keithley source meters (Keithley 2400) and the channel current was measured under a fixed gate voltage (V_G =0.6V) and a fixed source-drain voltage (V_{DS}=0.1V) controlled by a Labview program in a computer. Then epinephrine solution was added in the PBS solution during the measurement to get the responses of each sensor to different epinephrine concentrations. In the characterization of transfer curves of the OECTs, I_{DS} was measured as a function of V_G at the fixed V_{DS} of 0.1V.

CHI660B electrochemical workstation (CH Instruments, Inc) and a standard three-electrode electrolytic cell were employed for the CV measurements of Nafion and nanomaterials -modified Pt electrodes (size: 3mm × 3mm) in an epinephrine (1mM) PBS solution. The voltage scan rate is 50mV/s relative to a standard Ag/AgCl reference electrode and Au counter electrode (size: 3mm × 3mm).

3. Results and Discussion

3.1 Working principle of OECT-based epinephrine sensors

The conductance of the PEDOT:PSS channel of an OECT can be modulated by the gate voltage due to the electrochemical doping by cations from the electrolyte.[18] The channel current I_{DS} of the device at different source-drain voltage V_{DS} and gate voltage V_G is given by the following equation:[21,38]

$$I_{DS} = \frac{q\mu p_0 tW}{LV_p}(V_p - V_G^{eff} + \frac{V_{DS}}{2})V_{DS}, \quad (\text{when } |V_{DS}| << |V_p - V_G^{eff}|)$$
$$V_p = qp_0 t / c_i, \qquad (1)$$
$$V_G^{eff} = V_G + V_{offset},$$

where q and μ are electron charge and hole mobility, respectively; p_0 is the initial hole density in the channel; V_p and $V_G{}^{eff}$ are the pinch-off voltage and the effective gate voltage on the transistor, respectively; V_{offset} is an offset voltage at gate/electrolyte interfaces; t is the thickness of the active layer; W and L are the channel width and length of the OECT, respectively; c_i is the effective gate capacitance.

The working mechanism of the OECT-based epinephrine sensors is shown in Fig. 1. The direct electro-oxidation of epinephrine frees two electrons per epinephrine molecule and produce faradic current between the gate electrode and the electrolyte. The direct electro-oxidation of epinephrine in PBS is given by the formula:[39-41]

$$epinephrine \rightarrow epinephrine\ quinone + 2H^+ + 2e^- \qquad (2)$$

The faradic current produced by the direct electro-oxidation of epinephrine at the gate electrode can change potential difference between the electrolyte and the gate electrode and hence change the effective gate voltage $V_G{}^{eff}$ of the transistor given by: [21, 38]

$$V_G^{eff} = V_G + \alpha \log[EPI] + constant \quad ,$$
$$\alpha = 2.3(1+\gamma)kT/2e \ , \qquad (3)$$

where γ is the ratio between the electrical double layer capacitances of the electrolyte/channel interface (C_C) and the electrolyte/gate interface (C_G), $\gamma = C_C/C_G$; k is Boltzmann constant; T is room temperature and [EPI] is the concentration of epinephrine. Therefore, the increase of the epinephrine concentration in the beaker will increase the effective gate voltage of the OECTs and thus decrease the channel current. In other words, the transfer curve of the OECT will shift to lower gate voltage after the addition of epinephrine in the solution. (See supporting information, **Figure S1**).

As shown in Fig. 1, the gate electrode is modified with Nafion and nanomaterials. Due to pK_{a1} of epinephrine is about 8.02,[39] epinephrine molecules have positive charge in neutral PBS solution while Nafion is negatively charged at neutral aqueous solution.[29] So Nafion will attract epinephrine molecules in PBS solution by electrostatic interaction. On the other hand, nano-materials have been shown to be able to increase the sensitivity and decrease the detection limit of OECT-based biosensors.[26-29, 40-43] Hence, the surface modification on the gate electrodes is important

to the performance of the devices, which has been optimized in our experiments.

3.2 Epinephrine sensors with bare Pt gate electrodes

Fig.2a shows the normalized channel current responses (I/I_0, where I_0=the stabilized current with no epinephrine added) of an OECT-based epinephrine sensor with a bare Pt gate electrode to the additions of epinephrine. We can find that the channel current decreases with the increasing concentration of epinephrine, indicating the direct electro-oxidation of epinephrine molecules at the Pt gate electrode even though there is no modification on the surface. The device shows the channel current noise level of ~0.05 μA, which is much lower than the channel current (>100 μA) of the device. As shown in the inset of Figure 2a, the detection limit (signal/noise ratio > 3) of the device to epinephrine is ~30nM. The channel current change is due to the change in the effective gate voltage V_G^{eff} of the OECT given by Equation (3). The effective gate voltages corresponding to different epinephrine concentrations can be decided according to the transfer curve (I_{DS} vs. V_G) of the OECT shown in the inset of **Fig2b**. By subtracting the corresponding gate voltage before adding epinephrine, we can calculate the changes of the effective gate voltage (ΔV_G^{eff}).[29,44] Therefore, the response of the device to epinephrine can be presented as ΔV_G^{eff} versus [*EPI*], as shown in **Fig 2b**.

Fig. 2

3.3 Surface modification of Pt electrodes

To improve the sensitivity of the OECT-based epinephrine biosensors, Pt gate electrodes were modified with nanomaterials, including SWNTs, Gr and GO, which can promote electron-transfer reactions and enhance the electrocatalytic activity of the gate electrodes.[15,42] Nafion, an acidic polymer with the stable Teflon backbone and the acidic sulfonic groups, was employed as a matrix to modify the Pt electrodes together with the nanomaterials. Composites films of Nafion and different nanomaterials were uniformly coated on the Pt electrodes by drop coating and characterized by atomic force microscopy (AFM). The average thickness of each film was measured by reading the height difference under AFM across scratched edges. The surface morphology of the gate electrodes modified with (a) Nafion film (average thickness: 1.2μm), (b) Nafion film (2.3μm), (c) Nafion+SWNT film (2.1μm), (d) Nafion+Gr film (2.0μm) and (e) Nafion+GO films (2.2μm) were characterized under atomic force microscopy (AFM), as shown in the supporting information (Figure S2). Because the nanomaterials have low weight percentages (~2 wt.%) in the composite films, we find little influence of them on the surface morphology. The surface roughness values (rms) of all films are very similar (~3.8 nm).

The electrocatalytic properties of the electrodes were characterized by CV measurements in epinephrine (1mM) PBS solution. Fig. 3 shows the CV curves of the Pt electrodes modified with Nafion and different nanomaterials. The Nafion/nanomaterial modified electrodes and clean Pt electrode exhibit the oxidation peaks at about 0.6V and about 0.3V, respectively (vs Ag/AgCl electrode). The increased peak voltage after the modification of Nafion can be attributed to the Nafion film that limits the diffusion rate of epinephrine. On the other hand, the modification of Nafion on the Pt electrode can obviously increase the peak value of the redox current due to the fact that the negatively charged Nafion can attract positively charged epinephrine molecules in the PBS solution to increase the concentration of epinephrine near the electrode. Although the addition of GO in the Nafion film cannot increase the electrocatalytic activity of the electrode, the added graphene flakes and SWNTs lead to substantial enhancement of electrocatalytic activity as well as the effective surface area of the electrodes. We can find that the addition of SWNTs in Nafion increases the peak current for more than 60% compared with the electrode modified with Nafion only.

3.4 Epinephrine sensors with modified Pt gate electrodes

The Pt gate electrodes of OECTs were modified with pure Nafion films with two different thicknesses, including 1.2 μm and 2.3μm, by drop-coating Nafion solutions with different concentrations. Then the OECTs were characterized in PBS solution with the addition of epinephrine for different concentrations. As shown in **Fig. 4a** and **4b**, the OECTs exhibit channel current responses to additions of epinephrine and their detection limits are ~10nM, which are slightly lower than that of the OECT with bare Pt gate. The improvement of the sensitivity can be attributed to the increased concentration of epinephrine near the gate attracted by Nafion. So epinephrine molecules would diffuse across the Nafion micropores to the Pt electrode and undergo electro-oxidation. We can find that the device with thicker Nafion film shows higher current response. The slope α for the effective gate voltage change ΔV_G^{eff} versus epinephrine concentration in logarithmic axis (log[EPI]) is also higher for the device with a thicker Nafion film, as shown in **Table I**. On the other hand, too thick Nafion films can impede the transfer of epinephrine to the gate surface. Therefore, we chose the Nafion thickness of ~ 2μm in the following experiments.

Fig. 4

Then the OECTs co-modified with Nafion and different nanomaterials (SWNT, Gr and GO) were characterized at the same conditions. **Fig. 5a** shows the normalized channel current responses of the OECT with Nafion+GO/Pt gate to epinephrine addition in PBS solution. The detection limit is ~ 10nM, which is similar to that of the device with Nafion/Pt gate. Therefore, the modification of GO on the Pt gate has little effect on the OECT-based epinephrine biosensors. Moreover, GO leads to lower slope α in sensing epinephrine, which is probably due to the slow diffusion of epinephrine impeded by GO.[45] **Fig. 5b** shows the normalized channel current response of the OECT with Nafion+Gr modified on the Pt gate. The device exhibits an obvious channel current response down to the concentration of 1nM, due to the enhanced electrocatalytic activity of the gate electrode to epinephrine. **Fig 5c** shows the normalized channel current response of the device modified with Nafion+SWNTs on the Pt gate to additions of epinephrine. The detection limit of the device

is as low as 0.1nM, which is much lower than those of the aforementioned devices. This result is consistent with the CV measurements of the gate electrodes in epinephrine PBS solution. So the lowest detection limit of the device can be attributed to the highest electrocatalytic activity of the Nafion+SWNT modified Pt gate.

The changes of the effective gate voltage ΔV_G^{eff} of all devices at different epinephrine concentrations are calculated according to the channel current responses and shown in Fig 5d. The slope α of ΔV_G^{eff} versus epinephrine concentration in logarithmic plot (log[EPI]) is fitted for each device. As shown in **Table I,** the OECT with the Nafion+SWNT/Pt gate shows the highest α and the lowest detection limit in all of the devices, indicating that SWNT is the most effective nanomaterial in improving the sensitivity of the OECT-based epinephrine sensors.

For practical applications, the selectivity of the device is very important. As reported before, OECTs can be used as many types of electrochemical biosensors.[21] So the major interferences including ascorbic acid (AA) and uric acid (UA) were tested by the device with the Nafion+SWNT/Pt gate. We found that the device showed obvious responses to AA and UA at the minimum concentrations of 0.1 μM and 1 μM (See supporting information, Figure S3), respectively, which are 3-4 orders of magnitude worse than that of the device in sensing epinephrine. AA and UA have negative charges in neutral PBS solution (pH=7.4) while Nafion is also negatively charged in PBS.[44] So the Nafion film can effectively block the diffusion of AA and UA to the Pt gate electrodes of OECTs by electrostatic interaction. On the other hand, epinephrine is positively charged in PBS solution and will be attracted by Nafion film to the Pt gate electrode. Therefore, the Nafion film modified on the Pt gate can improve the selectivity of the devices.

Fig. 5

The best OECT-based epinephrine sensor gave the detection limit of 0.1nM that is much better than those of other electrochemical epinephrine sensors reported before (20-10μM),[8-12] as shown in **Table II**. For the cotton-fiber OECTs reported by Coppedè et al,[16] the detection limit to epinephrine is (only ~1 μM) much higher than that of our devices probably due to the poor stability of their devices, as evidenced by the big error bars of the current responses of the devices. Compared with the epinephrine sensors based on conventional ion−sensitive field effect transistors (ISFETs) with the detection limit of only 1μM,[9] the OECT-based sensors are much more sensitive and the detection limit is 3-4 orders of magnitude better, which can be attributed to the following two factors. One is the low operation voltage (less than 1 V) of the OECT. For a Si-based field-effect transistor, the operational voltage is around 10V that is one order of magnitude higher than that of the OECT. So the OECT-based sensor is much more sensitive to potential change than typical FET-based transistors. Another factor is the sensing mechanism of the OECT based on the detection of the electrochemical reaction of epinephrine on the gate. So the sensitivity of the device can be enhanced by improving the electrocatalytic activity of the gate electrode. Besides the nanomaterials used in this work, many other functional materials can be used to enhance the sensitivity of the OECT-based epinephrine biosensors.[42] There is a grand challenge in using conventional electrochemical epinephrine biosensors in medical applications because the epinephrine level in plasma of a healthy human is less than 2×10^{-10} M.[16] Based on the OECT platform, the epinephrine sensors able to detect the concentration down to 10^{-10}M can be further developed for practical applications in the future.

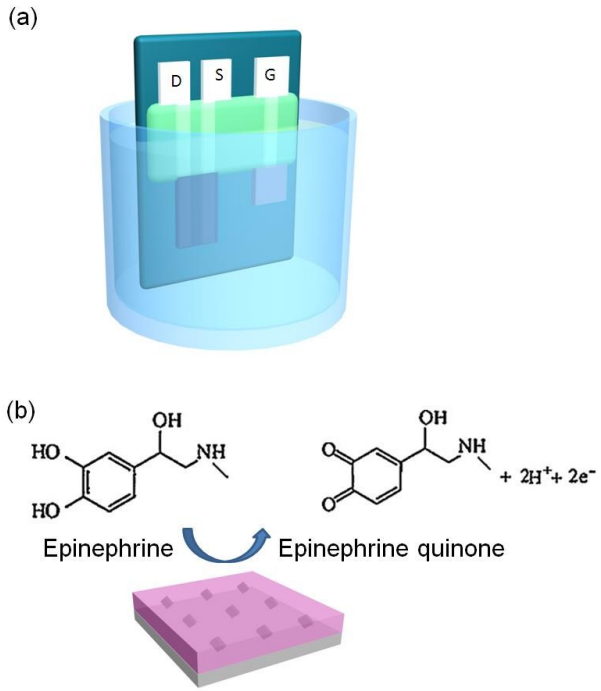

Fig. 1 (a) The schematic diagram of an OECT-based epinephrine sensor with a Nafion and nanomaterial -modified gate electrode. **(b)** The oxidation of epinephrine at the gate electrode modified with Nafion and carbon-based nanomaterials.

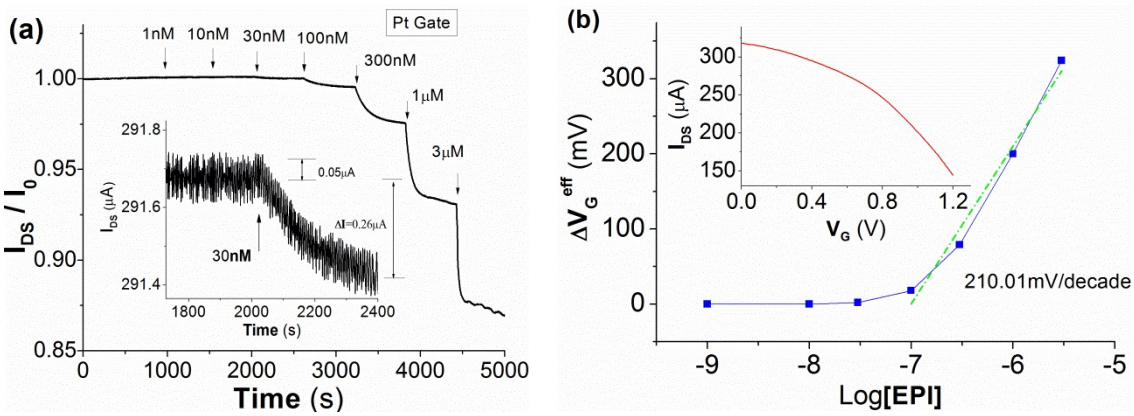

Fig. 2 (a) The normalized current response of an OECT with a Pt gate to the increasing epinephrine concentration in PBS solution measured at V_{DS}=0.1V and V_G=0.6V. I_0=291.67 μA. Inset: the enlarged current response at the detection limit of the device (30nM). (b) The offset voltage change as a function of the logarithmic value of epinephrine concentration ([EPI]). Inset: Transfer curve (I_{DS} versus V_G) of the OECT measured in PBS solution with V_{DS}=0.1V.

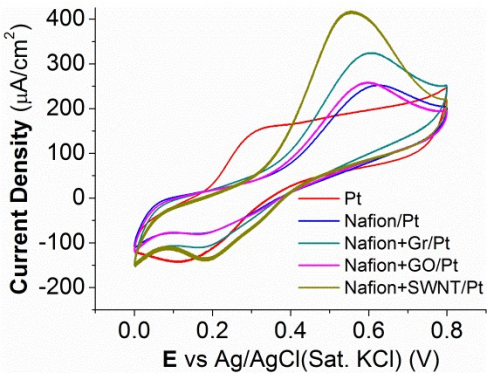

Fig. 3 Cyclic voltammograms of Pt electrodes modified with different films measured in 1mM epinephrine PBS solution. Voltage scan rate: 50mV/s.

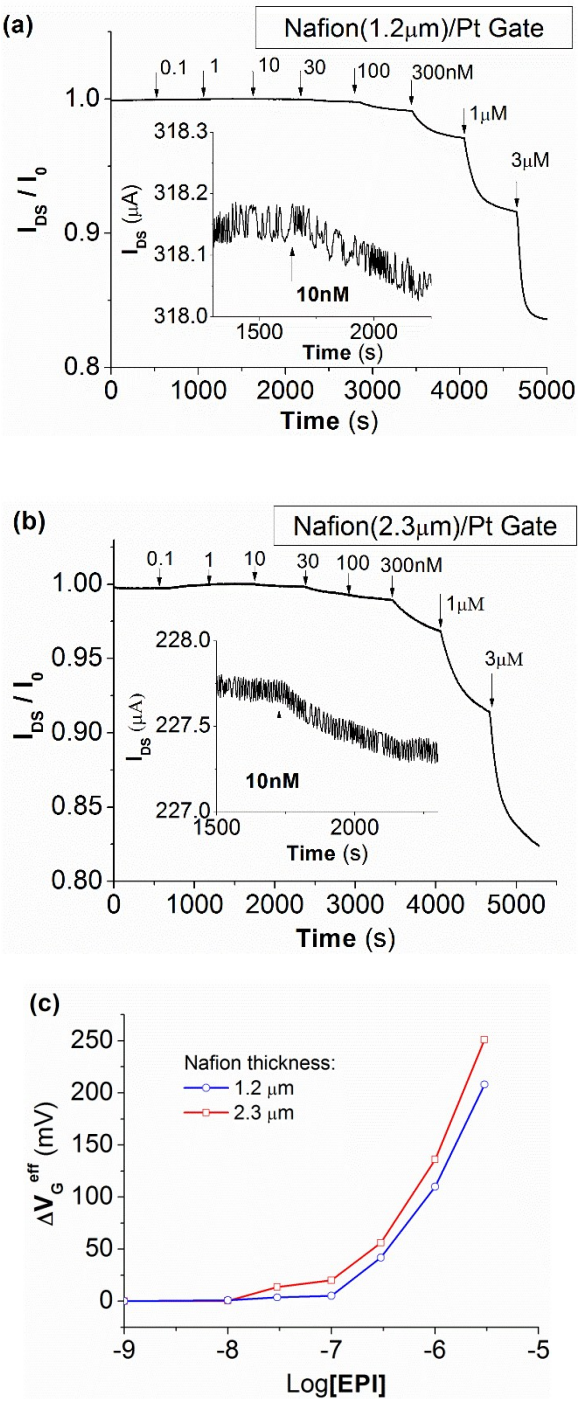

Fig. 4 The normalized current responses of OECTs with (a) 1.2μm thick (I_0=317.79 μA) (b) 2.3 μm thick Nafion films modified on Pt gates to the increasing epinephrine concentration in PBS solution (I_0=227.20 μA). V_{DS}=0.1V, V_G=0.6V,. Insets: The enlarged current responses at the detection limits (10nM). (c) The effective gate voltage change (ΔV_G^{eff}) of the two OECTs as a function of the logarithmic value of epinephrine concentration (Log[EPI]).

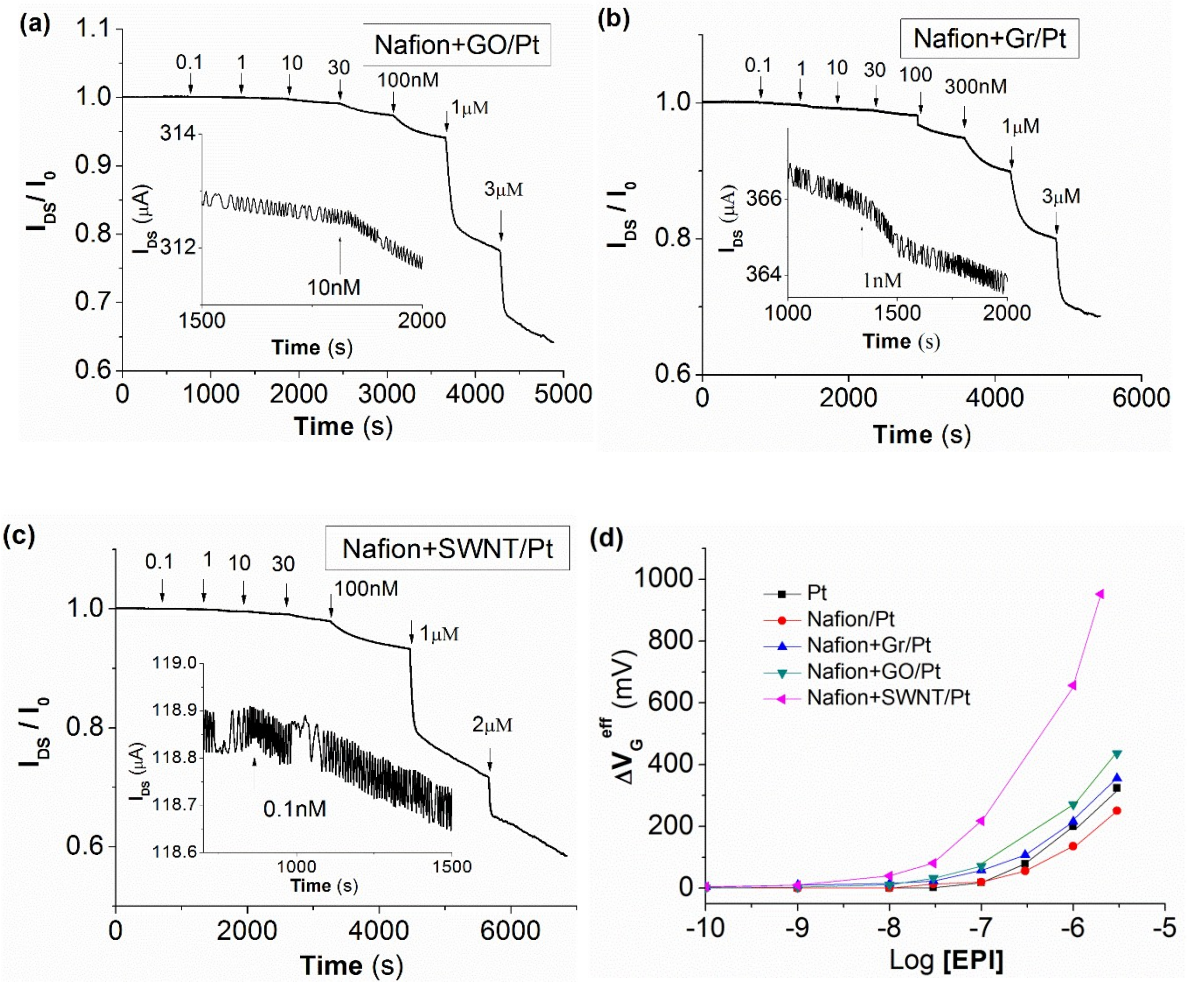

Fig. 5 The normalized current responses of OECTs with (a) Nafion+GO (I_0=313.13 μA); (b) Nafion+Gr (I_0=367.53 μA) and (c) Nafion+SWNT films modified on Pt gates to the increasing epinephrine concentration in PBS solution (I_0=119.02 μA). V_{DS}=0.1V, V_G=0.6V. Insets: the enlarged current responses at the detection limits ((a) 10nM, (b) 1nM; (c) 0.1nM). (d) The effective gate voltage change (ΔV_G^{eff}) of the OECTs with different gate electrodes as a function of the logarithmic value of epinephrine concentration (Log[EPI]).

Table I. The detection limit and the slope of effective gate voltage per decade of the epinephrine concentration (α) of OECT-based epinephrine biosensors.

Gate of OECT	**Detection limit** (nM)	α (mV/decade)
Pt	30	210
1.2μm-thick Nafion/Pt	10	136
2.3μm-thick Nafion/Pt	10	194
Nafion+GO/Pt	10	239
Nafion+Gr/Pt	1	248
Nafion+SWNTs/Pt	0.1	533

Table II. Comparison of different epinephrine biosensors.

Method	Modification	Detection limit(nM)	Reference
Square wave voltammogram	pyrolytic graphite electrode	170	8
ISFET	Au nanoparticles immobilized on the electrolyte/Al_2O_3 sensing interface	1000	9
CV	White rot fungi cells immobilized on Pt electrode	1040	10
Differential pulse voltammetry	Over-oxidized polypyrrole/multi-walled carbon nanotube composite on glassy carbon electrode	40	11
Amperometric detection	Multiwall carbon nanotubes on basal plane pyrolytic graphite electrode	20	12
Cotton-fiber OECT	Pt gate with no surface modification	~1000	16
OECT	Nafion and different carbon based nanomaterial immobilized on the Pt gate surface.	0.1-30	this Work

Conclusion

In summary, OECTs with Pt gate electrodes modified with biocompatible polymer (Nafion) and carbon-based nano-materials (SWNT, graphene flakes or GO) show high sensitivity to epinephrine. Nafion can enhance the sensitivity of the device by attracting epinephrine molecules to the gate electrode. SWNTs and graphene flakes modified on the gate electrode can further improve the sensitivity and decrease the detection limit of the device due to the enhanced electrocatalytic activity of the gate electrode. The device modified with Nafion and SWNTs shows the lowest detection limit of 0.1nM, which is sensitive enough for practical applications. Considering that the OECT-based epinephrine sensors can be prepared by low-cost and convenient solution process,[46] this type of devices are promising transducers for disposable applications in the future.

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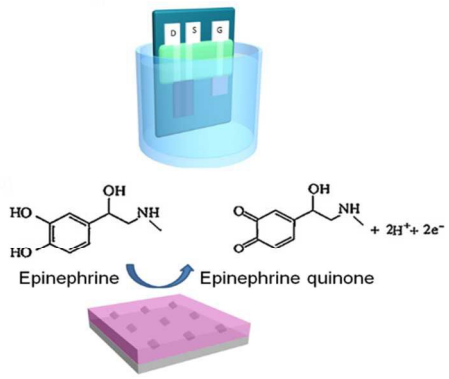
Reference

1. K. H. Berecek, M. J. Brody, *Am. J. Physiol.* 1982, **242**, H593.
2. K. E. Barrett, S. M. Barman, *Review of Medical Physiology*, 23rd edition, Mc Graw Hill.
3. H. Beitollahi, I. Sheikhshoaie, *Anal. Methods*, 2011, **3**, 1810.
4. N. A. Paradis, E. M. Koscove, *Ann. Emerg. Med*. 1990, **19**, 1288–1301..
5. F.D.P. Ferreira, L.I.B. Silva, A.C. Freitas, T.A.P. Rocha-Santos, A.C. Duarte, *J. Chromatogr. A*, 2009, **1216**, 7049.
6. L.I.B. Silva, F.D.P. Ferreira, A.C. Freitas, T.A.P. Rocha-Santosa, A.C. Duarteb, *Talanta*, 2009, **80**, 853.
7. E. Kojima, M. Kai, Y. Ohkura, *J. Chromatogr.* 1993, **612**, 187.
8. R.N. Goyal, A.R.S. Rana, H. Chasta, *Electrochimica Acta*, 2012, **59**, 492
9. A.B. Kharitonov, A.N. Shipway, I. Willner, *Anal. Chem*., 1999, **71**, 5441.
10. E. Akyilmaz, M. Turemis, I. Yasa, *Biosens. Bioelectron*., 2011, **26**, 2590.
11. S. Shahrokhian, R.S. Saberi, *Electrochimica Acta*, 2011, **57**, 132
12. A. Salimi, C. E. Banks, R.G. Compton, *Analyst*, 2004, **129**, 225
13. T. Pradhan, H.S. Jung, J.H. Jang, T.W. Kim, C. Kang, J.S. Kim, *Chem. Soc. Rev.*, 2014, **13**, 4684.
14. T.H. Tsai, S. Thiagarajan, S.M. Chen, C. Y. Cheng, *Thin Solid Films*, 2012, **520**, 7, 3054.
15. F. Valentini, G. Palleschi, E.L. Morales, S. Orlanducci, E. Tamburri and M.L. Terranova , *Electroanalysis*, 2007, **19**, 859.
16. N. Coppedè, G. Tarabella, M. Villani, D. Calestani, S. Iannotta and A. Zappettini, *J. Mater. Chem. B*, 2014, **2**, 5620.
17. C. Dodt, U. Breckling, I. Derad, H. L. Fehm, J. Born, *Hypertension*. 1997, **30**, 71.
18. H. S. White, G. P. Kittlesen,M. S. Wrighton, *J. Am. Chem. Soc*. 1984, **106**, 5375.
19. D. Nilsson, N.Robinson, M. Berggren and R. Forchheimer, *Adv. Mater.*, 2005, **17**, 353.
20. L. Torsi, M. Magliulo, K. Manoli, G. Palazzo, *Chem. Soc. Rev.*, 2013, **42**, 8612.
21. P. Lin, and F. Yan, *Adv. Mater*. 2012, **24**, 34.
22. P. Lin, F. Yan and H. L. W. Chan, *ACS Appl. Mater. Interfaces*, 2010, 2, 1637.
23. R. He, M. Zhang, F. Tan, P. H. M. Leung, X. Zhao., H. L. W. Chan, M. Yang and F. Yan, *J. Mater. Chem.*, 2012, **22**, 22072.
24. Z. T. Zhu, J. T. Mabeck, C. Zhu, N. C. Cady, C. A. Batt and G. G. Malliaras, *Chem. Commun*. 2004, 1556.
25. S. Y. Yang, J. A. DeFranco, Y. A. Sylvester, T. J. Gobert, D. J. Macaya, R. M. Owens and G. G. Malliaras, *Lab Chip*, 2009, **9**, 704.
26. H. Tang, F. Yan, P. Lin, J. Xu and H. L. W. Chan, *Adv. Funct.Mater*., 2011, **21**, 2264.
27. L. Kergoat , B. Piro , D.T. Simon , M.C. Pham , V. Noël , M. Berggren, *Adv. Mater*. 2014, **26**, 5658.

28. H. Tang, P. Lin, H.L.W. Chan, F.Yan, *Biosens. Bioelectron.*, 2011, **26**, 4559.
29. C.Z. Liao, M. Zhang, L.Y. Niu, Z.J. Zheng and F. Yan, *J. Mater. Chem. B*, 2014, **2**, 191.
30. P. Lin , X.T. Luo , I.M. Hsing , F. Yan, *Adv. Mater.*, 2011, **23**, 4035.
31. P. Lin , F.Yan, J. J. Yu , H. L. W. Chan, M. Yang, *Adv. Mater*. 2010, **22**, 3655.
32. D. Khodagholy, V. F. Curto, K. J. Fraser, M. Gurfinkel, R. Byrne, D. Diamond, G. G. Malliaras, F. Benito-Lopez, R. M. Owens, *J. Mater. Chem*. 2012, **22**, 4440.
33. G. Tarabella, F. M. Mohammadi, N. Coppedè, F. Barbero, S. Iannotta, C. Santato, F. Cicoira, *Chem. Sci*. 2013, **4**, 1395.
34. D. Nilsson, T. Kugler, P.O. Svensson, M. Berggren, *Sensors and Actuators B*, 2002, **86**, 193.
35. D.J. Kim, N.E. Lee, J.S. Park, I.J. Park, J.G. Kim, H.J. Cho, *Biosens. Bioelectron*., 2010, **25**, 2477.
36. D. Khodagholy, J. Rivnay, M. Sessolo, M. Gurfinkel, P. Leleux, L. H. Jimison, E. Stavrinidou, T. Herve, S. Sanaur, R. M. Owens, G. G. Malliaras, *Nat. Commun*. 2013, **4**, 2133.
37. C. Z. Liao, M. Zhang, M. Y. Yao, T. Hua, L. Li and F. Yan, *Adv. Mater.* 2015, doi: 10.1002/adma.201402625.
38. D.A. Bernards, D.J. Macaya, M. Nikolou, J.A. DeFranco, S. Takamatsu and G.G. Malliaras, *J. Mater. Chem.*, 2008, **18**, 116.
39. S. Corona-Avendaño, G. Alarcón-Angeles, A. Rojas-Hernández, M.A. Romero-Romo, M.T. Ram´ırez-Silva, *Spectrochimica Acta Part A*, 2005, **61**, 305.
40. R.N. Goyal, A.R.S. Rana, H. Chasta, *Electrochimica Acta,* 2012, **59**, 492.
41. S.M. Chen, K.T. Peng, *J. Electroanal. Chem.*, 2003, **547**, 179.
42. A. Salimi, C.E. Banks and R.G. Compton, *Analyst*, 2004, **129**, 225.
43. X. Luo, A. Morrin, A.J. Killard, M.R. Smyth, *Electroanalysis*, 2006, **18**, 319.
44. C.Z. Liao, M. Zhang, L.Y. Niu, Z.J. Zheng, F. Yan, *J. Mater. Chem. B*, 2013, **1**, 3820.
45. Y. D. Zhao, Y. Z. Xie, Z. K. Liu, X. S. Wang, Y, Chai, and F. Yan, *Small* 2014, **10**, 4521.
46. C. Z. Liao, C. H. Mak, M. Zhang, H. L.W. Chan and F. Yan, *Adv. Mater.* 2015, **27**, 676.

Table of contents entry:



Text: (one sentence, of maximum 20 words, highlighting the novelty of the work)

The sensitivity of OECT-based epinephrine sensors has been dramatically improved by modifying carbon nanomaterials on the Pt gate electrodes