



A New Highly Sensitive Sensor for Detecting Glucose Concentration

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Glucose sensors detection is a common method for glucose detection. Organic electrochemical transistors (OECTs) are considered to highly sensitive glucose sensors. The sensors show linear range from 0.1 μM to 100 μM , and its detection limit is about 0.1 μM . In addition, its sensing mechanism is discussed in detail. Glucose detection results show that the devices are sensitive to the gate voltage changes caused by the glucose enzymatic reaction. A glucose sensor detection system based on high-performance OECT-based glucose sensors is proposed. It is expected that the OECT devices have potential application on the low-cost and disposable glucose detection.

1. Introduction

Glucose also known as blood sugar, corn glucose, corn sugar, even referred to as glucose, is one of nature's most widely distributed and very important a monosaccharide. Glucose plays an important part in the biology. It is the energy source of living cells and the intermediate products of metabolism. Plants can produce glucose by the process of photosynthesis. Glucose detection is widely used in medical, food, biological technology and industry. For example, in medicine, the glucose detection test to the patient's blood, urine or saliva in the detection of glucose, thereby guiding the diet adjustment or adjust the diabetes medication, help diabetes treatment and control of diabetes. In food, glucose is a common carbohydrate, and it is also necessary to analyze the glucose content in foods (such as beverage, fruit juice, etc.). The amount of glucose has a certain effect on the fermentation process of microorganism. Moreover, the glucose detection is also used to detect the content of glucose in industrial wastewater.

The glucose sensor is usually composed of a recognition part and a signal converter. The recognition part is a bioactive substance, which is stimulated by the substrate, and the corresponding reaction is made. Signal converter is a kind of energy conversion, which can convert glucose concentration to another signal, such as electrochemical signal, optical signal, etc. By studying these signals, the content of glucose can be obtained. Glucose sensor is the most studied enzyme electrode sensor, which can be simple and rapid determination of glucose.

As one of the most important research contents in the biosensor, glucose biosensor has made great progress in the development of several decades. In recent years, it has been developed rapidly, and has become the most research and application of biological sensors. Organic thin film transistors (OTFTs) are being widely used in glucose sensors. Because it has the advantages of high sensitivity, low-cost, flexible and simple manufacturing process (Duarte and Dodabalapur 2012, Liao and Yan 2013, Lin and Yan 2012, Someya et al. 2010). Organic electrochemical transistors (OECTs) are an important kind of OTFT. In 1984, Wrighton first fabricated the OECT (White et al. 1984), which is an electronic device. Its active layer is made of a conducting polymeric thin-film comprised between two metallic electrodes. They are named the source and drain electrodes. The third electrode is called by gate (Romeo et al. 2014).

Lately, glucose sensors based on OECTs is proposed in a good few papers (Bernards et al. 2008, Liu et al. 2008, Macaya et al. 2007, Yang et al. 2010, and Zhu et al. 2004). For example, Liao et al. reported highly sensitive OECT-based glucose sensor with graphene modified gate electrodes (Liao et al. 2013). The device gives that detection limit down is 10 nM. The device without the graphene modification is two orders of magnitude worse than the devices. Furthermore, after modified with other nanomaterial (Pt nanoparticles), the detection limit can be extended to 5 nM (Tang et al. 2011b). The high sensitive OECT-based glucose sensor

with TiO₂ nanotube gate electrodes is reported in the paper. It is well-known that TiO₂ is a biocompatible material, thus it is expected to adsorb more glucose oxidase (GOx), which is benefit to improving the performance of the devices.

2. Experimental section

2.1 Device fabrication

The schematic diagram of the device structure is as shown in Figure 1. The device manufacturing substrate adopts a glass slide. Patterned Au/Cr source and drain electrodes were deposited on the surface of glass substrate by thermal evaporation through a shadow mask. The adhesion layer for the Au film (thickness: 50 nm) thin adopts the layer of Cr (thickness: 5 nm). After the surface of the sample was cleaned by a UV-ozone cleaner, a PEDOT:PSS layer (thickness: 80 nm) was spin-coated on top of the channel area. Then the device was annealed at 200 °C for 60 min in high purity N₂. The device's channel length was 0.2 mm. Its channel width devices were 6.0 mm. Nafion/GOx/Pt-NPs/TNTAs gate electrode was prepared according to our previous report (Liao et al. 2015).

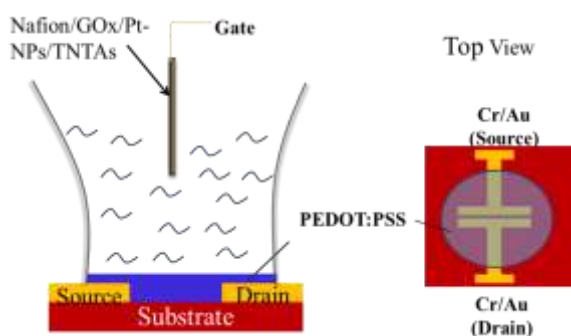


Figure 1: The schematic diagram of the device structure

2.2 Device characterization

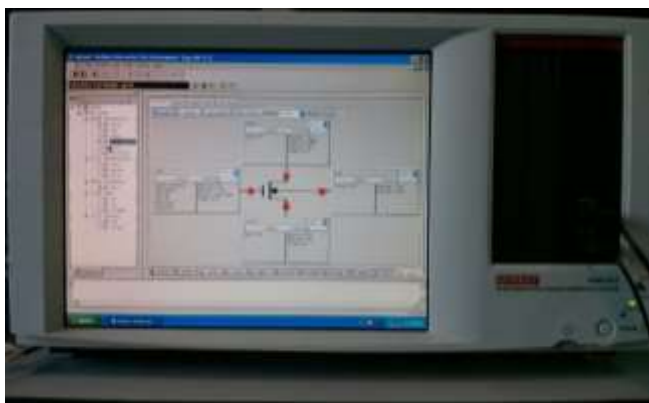


Figure 2: The digital image of Keithley 4200 semiconductor parameter analyzer.

The OECTs were analyzed by Keithley 4200 semiconductor parameter analyzer. The equipment picture is shown in Figure 2. The 4200 semiconductor parameter analyzer is a complete solution for the analysis of electrical properties of devices, materials and semiconductor processes. The advanced parameter analyzer has an unparalleled measurement sensitivity and accuracy. At the same time, it is the integration of embedded windows operating system and Keithley interactive test environment. This provides an intuitive and advanced function for the user to analyze the characteristics of semiconductor devices. It is a powerful stand-alone solution. Three basic electrical measurement techniques are needed to obtain the characteristics of a device or material. The 4200 semiconductor parameter analyzer provides these three functions.

Precise direct current voltage (I-V) measurement is the basis of the analysis of the electrical characteristics of the device. AC impedance, including the well-known capacitance voltage (C-V) technology, is capable of

providing the device characteristics that are not available in DC measurement. The 4200 semiconductor parameter analyzer, which adds the function of pulse signal generation and measurement, supports the analysis of the characteristics of the pulse type. The new pulse I-V (PIV) subsystem is more convenient for the advanced technology of high dielectric materials, thermal sensitive devices and advanced memory chips. It makes the measurement more accurate. The product is put into the market more quickly. This is the first commercial integration of precise, repeatable pulse and DC measurement in one solution, and the use is very convenient. The 4200 semiconductor parameter analyzer is suitable for the laboratory level of precision DC characteristics measurement and analysis. It has a very low micro current resolution and real-time graphics, data analysis and processing capabilities.

The critical information needed for the response of OECT devices were provided by the 4200 semiconductor parameter analyzer. The response of each sensor to the addition of glucose was measured at constant gate voltage V_G ($V_G=0.4$ V) and drain voltage V_{DS} ($V_{DS}=-0.1$ V) as a time function.

3. Glucose sensors

3.1 Working principle

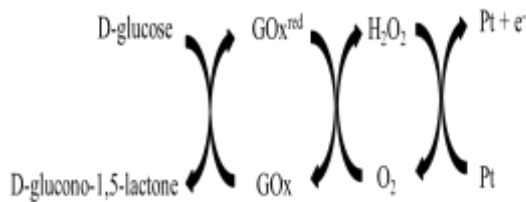


Figure 3: Working principle of OECT glucose sensors.

The enzyme sensor is constructed by the immobilized enzyme and the electrode combination. Using the high specificity and catalytic activity of the enzyme, the enzyme is used as the sensitive element of the biosensor in order to achieve the biological molecules (such as sugar, alcohols, organic acids, amino acids) concentration detection. The enzyme used for glucose detection is often glucose oxidase. According to the mechanism of charge transfer in the detection process, there are several types of current glucose sensors. (1) Oxygen as electron transfer mediator. In the presence of glucose oxidase, glucose and oxygen react to produce glucose acid and hydrogen peroxide, and the change of glucose concentration is linear with the concentration of hydrogen peroxide or oxygen. Electrochemical method for detecting the concentration of oxygen peroxide and oxygen concentration can achieve detection of glucose concentration. (2) Electron mediator instead of oxygen as electron acceptor. Electronic mediator is a molecular conductor that can transfer the electrons from the enzyme reaction center to the electrode surface, which can be changed by the electrode. It overcomes the shortcomings of the oxygen limitation of the glucose enzyme sensor. (3) No dielectric sensor. The main characteristic is that the electron transfer between the enzyme and the electrode is directly carried out without the electronic exchange between the enzyme and the electrode. In general, the enzyme is used to modify the surface of the electrode and the enzyme is immobilized on the surface of the conductive polymer modified electrode, which can achieve the specific and efficient catalytic reaction. Figure 3 shows the working principle of the OECT glucose sensor. The channel current IDS of an OECT is given by the following equation (Bernards et al. 2008, Lin and Yan 2012, Tang et al. 2011a):

$$\begin{cases} I_{DS} = \frac{q\mu p_0 t W}{LV_p} \left(V_p - V_G^{eff} + \frac{V_{DS}}{2} \right) V_{DS} \left(\text{when } |V_{DS}| \ll |V_p - V_G^{eff}| \right) \\ V_p = \frac{q p_0 t}{c_i} \\ V_G^{eff} = V_G + V_{offset} \end{cases} \quad (1)$$

Where electronic charge is expressed by q , the hole mobility is expressed by μ , the initial hole density in the channels is expressed by p_0 , the organic semiconductor film's thickness is represented as t , the channel width is represented as W , the channel length is represented as L , the transistor's effective capacitance per unit area is represented as c_i , the pinch-off voltage is represented as V_p , the effective gate

voltage is represented as V_G^{eff} , the offset voltage at interfaces is represented as V_{offset} .

The offset voltage V_{offset} can be changed by the H_2O_2 's oxidation at the gate voltage. The transistor's effective gate voltage V_G^{eff} is given by (Bernards et al. 2008, Cicoira et al. 2010):

$$V_G^{eff} = V_G + (1 + \gamma) \frac{kT}{2q} \ln[H_2O_2] + \text{constant} \quad (2)$$

Where γ is the ratio between the capacitances of the electrolyte-channel interface, Boltzmann's constant is represented as k , the temperature is represented as T , the concentration of H_2O_2 is expressed by $[H_2O_2]$. Therefore, the effective gate voltage of the OECT influenced by the glucose concentration is given by:

$$V_G^{eff} = \alpha \ln[\text{Glucose}] + \text{constant} \quad (3)$$

Where α represents constant, is the concentration of glucose is expressed by $[\text{Glucose}]$. Normalized current response (NCR) is used to compare the different devices. Its equation is as follow (Bernards et al. 2008, Tang et al. 2011a):

$$NCR = \left| \frac{I_{DS}^{conc} - I_{DS}^{conc=0}}{I_{DS}^{conc=0}} \right| \quad (4)$$

Where the drain current before an addition of glucose at the concentration of interest is expressed by $I_{DS}^{conc=0}$, the drain current after an addition of glucose at the concentration of interest is represented as I_{DS}^{conc} .

3.2 Glucose detection

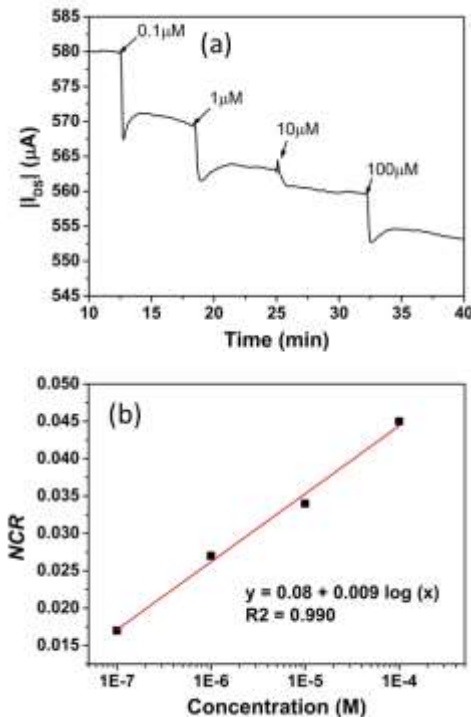


Figure 4: (a) The current response of the OECT device to successive additions of glucose. (b) The normalized current response (NCR) as a function of glucose concentration.

Figure 4. (a) depicts the real-time channel current I_{DS} response of an OECT device to successive additions of glucose ($V_{GS}=0.4V$ and $V_{DS}=-0.1V$). The device starts to exhibit a current response (signal/noise > 3) to the addition of 0.1 μM glucose. The change of I_{DS} decreases with the increase of glucose concentration. As shown

In Figure 4. (b), the device has a linear current response to the logarithm of glucose concentration from 0.1 μM to 100 μM . A sensitivity of 0.009 NCR per decade is obtained, and the detection limit is estimated to be 0.1 μM . In addition, as shown in Figure 5, the output current I_{DS} of the devices also decreases after the addition of 100 μM glucose, which indicates that the as-prepared OECT devices can be used as glucose sensors.

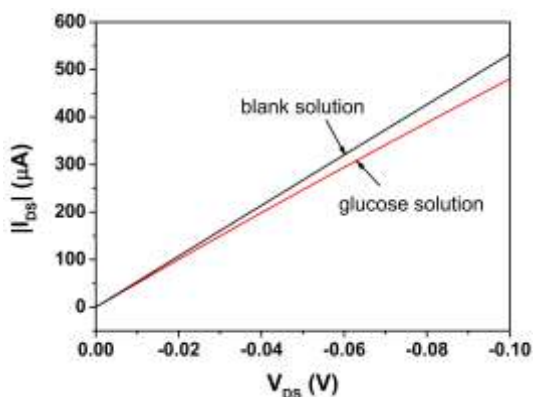


Figure 5: Output characteristic of the OECT device to the addition of glucose solution.

4 Glucose sensors detection system

In summary, when the high-performance OECT-based glucose sensors using TiO₂ nanotube gate electrodes detect glucose, the linear detection range is wide and the sensitivity is high. It is a kind of current type glucose sensor with good performance. So the paper designs a glucose sensor detection system based on high-performance OECT-based glucose sensors using TiO₂ nanotube gate electrodes. The overall design of the glucose sensor detection system is shown in Figure 6.

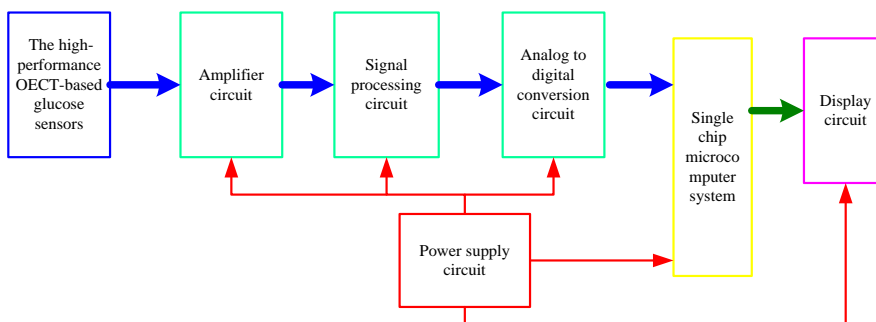


Figure 6: The glucose sensor detection system

A power supply circuit can provide a variety of voltage output; it is mainly for the microcontroller system and other circuits to provide working voltage. Glucose concentration is converted to current signal by the high-performance OECT-based glucose sensors. The current signal is relatively weak, which need to be amplified by the amplifier circuit. The amplified signal is processed by the signal processing circuit, and then be collected by analog to digital conversion circuit under the control of single chip microcomputer system. Display circuit displays glucose concentration. The glucose sensor detection system can drive the work of the glucose sensor, which is of great significance for the development of low cost, portable and high performance glucose sensor.

5. Conclusions

In conclusion, a high sensitively OECT-based glucose sensor is presented. The sensors show linear range from 0.1 μM to 100 μM , and the detection limit is about 0.1 μM . Through the sensing mechanism discussion, we think that the low detection limit can be ascribed to the signal magnification of OECT transistor. Due to the device can be easily produced in the solution process; they are particularly suitable for disposable sensing applications.

Acknowledgements

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