An ISFET sensor based on In₂O₃ nanoribbon for pH detection of micro solutions

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Abstract. In this paper, an ISFET sensor based on In2O3 nanoribbon is developed for pH detection of micro solutions. A double channel ISFET is designed which includes the In2O3 nanoribbon top channel and silicon substrate bottom channel so as to realize the pH detection of the micro solutions. Through experiments, the sensitivity of the sensor is 70 mV/pH in the range of pH 6 to pH 10, which exceeds the Nernst limit of 59.2 mV/pH (300 K) at room temperature. Taking the detection of cTnI as an example, the pH sensor can be used to detect the concentration of biomarkers.

1.Introduction

The pH detection has important applications in industry, biomedicine, environmental protection and so on [1]. The test strip and the glass electrode are widely used pH sensors. However, the subjective reading of the pH test paper is not accurate. The glass electrode is fragile, and is difficult to further miniaturization. Moreover, the glass electrode is particularly insensitive to strong acid or alkali [2]. Therefore, it is urgent to develop a new material to detect the pH value of the micro solution which may realize the miniaturization. In 1970, P. bergveld first proposed the ISFET structure for the detection of pH (H^+ ion) value [3]. Compared with the traditional pH sensors, the ISFET has more advantages in durability, rapidity, accuracy, sensitivity and miniaturization.

In recent years, the addition of biocompatible nanomaterials to the gate region of ISFET biosensors has attracted extensive attention of more and more researchers [4]. ISFET sensors based on silicon nanowires, zinc protonated (positively charged) or deprotonated (negatively charged) depending on the concentration of hydrogen ions in the electrolyte. The phenomenon may induce the Nernst response potential which is sensitive to H^+ at the interface between the sensitive membrane and electrolyte solution, so that the current between source and drain may be regulated.

According to the theory of electric double layer, there exists ionic charges on the surface of insulating layer and the electrolyte. The charges distributed on the surface of insulating layer may inevitably attract the same amount of electric charges in the electrolyte, forming an anti-ion layer. Hence, an electrical double layer between the insulating layer and the electrolyte interface has the same amount of the electricity, and opposite polarity. Therefore, a potential difference is generated between the surface of the insulating layer and the electrolyte solution, which is

oxide nanowires, carbon nanotubes, graphene and other nanomaterials are spread to apply for the detection of pH value, the protein, the DNA and other biological substances [5-8].

In this paper, we propose a nanostructured ISFET device to detect the pH value of the micro solutions. Rest of the paper is organized as follows. The operation mode of the sensor and the measurement results are explained in detail in section 2. The structure and pH performance of ISFET are analyzed in section 3. Some conclusions are given in the conclusion part.

2.Materials and method

2.1 Detection principle

The sensitive mechanism of ISFET is based on surface base theory and double layer theory [9-10]. According to the surface basis theory, there are an amount alcohol groups (-OH) on the surface of the insulator, which can be called the interface potential E. The relationship between the interfacial potential and the logarithm of H^+ activity in electrolyte solution is linear and it is expressed as,

$$E = E_0 + \frac{RT}{F} ln\, a_{H^+}\ ,\qquad (1)$$

where R, T, Tre, F, a_{H^+}, E_0, respectively represents the gas constant，the absolute temperature，the Faraday constant, the activity of hydrogen ion and a constant.

The dielectric layer is usually very thin, and the interface potential E may change the charge density on the semiconductor surface, which may further regulate the source leakage current. The relationship between source leakage current and interface potential is written as follows,

$$I_{DS} = \frac{\mu_n C_o W}{L}\left[\left(V_{GS} - E_{ref} + E - V_T\right)V_{DS} - \frac{1}{2}V_{DS}^2\right],\ (2)$$

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where μ_n, C_o, V_{GS}, V_{DS}, w/L, V_T, E_{ref} respectively stand for the carrier mobility, the gate capacitance per unit area, the gate source voltage, the drain source voltage, the channel width length ratio, the threshold voltage, and the reference electrode and solution interface potential.

Combining Eq. (1) and (2) may get following relation,

$$I_{DS} = \frac{\mu_n C_o w}{L}\left[\left(V_{GS} - E_{ref} + E_0 + \frac{RT}{L}\ln a_{H^+} - V_T\right)V_{DS} - \frac{1}{2}V_{DS}{}^2\right]. \qquad (3)$$

As I_{DS}、E_{ref}、V_{DS} are all constant, we have the following relation,

$$V_{GS} = A + B\ln a_{H^+} \ . \qquad (4)$$

As V_{GS}、E_{ref}、V_{DS} are all constant，we may get,

$$I_{DS} = C + D\ln a_{H^+} \ . \qquad (5)$$

From Eq. (4) and (5), the relationship between the gate source voltage and the source leakage current is linear with logarithm of the H^+ activity in solution. The pH value of the solution may be acquired through the measurement of the hydrogen ion activity in the solution by the gate source voltage or the source leakage current.

2.2 In$_2$O$_3$ nanoribbon ISFET

In$_2$O$_3$ has stable chemical properties, wide band gap and low resistivity. Applying the field effect transistor with nanostructured In$_2$O$_3$ to the channel material has the advantages of high signal-to-noise ratio, label free and easy to multi-channel integration. Nanomaterials can be considered as one-dimensional. As one-dimensional metal acts as a "flexible" electron channel, the atomic stress within or between molecules may lead to the change of electrochemical behavior several orders of magnitude larger than that of bulk materials [11]. Using one-dimensional FET for biochemical sensing may greatly improve the sensitivity of the device [12].

The structure of In$_2$O$_3$ nanoribbon ISFET is showed in Fig. 1. The length and width of the device are respectively 15 mm and 10 mm. Si$_3$N$_4$ is used as the pH sensitive film material which is solidified on silicon substrate. The nanoribbon is made by In$_2$O$_3$ material and Ti/Au is applied to make the source and drain. The nanostructured field-effect transistors (FET) is fabricated by plasma enhanced chemical vapor deposition (PECVD), electron beam evaporation, photolithography and magnetron sputtering.

The preparation process of In$_2$O$_3$ nanoribbon ISFET is introduced as follows. Firstly, the Si$_3$N$_4$ film is grown on Si substrate by the plasma enhanced chemical vapor deposition (PECVD). Secondly, source and drain are fabricated by one-step photolithography, and source and drain masks are formed by coating photoresist on Si$_3$N$_4$ film. Thirdly, Ti/Au metal is deposited by electron beam evaporation, and the source and drain are generated after stripping the metal. Fourthly, the gate is fabricated by secondary lithography. Then coating the gate with photoresist may form a gate mask. Finally, the In$_2$O$_3$ nano film is deposited by magnetron sputtering which may result a channel. It has a growth/width ratio of

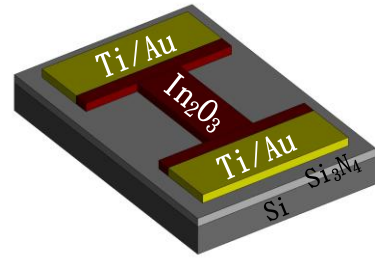800μm/50μm and a thickness of 50nm. The grid is formed after stripping coats.

Fig.1. The structure of ISFET

2.3 Micro Device

In order to make the electrolyte solution fully contact with the ISFET surface of In$_2$O$_3$ nanoribbon, a solution filling device with a capacity of 2 mL is designed in this paper. The overall structure of the equipment is showed in Fig. 2. A cylinder with a diameter of 3.2cm and a height of 1.5cm is embedded with a hollow conoid with a diameter of 1.5cm and a height of 2.2cm. The bottom of the conoid is a circle with a diameter of about 2 mm and an outer wall of about 1 mm, which can very well fit the surface of ISFET. The cylinder is fixed by four screws. All of tests have been performed by the device.
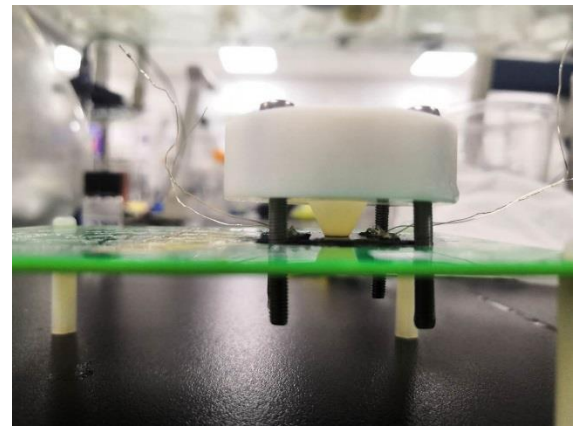

Fig.2. Micro detection cell

2.4 Measurement setup of In$_2$O$_3$ nanoribbon ISFET

Aiming at studying the electrical and pH characteristics of nanostructured ISFET, the output characteristic curve (I$_{DS}$-V$_{DS}$) and transfer characteristic curve (I$_{DS}$-V$_{GS}$) are detected by our own detection circuit. All the detected liquid gate potentials are applied through the Ag/AgCl reference electrode. The output and transfer characteristics are measured at room temperature and in 0.1 * PBS buffer solution. We use DP1308A (Beijing Puyuan Jingdian Technology Co., Ltd.) to supply a fixed potential of -1V to the liquid gate, and scan the voltage from -4V to 0V between the source and drain to measure the output characteristics. The transfer characteristics are

measured under fixed -0.5V source drain voltage, and the liquid gate potential is scanned from 0V to 2V.

For the purpose of detecting the pH sensitivity, the I_{DS}-V_{GS} curves of In_2O_3 nanoribbon ISFET are measured at room temperature using commercial standard pH solutions with pH values ranging from 6 to 10. The liquid gate voltage is scanned from 0V to 1.3V, and the source drain voltage is fixed at -1V.

3. Results and discussion

The output characteristic curve and transfer characteristic curve of In_2O_3 nanoribbon ISFET are illustrated in Fig. 3 and Fig.4. Firstly, the In_2O_3 nanoribbon ISFET biosensor is prepared by aforementioned method. Then, after the chip is placed on the electrochemical stage, the gate and source drain electrodes are connected to detect the electrical signal. As 1.5ml solution is added, due to the existence of H^+ in the solution and H^+ formed by hydration of In_2O_3 film surface, a double electric layer is formed at the interface of one side of the solution. Thus, an interface potential is generated. The formed interface potential changes the charge density of the In_2O_3 surface and generates the interface potential difference, which regulates the channel current. As different grid voltages are applied, the interface potential may correspondingly vary. The high gate voltage results the small interface potential difference, and the small source leakage current.
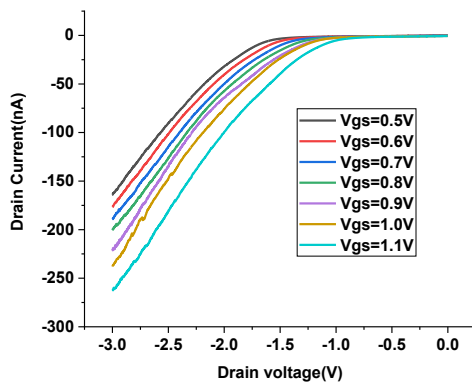
The voltage between the source and drain is set to -1V, since the ISFET device is in deep saturation. In the saturated region, the current (I_{DS}) between source and drain is weakly dependent on the voltage between source and drain (V_{DS}), which is mainly controlled by the voltage between gate and source. Even if the V_{GS} change very tiny, the I_{DS} may significantly increase. As shown in Fig. 5, a family of I_{DS}-V_{GS} curves is displayed with pH values from 6 to 10. As adding solutions with different pH values, the current obtained is changed since the H^+ concentration is different. From the Fig. 6, it can be seen that the I_{DS} is enhanced with increasing of pH value.

At 10μ a drain source current, the sensitivity of In_2O_3 nanoribbon ISFET is 70±5mV/pH, which exceeds the Nernst limit at room temperature. The sensitivity structure is presented in Fig. 5. Compared with the traditional ISFETs, the advantage of the proposed device is obvious that our device is not only has semiconductor silicon channel, but also has In_2O_3 nanoribbon acting as conductive channel. Under dual channel operation, the pH sensitivity of the device easily exceeds the Nernst limit. From results, it can already achieve the desired effect in the detection of biomaterial concentration depending on the change of pH value.

On the basis of the successful detection of pH value by In_2O_3 nanoribbon ISFET sensor, we tried to detect cTnI at 100 pg/ml. Enzyme linked immunosorbent assay (ELISA) is used to detect the source leakage current of cTnI at 100 pg/ml through fixed liquid gate potential and source drain voltage. Results of tests are investigated in Fig. 7. Firstly, taking 0.5ml 0.1*PBS solution, the measured source leakage current is stable at -0.5294 mA. Then, after we add 1ml of 1mg/ml urea solution, the measured source leakage current is stable at -0.4126 mA. The change of cTnI concentration in solution makes the change of the surface potential of ISFET, resulting to the difference of source leakage current. The variation of source leakage current reflects the concentration of different cTnI.
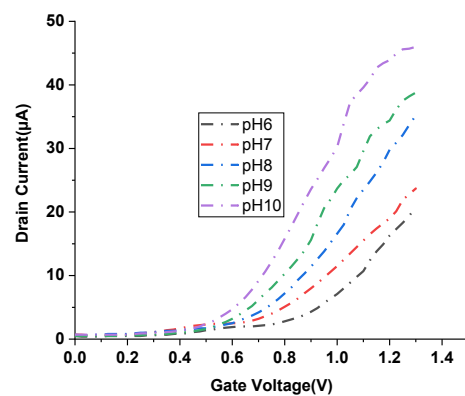

Fig.3. The output characteristic of nano structure based ISFET

Fig.4. The transfer characteristic of nano structure based ISFET

Fig.5. The family of I_{DS}-V_{GS} curves with pH values from 6 to 10
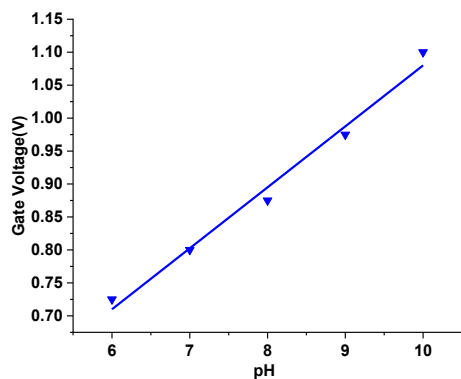
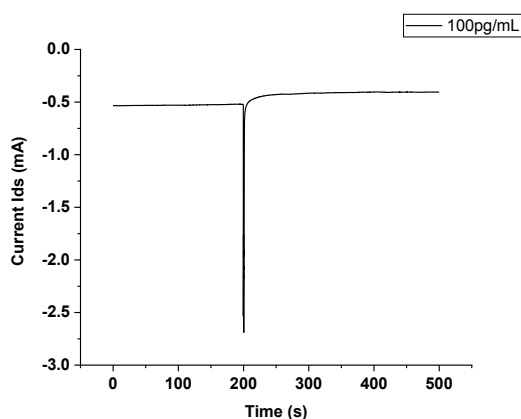**Fig.6.** The linearity of pH values from 6 to 10

Fig.7. The results of 100pg/mL cTnI by In$_2$O$_3$ Nanoribbon ISFET

4. Conclusion

A kind of pH sensor based on In$_2$O$_3$ nanoribbon ISFET is introduced for the detection of pH value of micro solution in this paper. Through dual channel operation of the proposed ISFET, the device performs high pH sensitivity, reaching at 70 mV/pH. In$_2$O$_3$ nanomaterials have good biocompatibility so that it is widely used to detect biomolecules based on pH detection, such as cTnI, NMP22 protein of bladder cancer, amyloid beta peptide of Alzheimer's disease. Therefore, the proposed device has a very good application prospect.

5. Acknowledgement

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