A novel biomedical sensor for tumor marker based on Flexible supported solution gated graphene field effective transistor

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Keywords: Tumor Marker; Field Effective Transistor; Graphene

Abstract. Graphene is a kind of two dimensional material. Great attentions have been paid on graphene based components due to its perfect and mysterious electronic characteristics. Flexible supported graphene field effective transistor (GFET) were prepared, solution gated by an Ag/AgCl reference electrode in the phosphate buffer solution (PBS) and applied in the label free detection of tumor marker which was alpha fetal protein (AFP) in this presented work. It is verified in this work that the flexible GFET would be a potential low cost solution for disposable medical components..

Introduction

Tumor marker is a kind of clinical index used in the diagnosis of cancer diseases. Traditional methods for tumor marker detections were based labeled protocols (such as immumofluorescence and electrochemiluminescence). With the development of solid-state electronic components, such as field effective transistor (FET) and light addressable potentiometric sensor (LAPS), some directly electronic ways for tumor markers' measuring were proposed with the merits of label-free.

The so-called solution gated graphene field effective transistor (SGFET)[1], also named as the electrolyte or liquid gated field effective transistor [2], is a complex of the classical semiconductor sensor's structure and the perfect two-dimensional carbon material, which were named as the ion sensitive field effective transistor (ISFET) and graphene, respectively. Graphene was used as the substitute for the traditional semiconducting channel material, silicon. The theoretical prediction was proved to be true experimentally, which was the conductance of GFET's channel could be altered by the adsorption of hydroxyl (OH^-) and hydroxonium (H_3O^+) ions[1]. More scientific works have testified that the conductance of SGFET's channel could be modulated not only by the value of pH, but also by the adsorbed biochemical molecules and exhibited a proportional relation with their concentrations. For example, the molecules of bovine serum albumin (BSA) could be detected by EGFET, responded as the variation of the transferring conductance, and exhibited a the BSA-concentration dependence [2]. The comparison between GFET and carbon nanotube FET was carried out in the experiments for the detection of glucose or glutamate molecules[3]. The unlabeled monitoring of deoxyribonucleicacids (DNA) hybridization could also be executed by SGFET as low as 1 pM (1 mol per liter) of the target DNA[4].It was postulated that there are promising potentials of graphene in nanoelectronic biosensing[1-4]. Theses scientific works inspired lots of researching efforts on SGFET's applications in the domain of biological and chemical sensors [5-8], as well as in some of practical areas, such as environmental monitoring [9-11] and food safety [12].

It is believed that the main sensing principle in SGFET should be the conductivities' changing in FET's channel area which were induced by the specific adsorption or desorption of the analytes, such as ion, molecule, cell, protein, and so on [13, 14]. Based on this mechanism, GFET was prepared on a flexible substrate and immerged in the phosphate buffer solution (PBS). The flexible supported SGFETs were applied in the label-free detection of alpha fetal protein (AFP) which is a universal index in the clinical examinations. The presented work identified the potential of the flexible supported SGFET to be explored as a medical device or apparatus.

Experiments and Equipments

A. Synthesis of graphene film on PDMS substrates.

The graphene material were prepared according to the modified Hummers methods [15]. After the synthesis of traditional graphene oxide (GO) suspension (0.5 mg/mL), carboxylate treatment was executed to obtain carboxylated graphene oxide (GO-COOH) by sodium hydroxide and hypochlorous acid. Reducing progress was performed after the deposition of GO-COOH film on the flexible substrates which were prepared by polydimethylsiloxane (PDMS). In this progress 1-ethyl-3-(3-dimethyl-aminopropyl) carbo- diimide (EDC)/N-hydroxysuccinimide (NHS) were used as activator [16].

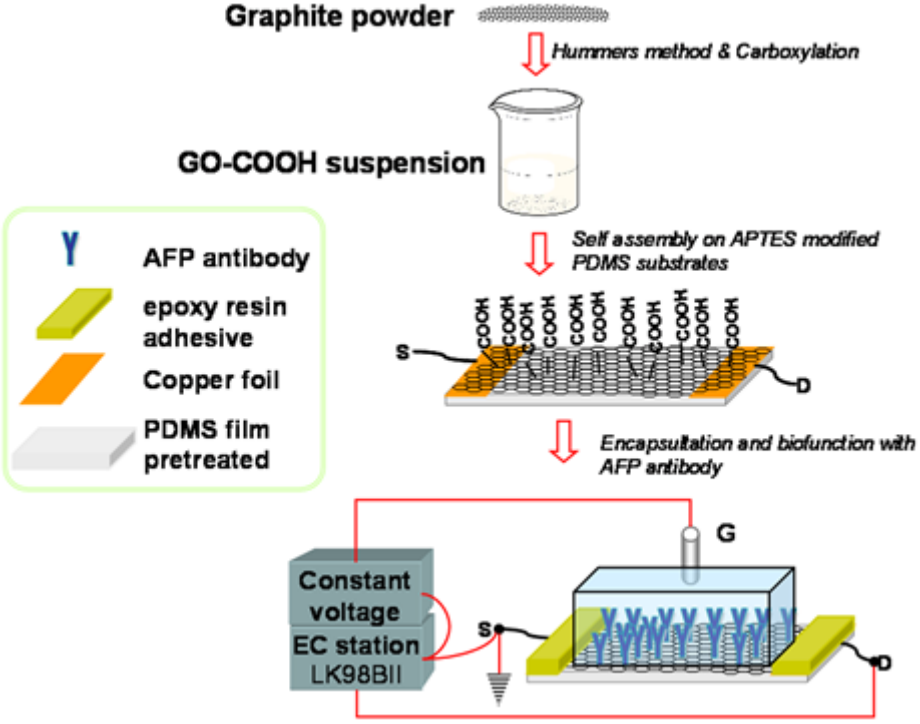


Fig.1. Scheme of the flexible supported SGFET and its system for the label free detection of AFP.

B. Preparation for GFET

Firstly, flexible PDMS substrates were modified by APTES to get the amino-group-ended surface.

Secondly, copper foils were attached onto the left and right sides of PDMS substrates as shown in Fig. 1. Then electrodes of S and D were weld by indium to get the electronic contacts between SGFET and measuring system.

Thirdly, the films of graphene materilas were self-assembled by covalent bonding on the amino-PDMS substrates and reduced in situ..

C. Equipments

The prepared devices were tested in a modified electrochemical detection system which was composed of a LK98BII microcomputerbased electrochemical analyzer (Lanlike Chemical and Electron High Technology Co., Ltd., Tianjin, China), a constant voltage power supply and a computer. The electrodes of SGFET which were gate (G), source (S) and drain (D) were connected into the system as depicted in Fig. 1.

D. Experimental procedure

Firstly, cyclic voltammetry experiments were conducted on the unfunctionalized GFET to investigate the original device current-voltage characterization.

Secondly, anti-AFP molecules were immobilized on the gate area of GFET by covalent bondings, as well. AFP antibody solution (84.8 ng/ml) was incubated on the gate area of the prepared GFET, as depicted in Fig. 1. Then the sensing sites on GFET were blocked by bull serum albumin (BSA, 1%) to avoid unspecific adsorption of AFP antigen in the following detection.

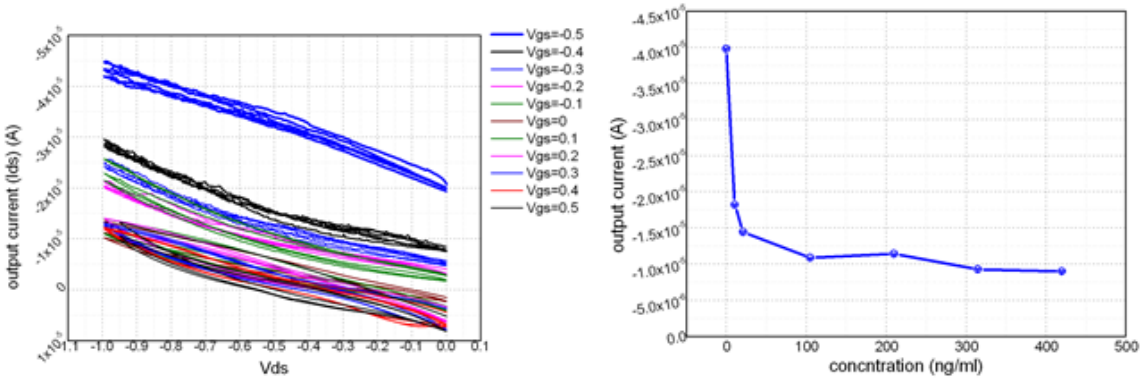
Thirdly, under the optimized working conditions, unlabeled tumor marker detections were

performed by as-prepared SGFET. The collected output currents (Ids) were plotted in the coordinates of currents vers concentrations, as shown in Fig. 3.

All the agents in this work were in the degrade of analytical reagents (AR). Deionized water was used for dilution and rinse.

Results and Discussions

The cyclic voltammetry examinations of SGFET were executed before the detection AFP antigen, the results were presented in Fig.2 (a) . According to Fig. 2, SGFET was tested in tumor maker detections when Vgs and Vds were maintained as -0.4V and -1V, respectively. The measured currents under different AFP concentrations were plotted in a curve shown in Fig. 2 (b). While the reason for choosing this working conditions is that more varied output currents (Ids) could be measured. As shown in Fig. 2 when the voltages of Vgs were changed around -0.4V (the black line in Fig. 2) the output currents were shifted from bold blue lines (-0.5V) to pink lines (-0.2V) or others. On the contrary, under other bias voltages, for examples -0.3 or 0.4 V, the lines were crowded together, the negatively changed Vgs could not be transduced a obviously identified output currents.



(a) Cyclic voltammetry of blank SGFET (b) the responding for AFP of SGFET

Fig.2. Cyclic voltammetry examinantions for blank SGFET

Conclusion

The presented tumor markers' detection strategy based on PDMS supported SGFETs possesses the merits of stretchability, inexpensive and label-free. The upper limit of this method for AFP was 300 ng/ml, it is proved that it could be developed as an alarming clinical assay for tumor diseases..

Acknowledgement

This work was supported by the National Natural Science Foundation of China (Grant No. 61371028), Tianjin Natural Science Foundation (Grant No. 12JCZDJC22400).

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