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High Performance CNTENFET with K/PPy/CNT nanocomposite biosensing layer for Cholesterol Detection

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Abstract—We have reported a high-performance dual gated carbon nanotube enzyme modified field-effect transistor (CNT-ENFET) for cholesterol detection. To improve the device performance, we have used dual-gate design with high κ dielectric as top gate and low κ dielectric as bottom gate and a nanocomposite of potassium doped carbon nanotube with polypyrrole (K/PPy/CNT) as the biosensing membrane. The device exhibited a good sensitivity (~ 1.0 V/decade), low response time (~ 1 s), wide dynamic range (0.1 - 25) mM, wide linear range (2-20 mM), low detection limit (0.11 mM), good stability (7 months) and high selectivity (interference ~ 1.8 %).

Index Terms— Carbon nanotube (CNT), cholesterol, dual-gate, ENFET, K/PPy/CNT.

I. INTRODUCTION

Carbon nanotube based ENFETs have been found as ideal biosensor with high selectivity, real-time response and have capability of label free detection [1], [2]. Polyethylenimine (PEI) doped carbon nanotubes as channel material exhibit excellent n-type FET characteristics and has advantages over other types of n-doping techniques [3], [4]. The response time, selectivity, stability and dynamic range of ENFET devices depend on the number of enzyme molecules and therefore, immobilization of enzyme on the top of the inorganic gate insulator layer of ISFET is a crucial step. Various advanced materials such as CNT, gold nanoparticles and porous materials have been used for firm immobilization of the enzyme. In general, these materials cannot support enzyme directly, and hence selection of an enzyme-loaded matrix compatible to both the insulating layer and the enzyme has importance in ENFET construction. Nanocomposite of potassium doped carbon nanotube with polypyrrole (K/PPy/CNT) is suitable to use as bio-sensing layer for its high compatibility with enzyme, fast electron transfer and better dispersion [5]. The sensitivity of ENFET device is an important factor for molecular detection [6], [7]. The sensitivity of single gate ENFET beyond the Nernstian sensitivity limit (usually 59 mV/pH at room temperature) can be enhanced by introducing double gates in the device structure [8]. Sensitivity of such dual gate ENFET is dependent on the capacitive coupling between the top gate and bottom gate dielectrics that can be increased by using high- κ dielectric as top gate material and low- κ dielectric as bottom gate material [9].

Referring to cholesterol biomolecule, it is an essential steroid metabolite found in most of the human cells and is carried through

blood by lipoproteins [10]. It contributes to the structure of cell walls, helps in synthesis of bile acids in the intestine, allows the body to produce vitamin D and enables the body to make steroid hormones. However, elevated level of cholesterol is a biomarker for myocardial infarction, type 2 diabetes, thrombosis, high blood pressure and cardiovascular diseases [11]. Therefore, development of a low cost, integrated, disposable and reliable technique for its detection is essential and significant in medical and clinical applications.

ENFET is constructed by immobilizing an enzyme on the top of the gate insulator of an ion sensitive field effect transistor (ISFET). The Simplest physics picture behind the working of ENFET is the exploitation of field effect concept introduced by an electrolyte gate electrode, which is capacitively coupled through a thin dielectric layer with semiconducting channel. The enzyme reacts with the analyte of interest and generates or consumes protons which changes charge at the gate surface in accordance with site binding theory. This change in charge at the gate surface modulates the channel conductance and hence the channel current between the source and the drain of the ISFET. This output current can be related with the concentration of analyte under examination. In case of ChOx enzyme, for an example, it reacts with cholesterol in accordance with the following chemical scheme:

The number of released protons (H^+ ions) depends on concentration of electrolyte solution and are accepted by the insulating surface as per its buffer capacity. Acceptance of protons by the surface affects the electrolyte – insulator interface potential (ψ_0) and therefore, modulates the channel current.

In this letter, we have reported a high-performance carbon nanotube enzyme modified field-effect transistor (CNT-ENFET) for cholesterol detection with good sensitivity (~ 1 V/decade), low detection limit (0.11 mM), good stability (7 months) and high selectivity (interference ~ 1.8 %). To our knowledge, these are the best characteristics parameters that have been reported so far.

II. DUALGATECNTENFET

A. Fabrication

Fabrication of the dual gate CNT-ENFET has started with indium tin oxide (ITO) coated glass plate (dimension: 6 mm $\times$ 3 mm $\times$ 1.1 mm) as a substrate which has also served as the bottom gate. On the top of the ITO, a layer of ZnO ($\kappa \sim 1.5$) has been deposited (dimension: 5 mm $\times$ 3 mm $\times$ 10 nm) using electrochemical deposition (ECD) technique [12]. On the top of this bottom insulating layer, a thin film of PEI doped multi-walled carbon nanotube (MWCNT) ($> 8\%$ carboxylic acid functionalized, avg. dia. 9.5 nm, length 1.5 nm) has been deposited (dimension: 5 mm $\times$ 3 mm $\times$ 10 nm) by ECD technique. This CNT layer forms the n+ source (S), drain (D), and channel regions. A high κ dielectric ZrO_2 ($\kappa \sim 25$) layer has been then deposited on the top of the CNT layer (dimension: 3 mm $\times$ 3 mm $\times$ 10 nm) to act as top gate. Metal Al has been used to form the source (S) and drain (D) contact regions on the top of the CNT layer. The details of fabrication process of these layers and contacts can be obtained in our earlier publications [12], [13]. Referring to the nanocomposite K/PPy/CNT layer, a solution has been first prepared by adding two ml of (1.0 M) KOH solution (potassium cannot be directly doped as it is unstable in air and very reactive with water) to 10 ml of CNT solution. Pyrrole solution (8 μ l) prepared in formic acid with 10 μ l K-doped CNT solution has then been added in 10 ml acetonitrile. The solution has then been sonicated for 20 minutes and kept idle for 12 hours. This complex solution has then been deposited on top of the ZrO_2 layer by spin coating technique to form nanocomposite K/PPy/CNT layer (dimension: 3 mm $\times$ 3 mm $\times$ 10 nm). After the fabrication of the device, 10 μ L of ChO_x (~ 24 U/mg activity in PBS) solution has been immobilized (as per experimental results which is not shown) on the top of the sensing layer by physical adsorption technique for experimentation [14].

B. Characterization

Prior to being used as ENFET, the device has been biased for electrical characterization. Conventionally, for single gate operating mode, the bottom gate (BG) is grounded, whereas the top gate (TG) is grounded for double gate operation [15]. Using this methodology, TG voltage ($V_{GS(T)}$), BG voltage ($V_{GS(B)}$) and drain voltage (V_{DS}) have been fixed at 0.6 V, 1.0 V and 0.3 V respectively as shown in Fig.1.

Fig. 1. (a) Output characteristics of TG CNTENFET at pH 7. The inset shows a schematic diagram of the ENFET structure. (b) The output characteristics of BG ENFET at pH 7.

C. Sensor Characteristics

In order to determine the sensor characteristics, cholesterol stock solutions of different concentrations (0.1 mM to 25 mM) have been prepared using Triton X-100 as surfactant (as cholesterol is insoluble in water, therefore, need to be blended maintaining some processes). The output characteristics at different concentrations and linearity curve of the device are shown in fig. 2(a) and (b) respectively. From fig.2(a), it is observed that the dynamic range of the device is (0.1 - 25) mM and from fig.2(b) it is observed that the device is linear from 2 mM to 20 mM with regression coefficient 0.994. The current sensitivity has been found to be ~ 75.17 $\mu A/mM$.

Fig. 2. (a) Output characteristics of the dual gated CNT-ENFET. (b) The linearity curve of the device with regression coefficient 0.994.

ENFET being an electronic device basically measures the insulator-electrolyte interface potential, ψ_0 which is a function of solution pH dependent on concentration of solution. In general, for single gate CNT-ENFET, ψ_0 is related with its threshold voltage $V_{TH(ENFET)}$ by (2):

$$V_{TH(ENFET)} = E_{ref} - \psi_0 + \chi^{sol} - \frac{\phi_{CNT}}{q} - \frac{Q_{total}}{C_{insulator}} \quad (2)$$

Unlike MOSFET, the threshold voltage of ENFET varies with respect to the concentration of the analyte and therefore the sensitivity of the device can be expressed as:

$$S = \frac{\Delta V_{TH(ENFET)}}{\Delta C} \quad (3)$$

Where, ΔC is the change in electrolyte concentration and $\Delta V_{TH(ENFET)}$ is the corresponding change in threshold voltage of ENFET. The change in threshold voltage for different concentrations of analyte can be determined experimentally from transfer characteristic curves of ENFET using extrapolation in linear region (ELR) technique [16]. Using this technique (fig.3.a), the change in $V_{TH(ENFET)}$ with respect to cholesterol concentration has been plotted in fig.3(b). The slope of this curve gives the sensitivity of the device and found to be 1.0 V/decade. Limit of detection has been calculated using basic equation [17] and found to be 0.11 mM. Temperature dependence of the device has been tested and maximum response has been obtained at 30 °C in the temperature range of 20 to 40°C.

Fig. 3. (a) Extraction of threshold voltage from transfer characteristic curves using ELR technique. (b) Threshold voltage variation with respect to cholesterol concentration.

The specificity of the sensor has been studied by testing the device for interference of other biomolecules (fig. 4(a)). It was found that the interference of the device is negligible with other biomolecules such as glucose, uric acid, urea etc. The interference percentage has been calculated using (4) [20] and found to be $\sim 1.8 \%$.

$$\% \text{ Interference} = \frac{I_{chol} - I_{int}}{I_{chol}} \times 100 \quad (4)$$

For testing the stability of the device, the device has been tested few times every month over a period of 8 months and then curve has been plotted taking I_{DS} as a parameter. It is observed that the device is stable over a period of 7 months (fig. 4(b)). The reproducibility of the device has been proven by performing experiments with five fabricated devices under similar conditions. All the five devices have produced almost similar results. The repeatability test has been performed on the same device for 10 times (once a week) and almost similar results have been found. The fabricated sensor has been compared with other FET based cholesterol sensors available in the literature and shown in table I.

Fig. 4. (a) Interference of cholesterol with other biomolecules. (b) The stability of the device

Table 1. Comparison of different ENFET biosensors developed for cholesterol detection

Ref.	Bio sensing layer	Linearity (mM)	LOD (mM)	Sensitivity	Shelf Life (Day)
[19]	ZnO NRS	0.001-45	5×10^{-5}	$10 \mu A \text{ cm}^{-2} \text{ mM}^{-1}$	-
[20]	Ferrocenyl/alkanethiol	1.8-12.9		57 mV/decade	-
[18]	PANI/ZnO	0.5-16.6	0.25	60 mV/decade	150
This work	K/PPy/CNT	2-20	0.11	1 V/decade	210

III. CONCLUSION

We have presented a high-performance CNT-ENFET with K/PPy/CNT nanocomposite as sensing layer for cholesterol detection. Due to the use of K/PPy/CNT nano composite, the sensor has shown high dynamic range, low detection limit and good stability. Owing to the use of double gates, the resulting biosensor has shown high sensitivity which is desirable for nanobiosensing applications such as measurement of proteins

interactions, protein function, antibody-antigen reactions, DNA hybridization etc. Also the fabricated device has been found to be reproducible and repeatable with negligible interference. Hence, dual gated CNT-ENFET with K/PPy/CNT nano composite as sensing layer could be a valuable platform for cholesterol detection.

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