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Carbon Nanotube Based Dual-Gated Junctionless Field Effect Transistor for Acetylcholine Detection

Md. Abdul Barik, Rashmi Deka and J. C. Dutta

***Abstract*—A compact n-type carbon nanotube (n-CNT) based junctionless field effect transistor (JLFET) for acetylcholine detection has been fabricated by integrating chitosan/nickel oxide as sensing membrane with CNTFET using chemical solution process. To improve the sensing performances higher than Nernstian, dual gated junctionless CNTFET has been considered here. Electrical response has been carried out after immobilization of acetylcholine esterase using digital multimeter in presence of phosphate buffer saline of 50 mM & pH 7 in a glass pot. Experimental results show good linearity for acetylcholine concentration from 0.01 to 0.2 mM and improved sensitivity of 1.25 V/decade at room temperature. Limit of detection and Michaelis-Menten constant have been found to be 0.37 µM and 0.2 mM, respectively. Insignificant interference observed while the sensor was tested with other clinical parameters.**

***Index Terms*— Acetylcholine, acetylcholine esterase, carbon nanotube, junctionless field effect transistor, solution process.**

I. INTRODUCTION

RECENTLY, Field Effect Transistor (FET) based biosensors are interested for detection of chemical analytes, environmental hazardous, clinical disorders, food toxicity and for military safety due to the advantages such as on-chip integration, fast response, long life and high sensitivity [1], [2]. P. Bergveld in 1970 developed the first ion sensitive FET (ISFET) based pH sensor [3] and then integration of enzymes with ISFET known as enzyme modified FET (ENFET) was developed by Janata and Moss in 1976 [4]. Since then, many ENFETs were developed for detection of glucose, urea, acetylcholine, cholesterol and creatinine [5]-[7]. These FET based biosensors have some drawbacks such as scaling limitation (i. e. while gate length less than 20 nm), high threshold voltage, small on-off current ratio and low sensitivity (i.e. less than 59.2 mV/decade stated by Nernst) [8], [9]. The scaling limitation of traditional FET based devices can be overcome by CNTs as channel material due to easy to synthesize into nano form [10]. The high threshold voltage can be lowered and small on-off current ratio can be increased using junctionless CNTFET due to high mobility of charge carriers and low internal contact resistance [11]. A junctionless FET (JLFET) has no pn, n^+ n and p^+ p junction in the source-channel-drain path. It is a uniform resistor having either *n*-type or *p*-type material through which mobile charge carriers can be modulated by applying gate voltage. For turning on and off a FET, the simplest physics picture is that the gate and the semiconductor channel forms a parallel plate capacitor. When we change the gate voltage, the carrier density inside the semiconductor is changed and the Fermi level moves in and out of the gap, so that the channel changes from insulating state (off state) to conducting state (on state) i.e. large drain current due to the channel being heavily doped and mobile charge carriers becoming available or vice versa i.e. small drain current. The gate modulates the resistance of the heavily doped semiconductor; hence the device behaves like a gated single resistor [12]. The low sensitivity can be enhanced using dual-gated FET (DGFET) [9]. In DGFET, channel potential and electric field distributions along the channel can be controlled by adjusting the work function of metal and semiconductor. The complication and high cost of traditional techniques required for fabrication of semiconductor devices can be minimized using chemical solution process. Several FETs using chemical solution technique have been reported for detection of cholesterol [13], [14]. Like cholesterol, urea, glucose and creatinine; acetylcholine is also an important parameter available in the peripheral and central nervous systems. In the central nervous system, acetylcholine is involved in attention, learning, memory, consciousness, sleep and control of voluntary movements [15], [16]. Dysfunction of this cholinergic system causes the major neurological disorders such as Schizophrenia, Alzheimer, Parkinson and Huntington [17].

As far as Nanobiosensing area is concerned, nanostructured nickel oxide (NiO) has many applications due to its unique properties including high biocompatibility, electrocatalysis, high chemical stability and high electron transfer [18]-[20]. Composites of nano-NiO with chitosan (CH) are very attractive material for biosensor applications due to excellent film forming ability, mechanically strength and

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S. B. Author, Jr., was with Rice University, Houston, TX 77005 USA. He is now with the Department of Physics, Colorado State University, Fort Collins, CO 80523 USA (e-mail: author@lamar.colostate.edu).

T. C. Author is with the Electrical Engineering Department, University of Colorado, Boulder, CO 80309 USA, on leave from the National Research Institute for Metals, Tsukuba, Japan (e-mail: author@nrim.go.jp).

biocompatibility [21]. In this manuscript, an acetylcholine FET having CH/NiO nanocomposite as sensing membrane with integration of dual gated junctionless carbon nanotube field effect transistor has been reported. The fabrication part has been performed using solution technique and characterization part has been done using digital multimeter in a glass pot in presence of phosphate buffer saline (PBS) of 50 mM and pH 7.

II. EXPERIMENTAL

A. Preparation of solution

Acetylcholine esterase (AChE) with an activity of 301 U/mg and acetylcholine (ACh) were obtained from Sigma. 1 M of acetylcholine esterase solution has been prepared by dissolving 1 mg of AChE powder in 1 ml phosphate buffer saline (PBS) of 50 mM and pH 7 and stored at 4º C. Acetylcholine solution (0.2 mM) has been prepared in pure water. Sodium phosphate buffer saline has been prepared using sodium diphosphate (NaH_2PO_4) and sodium monophosphate (Na_2HPO_4) [22]. Single walled carbon nanotube (SWCNT) having carbon purity ~ 99 %, tube length ~ 20 µm and diameter ~ 100 nm was purchased from Alibaba and functionalized using polyethylene imine (PEI). Indium tin oxide (ITO) coated glass (sheet resistance ~ 15 Ω/cm^2) has been obtained from NANOCS. Hafnium dioxide (HfO_2), nickel oxide (NiO), chitosan (CH), zinc oxide (ZnO) and other chemicals and materials are of analytical grade.

B. Sensor fabrication

Dual gated junctionless carbon nanotube (DGJLCNTFET) has been fabricated using solution process. Glass with dimension ~ 5 mm × 2 mm has been used as substrate on which ITO is coated for bottom gate material. On this ITO coated glass, a thin layer of intrinsic ZnO (dimension~5 mm × 2 mm × 10 nm) has been deposited to act as bottom gate insulator. Due to small dielectric constant (~ 1.5) of ZnO, the drain current contributed by bottom gate is less than that contributed by the top gate (top gate insulator is HfO_2). For preparation of ZnO solution, 10 mg zinc acetate (Zn $(CH_3COO)_2$) has been dissolved in 10 ml distilled water and 2 ml ammonium hydroxide (NH_4OH) has been added and stirred at room temperature for several minutes. The thickness of ZnO has been measured using gravimetric analysis technique [23], [24]. On the top of the ZnO layer, uniformly PEI doped (doping concentration ~ 30 %) single walled carbon nanotube (SWCNT) has been deposited. PEI doped CNT acts as n-type source (S), drain (D) and channel regions (dimension ~ 5 mm × 2 mm × 100 nm) [25]. CNT (10 mg) has been dispersed in 10 ml PEI/methanol and sonicated for several minutes. This makes CNT as n-type semiconductor [25]-[26]. On the top of the channel region, a thin layer of HfO_2 (dimension ~ 1 mm × 2 mm × 10 nm) has been deposited as top gate insulator. The high κ-dielectric constant (~ 25) of HfO_2 increases capacity and reduces direct tunneling leakage current [27]-[29]. This capacity enhances drain current and thus, device performance can be increased. Since HfO_2 is insoluble in water, HfO_2 layer has been prepared as: 100 mg solid $HfCl_4$ has been dissolved in 10 ml de-ionized water and sonicated for several minutes. It has then been deposited on the top of the channel region by using solution process and heated at temperature ~ 180º C for getting dry HfO_2 film [30]. The thickness of HfO_2 film has been measured by gravimetric technique and found to be ~ 10 nm.

A sensing membrane (dimension ~ 1 mm × 2 mm × 50 nm) consisting of NiO and chitosan (doping concentration ~ 5 %) has been deposited on the top gate insulator. This sensing membrane has been prepared by using solution method: 20 ml (100 mM) of $NiCl_2.6H_2O$ and 20 ml (100 mM) NaOH have been dissolved in 20 ml distilled water at room temperature and heated at 290º C. This gives solid nanostructured NiO thin film [31]. Biocompatibility of NiO has been improved by doping 10 µl of chitosan (0.05 M prepared by 50 mg in 100 ml of acetate buffer) in NiO solution [20]. Prior to deposition of top gate insulator HfO_2, aluminum (Al) has been deposited on source and drain for contact purpose using filament evaporation technique. Aluminum has been chosen as contacts because of its low resistivity, low melting point, and excellent adhesion to dielectrics, ease of deposition and no contamination of Al [32]. Polydimethylsilaxane (PDMS) has been coated on the whole FET except the sensing region for passivation purpose at the time of acetylcholine measurement [33]. A complete schematic of dual gated JLCNTFET has been shown in the Fig. 1 (a) and proposed electrochemical mechanism of CH/NiO with ZrO_2 and PEI doped CNT for acetylcholine detection has been shown in the Fig. 1 (b).

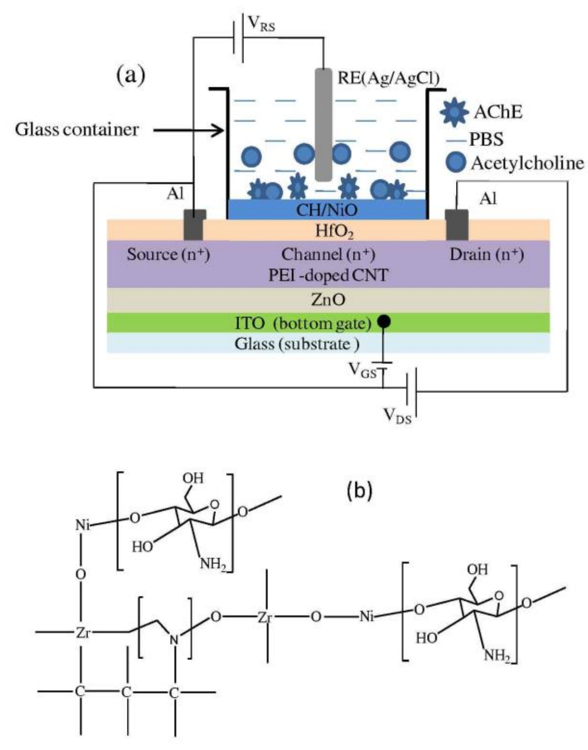

Fig. 1. (a) Schematic of dual gated JLCNTFET (b) Proposed electrochemical mechanism of CH/NiO with ZrO_2 and PEI/CNT

III. ENFET THEORY

An ENFET is analogous to an ion sensitive field effect

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transistor (ISFET) for which an additional sensing membrane is to be used on the top of the gate insulator for immobilization of biomolecules. ISFET is fundamentally a metal oxide semiconductor field effect transistor (MOSFET) and hence the theoretical description of MOSFET is essential to understand ISFET's theory. MOSFET is the basic building block of an ENFET. For conventional dual-gated MOSFET in the linear region (when $V_{GS} > V_{TH}$ and $V_{DS} < (V_{GS} - V_{TH})$), the total drain current (I_{DS}) (V_{GS} being the gate voltage, V_{DS} is the drain voltage and V_{TH} is the threshold voltage) is given by Eq. (1) [34], [35].

$$I_{DS,total}(MOS) = C_{ox,top}\,\mu\left(\frac{W}{L}\right)\left[(V_{GS,top} - V_{TH,top})V_{DS} + \frac{V_{DS}^2}{2}\right] + C_{ox,bottom}\,\mu\left(\frac{W}{L}\right)\left[(V_{GS,bottom} - V_{TH,bottom})V_{DS} + \frac{V_{DS}^2}{2}\right] \quad (1)$$

Where, $C_{ox,\ top}$ and $C_{ox,\ bottom}$ are the capacitances of top and bottom gate oxide respectively, W and L are the width and length of the channel, μ is the electron mobility. $V_{GS,\ top}$ and $V_{TH,\ top}$ are the gate voltage and threshold voltage of top gate respectively. Similarly, $V_{GS,\ bottom}$ and $V_{TH,\ bottom}$ are the gate voltage and threshold voltage of bottom gate respectively. Unlike MOSFET, introduction of electrolyte solution of biomolecules between the reference electrode and sensing membrane of ENFET produces additional voltages: a constant potential of the reference electrode, V_{Ref}, and the interfacial potential $\Psi_0 + \chi^{sol}$ at the liquid/ solid interface. Where Ψ_0 is the surface potential and is a function of pH of the solution and χ^{sol} is the surface dipole potential of the solvent having a constant value. For ENFET the equation of top gate threshold voltage is given by Eq. (2) [2], [36].

$$V_{TH,top}(EN) = V_{Ref} - \Psi_0 + \chi^{sol} - \frac{\Phi_{CNT}}{q} - \frac{Q_{OX,top} + Q_{SS,top} + Q_{B,top}}{C_{ox,top}} + 2\phi_f \quad (2)$$

Where ϕ_{CNT}/q is the work function of CNT, Q_{ox} is the accumulated charge in the oxide, Q_{ss} is the fixed surface-state charge, Q_B is the bulk charge and ϕ_f is the fermi potential of CNTs. If we proceed like MOSFET, the general expression for the drain current of dual gated ENFET in the linear region is given by Eq. (3).

$$I_{DS,total}(EN) = C_{ox,top}\,\mu\left(\frac{W}{L}\right)\left\{\left[V_{GS,top} - \left(V_{Ref} - \Psi_0 + \chi^{sol} - \frac{\Phi_{CNT}}{q} - \frac{Q_{OX,top} + Q_{SS,top} + Q_{B,top}}{C_{top}} + 2\phi_f\right)\right]V_{DS} + \frac{V_{DS}^2}{2}\right\} + C_{ox,bottom}\,\mu\left(\frac{W}{L}\right)\left[(V_{G,bottom} - V_{TH,bottom})V_{DS} + \frac{V_{DS}^2}{2}\right] \quad (3)$$

In ENFET, V_{DS} and V_{Ref} are kept constant. The parameter $V_{TH,\ top}$ (EN) can be chemically modified via the surface potential, Ψ_0 at the electrolyte/oxide interface and $V_{TH,\ bottom}$ (MOS) is same as conventional MOSFET which is kept constant during fabrication process. Using site binding and Gouy–Chapman–Stern (GCS) model, the surface potential (Ψ_0) at the top gate can be shown as a function of pH or concentration of the solution. According to this model, the surface potential change ($\Delta\Psi_0$) is given by Eq. (4) [9].

$$\Delta\Psi_0 = -2.3\,\alpha\frac{kT}{q}\Delta\log[M] \quad (4)$$

With k being the Boltzmann constant, q is the charge, T is the temperature at the time of experiment, α is the dimensionless sensitivity parameter (α = 0–1) and M is the concentration of electrolyte solution. The change in threshold voltage due to change in surface potential can be related as Eq. (5) [9].

$$\Delta V_{TH,top}(EN) = \frac{C_{top}}{C_{bottom}}\Delta\Psi_0 \quad (5)$$

Where, C_{top} and C_{bottom} are the capacitances of top and bottom gate respectively. Eq. (6) summarizes the biocatalytic transformations stimulated by acetylcholine esterase [37]. In presence of water, AChE transforms ACh to choline and acetatic acid by releasing H^+ ions to the electrolyte solution. The protons released from this reaction bind with the specific sites of the gate insulating surface in accordance with site binding theory and thereby affect the surface potential of the gate interface. The change in surface potential dependence on hydrogen ion concentration affects the CNT channel doping that modulates channel current. The site binding mechanism is a surface phenomena i.e. confined to insulating surface touching with the sensing membrane and therefore there is no affect of this electro chemical reaction [Eq. (6)] on source and drain electrodes as these are not connected with sensing membrane. Moreover, reference electrode with which the source is connected is a non-polarizable electrode.

$$CH_3COO(CH_2)_2N^+(CH_3)_3 + H_2O \xrightarrow{AChE} (CH_3)_3(CH_2)_2NOH + CH_3COOH + H^+ \quad (6)$$

IV. RESULTS AND DISCUSSIONS

After immobilizing AChE by physical adsorption technique on NiO/CH sensing membrane, the whole device has been sealed with polydimethylsilaxane except sensing membrane. ENFET with reference electrode (Ag/AgCl) has been inserted in a glass pot containing 20 ml PBS of 50 mM, pH 7 as shown in Fig. 2 (a). Drain to source voltage from 0 to 1 V in step of 0.2 V has been applied between source and drain where positive and negative supply have been connected to drain and source respectively. A fixed voltage of 0.6 V [where drain current is maximum as shown in Fig. 2 (b)] has been applied to reference electrode and bottom gate. The Positive supply has been connected to reference electrode and bottom gate (bottom gate connection is not shown) and negative supply has been connected to source. A digital multimeter has been used to record drain currents (I_{DS}). 100 μl stock solution of acetylcholine (0.01-0.2 mM) has been added by micropipette to PBS in the pot each time and corresponding I_{DS} against each acetylcholine concentration has been recorded.

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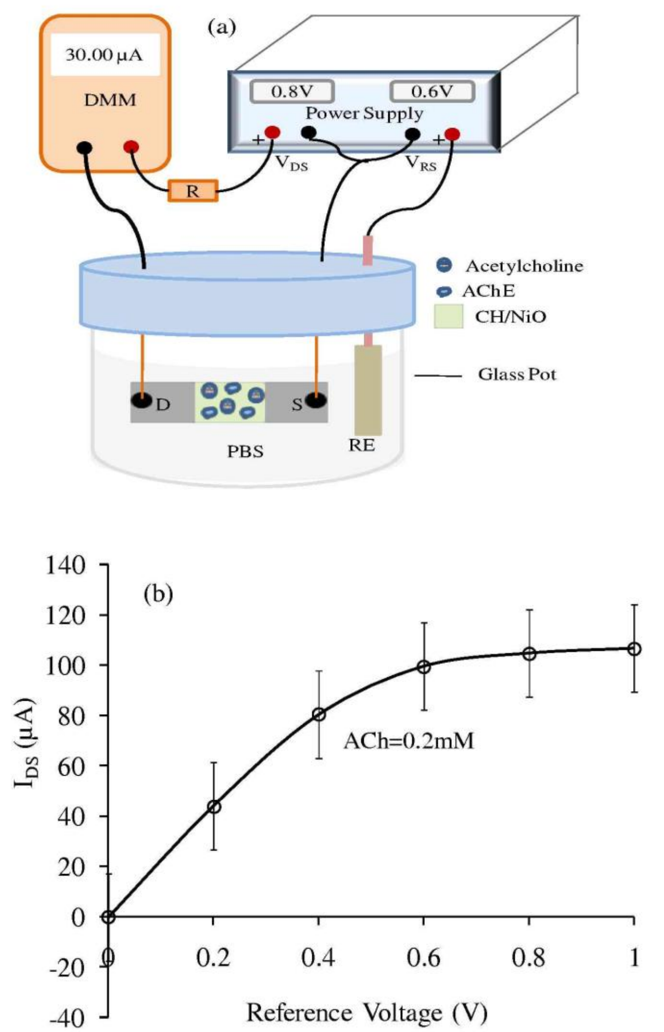

Fig. 2. (a) Setup for measurement of acetylcholine concentration using DMM at temperature 25º C and pH 7 (b) Plot of reference voltage Vs. drain current for acetylcholine concentrations 0.2 mM at temperature 25º C and pH 7 (with error bar/standard deviation).

Fig. 3 (a) is the dc output characteristics with different acetylcholine concentration from 0.01 to 0.2 mM. The linearity of the sensor is shown in Fig. 3 (b), which was obtained from Fig. 3 (a) by noting the drain currents for different concentrations from 0.2 to 0.6 V in steps of 0.1 V. This shows the linearity of the sensor from 0.01 to 0.2 mM corresponding to the drain voltage upto 0.4 V. This experiment was performed at 25º C and pH 7. The experiments were repeated 10 times for every acetylcholine samples (graph shown only for one time) using same procedure and condition as mentioned and only slight variation of the response has been observed. The standard deviation for these samples has been found to be 60 μM using basic relation and regression coefficient (R^2) ~ 0.999 [In Fig. 3 (b) at V_{DS} ~ 0.4 V]. The sensitivity in terms of drain current has been found to be ~ 500 μA/mM [From Fig. 3 (b)]. The Michaelis-Menten constant (K_m) is an enzyme kinetic that has significant roles in enzyme biosensors. It has been calculated from the Linweaver Burk plot (graph not shown) by plotting the inverse of acetylcholine concentration versus inverse of I_{DS} and has been found to be 0.2 mM. This lower value of K_m reveals high affinity immobilization of AChE with sensing membrane of enzyme FET resulting in enhanced biochemical reaction. Limit of detection (LoD) is the lowest quantity of a substance to be detected. In this experiment LoD has been calculated using the basic equation [13] and found to be 0.37 μM.

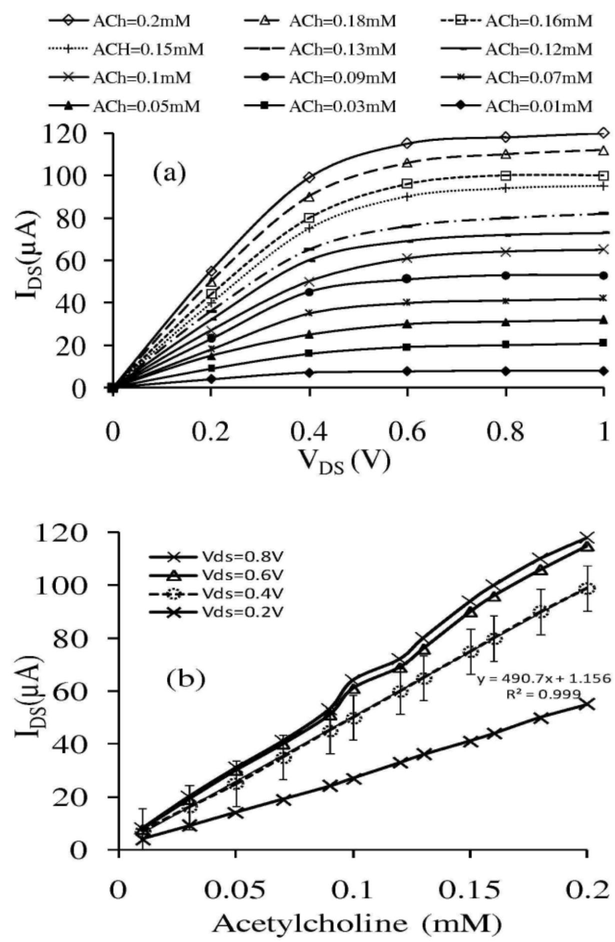

Fig. 3. (a) Drain characteristic curves for acetylcholine concentration (0.01-0.2 mM) at temperature 25º C and pH 7 (b) Sensitivity characteristic curves for different acetylcholine concentrations (0.01-0.2 mM) at temperature 25º C and pH 7. The curve is linear at V_{DS} ~ 0.4 V where regression coefficient has been calculated (with error bar/standard deviation).

The change in threshold voltage of dual-gated FET is equal to multiplication of shift in the surface potential and ratio of top to bottom gate capacitors. The surface potential has been calculated using Eq. (5) at room temperature as explained by Guoy–Chapman–Stern. The thickness of top gate insulator has been kept constant ~ 10 nm while thickness of bottom gate insulator has to be varied. It is because the large thickness of bottom gate insulator suppresses total drain current and acting as single gated FET. As a result, drain current corresponds to Nernstian response. Again low dielectric constant of bottom gate insulator provides bottom gate leakage current that affects sensitivity of device. Thus, optimum thickness of bottom gate insulator is required. Optimum thickness is found to be from 10 nm to 100 nm. Corresponding to these variations, the threshold voltage has changed from 196 mV to 1.9 V, where

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drain current sufficiently flows without affecting sensitivity. The maximum change in threshold voltage is more than as stated by Nernst [9] and depends on the ratio of capacitances of top and bottom gates. The change in threshold voltage with respect to acetylcholine concentration (0.01-0.2 mM) has been plotted [Fig. 4 (a)]. Mathematically the sensitivity in terms of threshold voltage is defined by Eq. (7) [13].

$$S = \frac{\Delta V_{TH}}{\Delta C_{in}} \tag{7}$$

Where, ΔV_{TH} is the change of threshold voltage due to change in the concentration of electrolyte solution, ΔC_{in}. The slope of the graph [Fig. 4 (a)] gives the sensitivity and has been found to be 1.25 V/decade at room temperature. The effect of temperature on this device has been investigated by measuring drain current using same procedure as mentioned earlier for 0.2 mM of acetylcholine solution in PBS of pH 7 and varying temperature from 15 to 45º C. The maximum response has been found in the temperature range from 30 to 37º C as shown in Fig. 4 (b).

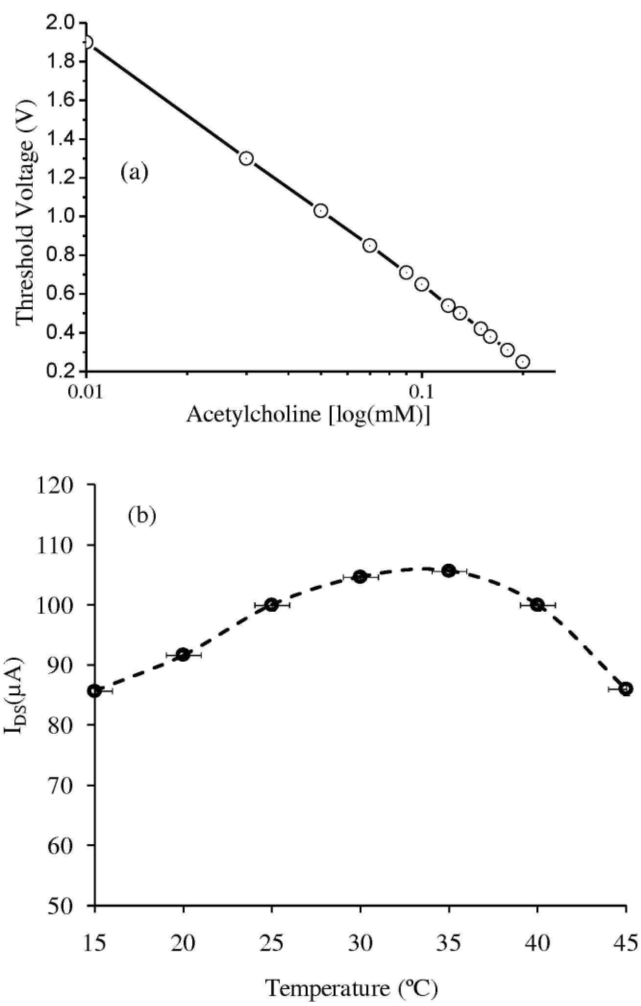

Fig. 4. (a) Change in threshold voltage with respect to acetylcholine concentration at 25º C and pH 7 (b) Effect of temperatures on drain current at pH 7 (with error bar/standard deviation).

Optimization of pH has been studied using the same procedure and varying pH from 5 to 9 at room temperature in PBS for 0.2 mM of acetylcholine solution. The maximum response has been found at pH 7–8. Above this value, reaction activity of acetylcholine esterase becomes slower and hence response decreases as shown in Fig. 5 (a). The interference on acetylcholine (0.2 mM) solution due to the presence of urea (0.2 mM), glucose (0.2 mM), uric acid (0.2 mM), ascorbic acid (0.2 mM), dopamine (0.2 mM), lactic acid (0.2 mM) and heparin sodium (0.2 mM) have been studied at the same environmental conditions. The results show no significance change in the response as shown in the Fig. 5 (b).

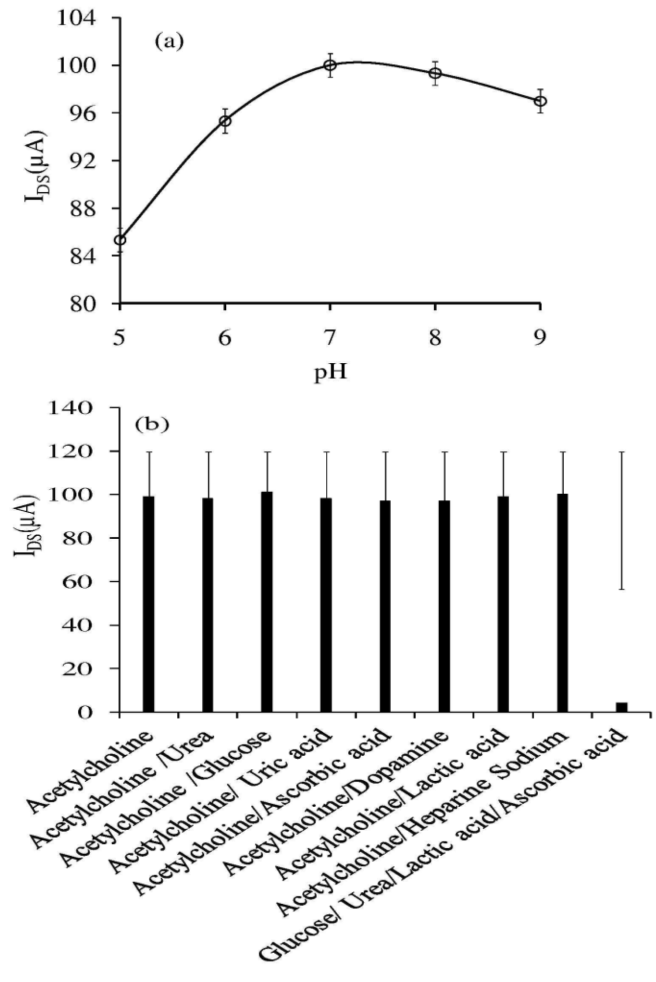

Fig. 5. (a) Effect of pH on acetylcholine responses at temperature 25º C (with error bar/standard deviation) (b) Interference of acetylcholine concentration with other biomolecules at temperature 25º C and pH 7 (with error bar/standard deviation).

The percentage of interference can be calculated by using Eq. (8) [14].

$$\%\ \text{Interference} = \frac{I_{ACh} - I_{Int}}{I_{ACh}} \times 100 \tag{8}$$

Where, I_{ACH} is the drain current for acetylcholine only and I_{Int} is the drain current for acetylcholine with other mixtures. It has been found that average percentage of interference of acetylcholine with other solution is~ 1.5 %. The experiment has been performed at the same environmental conditions in every week for 8 months and has been found that the device has ~ 99 % activity for acetylcholine detection. Two acetylcholine samples of 0.1 and 0.2 mM were studied using same experimental procedure and condition as mentioned above for about 10 times and only 1-2 % variation of the response has been observed. The errors and standard deviations have been shown in the relevant Figures [e.g. Fig. 2 (b), Fig. 3 (b), Fig. 4 (b), Fig. 5 (a) & Fig. 5 (b)].

In order to characterize the sensor behavior outside the liquid, an experiment has been performed as: After finishing the in-liquid measurements, Al metal has been deposited on the top insulating layer by filament evaporation technique. This Al electrode has worked as top gate material. The applied voltages to both the top and bottom gates were in the range from 0 to 1 V in step of 0.2 V. The drain currents show good linearity up to drain voltage ~ 0.4 V and then saturation occurs just like output characteristics of MOSFET as shown in Fig. 6. This has shown the gate dependence similarity of channel both outside and in-liquid measurements.

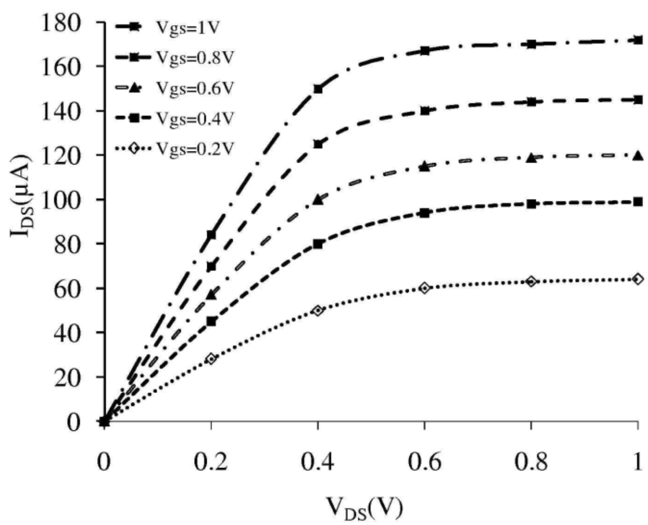

Fig. 6. Output characteristic curves at different top/bottom gate voltages and at temperature 25 º C.

V. CONCLUSIONS

In this work, a sensitive integrated n-type CNT based dual-gated junctionless field effect transistor has been fabricated for detection of acetylcholine. The sensitivity of this device has been found to be 1.25 V/decade with good linearity from 0.01 to 0.2 mM at temperature of 25º C. This technique has overcome the Nernstian limit (i.e. sensitivity~59.2 mV/decade at room temperature) because sensitivity depends on the ratio of coupling capacitor of top and bottom gates. It has been observed that this biosensor has reproducibility, repeatability and insignificant interference with other biological parameters. This FET based biosensor requires minimal instrumentation and can be easily fabricated. Thus, the efforts are being made to utilize this nano-structured dual gated JLCNTFET based biosensor in the field of bioelectronics and biomedical applications.

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Md. Abdul Barik was born in Assam, India. He received the M.Tech degree in Bioelectronics from the Department of Electronics and Communication Engineering, Tezpur University, Assam, India. Currently He has been pursuing Ph.D in the Department of Electronics and Communication Engineering, Tezpur University under the guidance of Professor Jiten Ch. Dutta. His current research interests include fabrication of nano materials based BioFETs using solution process.

Rashmi Deka was born in Guwahati, Assam, India. She received her B. Tech. from North Eastern Hill University and M.Tech from KIIT University, Bhubaneswar in Electronics and Communication Engineering. Currently she is pursuing Ph.D in the Department of Electronics and Communication Engineering, Tezpur University under the guidance of Professor Jiten Ch. Dutta. Her current research area is in fabrication of acetylcholine NEUROBIOFET for biomedical applications.

J. C. Dutta was born in Assam, India. He received the B. E. and M. E. degrees in Electrical Engineering from Dibrugarh University and Jadavpur University respectively. He obtained Ph.D degree in Engineering from Jadavpur University. He has been serving as faculty in the Department of Electronics & Communication Engineering, Tezpur University since 2001 and currently he is working as Professor. His research interests include Biosensors, Bioelectronic Devices and Neurobioengineering.