ABSTRACT

The present investigation is focused on developing a biologically inspired electronic circuit model of neuron using enzyme modified field effect transistor (ENFET) to reproduce the behavior of nerve axon. Electronic based model of neuron has advantages of obtaining signals in real time, helps to observe neuron signals in direct wave form and to study the effects of change of parameters. The developed electronic model is based on the Hodgkin – Huxley (H-H) conductance model of neuron and characteristics of conductances are based on their squid axon voltage clamp data. Experimental results indicate that the sodium and potassium conductances of H-H model are time and voltage dependent. Field effect transistor (FET) can be used as an ideal electronic element to simulate these axon membrane conductances. It is because FET is a voltage controlled device and it behaves as a variable resistor when operated at low drain to source voltage. As far as the generation of action potential of an excitable neuron membrane is concerned, the opening and closing of axon membrane channels are initiated by neurotransmitters. An acetylcholine (a neurotransmitter) sensitive field effect transistor (AchFET) which is an ENFET can, therefore, be used as electronic element to simulate the membrane axon conductances. ENFET is basically a metal oxide semiconductor field effect transistor (MOSFET) whose metal electrode is modified by an enzymatic layer and an electrolyte solution. Referring to the validation of the developed model, conductance based neuron models (e.g. H-H type models) are highly nonlinear and involve many electrophysiological parameters. Among these parameters, some of them can be measured experimentally while other parameters can only be estimated with successful estimation technique. Different methods have already been developed in order to estimate the parameters of conductance based model of neurons. A commonly used approach is the estimation method introduced by Hodgkin-Huxley which is associated with the voltage- clamp technique. Though this method may be taken as a reference method, but for every model, use of voltage clamp technique and finding the associated mathematical expression is very difficult to carry out for neurophysiologists. For this reason, parameter estimation of H-H type model has been traditionally carried out by optimization algorithm. However under circumstances, especially for the system which contains more than one parameters, successful estimation of unknown parameters depends on the estimation algorithm capable of giving parameters values which are in good agreement with established data.

In view of the above, in the first work, a compact n-type carbon nanotube (n-CNT) based acetylcholine sensitive field effect transistor (AchFET) was fabricated and characterized. It was fabricated by integrating chitosan/nickel oxide as sensing membrane with CNTFET using chemical solution process. After immobilization of acetylcholine esterase using physical adsorption technique, electrical response was carried out using digital multimeter in presence of phosphate buffer saline of 50 mM and pH 7 in a glass pot. Experimental results show the linearity for acetylcholine concentration from 0.01 mM to 0.2 mM and sensitivity of 57 mV/decade at room temperature. Stability and sensing time for this sensor was found to be 8 month and 1s respectively. Its characteristics was compared with its MOSFET counterpart and found to be similar. It has ensured that the fabricated device i.e AchFET can be used as variable resistor in an electronic circuit for reproduction of potassium and sodium conductances of axon membrane.

In the second work, an electronic circuit was developed using the fabricated AchFET for reproduction of conductances and action potential of axon membrane. It was developed by replacing conventional FET used in Guy ROY circuit model with AchFET. This physiologic based circuit was given the name NEUROAchFET. It is based on Hodgkin-Huxley model of neuron and their axon voltage clamp data. This biologically inspired circuit uses two AchFETs. One was used for sodium conductance and other was used for potassium conductance. The voltage across the drain to source of AchFET represents the membrane voltage and drain to source current of the AchFET represents the membrane current. The voltage and time dependent characteristics of the two conductances are realized by introducing a feed back and RC circuits respectively. Experimental results indicate that this circuit can reproduce a wide variety of membrane conductances and different types of action potentials. Due to inclusion of AchFET in the circuit model of neuron, it may open the possibility of measurement of concentration of acetylcholine neurotransmitters responsible for synaptic actions i.e. excitatory and inhibitory postsynaptic potentials. It is expected that such a NEUROAchFET will become a useful research unit in neurology for simulation of receptor function and electrical activity of neuron.

In the third work, the developed electronic model was validated using parameter estimation method applicable for conductance based model of neuron. In order to first find out the better estimation method, three biologically inspired algorithms namely Genetic Algorithm (GA),Particle Swarm Optimization (PSO) and Firely Algorithm (FA) was tested for estimating the parameters of original Hodgkin-Huxley conductance based model and found that FA is superior than others. These estimation methods were chosen due to the fact that they are based on evolutionary algorithms and are advanced optimization methods so far. These methods are easy to use and efficient in terms of computation. FA algorithm is then used for estimating the parameters of the NEUROAchFET. The estimated parameters are then compared with other models and found in good agreement with existing electronic models.

Graphically the abstract is shown in Fig. 1 to Fig.3. Fig. 1 shows the structure and sensitivity graph for acetylcholine detection using CNTFET. Fig. 2 shows the NEUROAchFET circuit for reproduction of sodium and potassium conductances. Fig. 3 shows the comparison of experimentally obtained action potential from the circuit with other models. It is found that the experimentally obtained action potential is in good agreement with the action potentials obtained from other models.

Graphical Abstract:

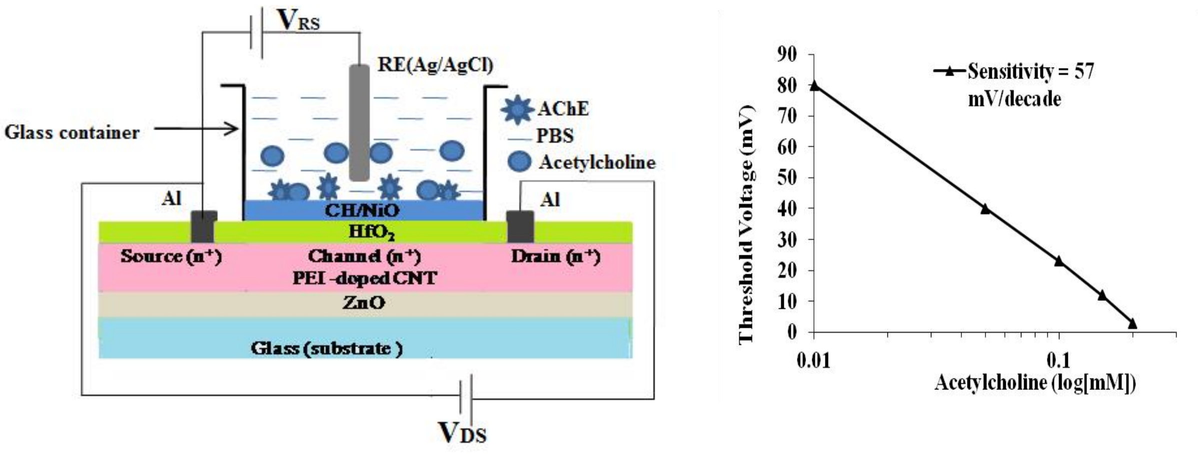

Fig.1: Structure and sensitivity of AchFET

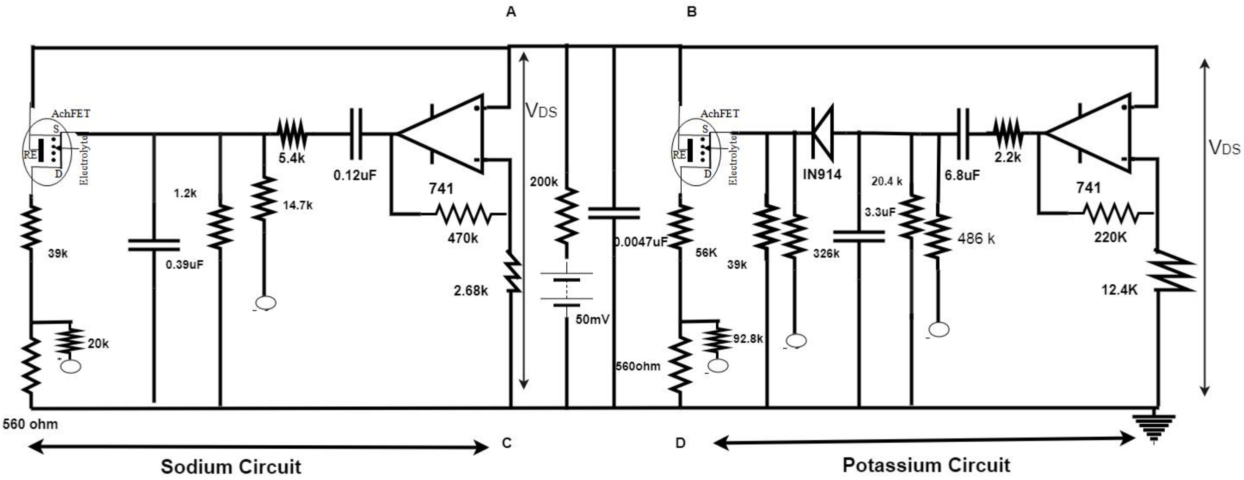

Fig.2: NEUROAchFET circuit

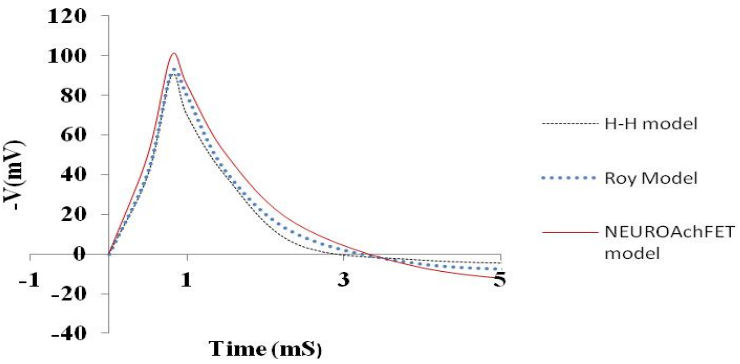

Fig.3: Action potential obtained from NEUROAchFET circuit and compared with H-H model and Guy Roy model.