Chapter 1

Introduction

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1.1 Introduction

Modeling neuron plays important role in describing aspects of neural coding, memory, network dynamics, network simulations, neuroscience for simulations of receptor function and electrical activity of neuron.

There are basically two types of neuron models. Integrate and fire (I & F) model neuron and conductance based model of neuron [12, 61]. In integrate and fire model neuron, many details of electrophysiology of neurons are not considered, instead it stresses on adequate description of phenomenon rather than biophysical basis of modeling i.e. Integrate and fire models are phenomenological models. Due to exclusion of details of electrophysiology of neurons, the utility of these models in biomedical science, more particularly in neurology, has been contrasted with more detailed conductance based models. Integrate and fire models have been the focus of theoretical and computational studies over decades and still widely used today. Unlike integrate and fire models, conductance based models are based on biophysical description of neurons. These models include many biological phenomena of membrane through conductances. Lot of conductance based models has been developed in the past, but among these models, neuroscientists have so far utilized Hodgkin-Huxley (H-H) model as a circuit analog of the axonal membrane. It is because the H-H equations are simple and elegant tool, capable of explaining the activity of neuron with the help of variable permeability (or conductance) of membrane for different ions.

Based on Hodgkin-Huxley type conductance based model, electronic circuits have been developed in the past to reproduce the behavior of nerve axons. 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. Among all electronic models developed so far, only Lewis electronic model could reproduce the details of the squid axon membrane conductances. But this circuit was quite complex and expensive to build. Guy Roy developed a simple electronic model known as NEUROFET using using field effect transistor (FET) as variable resistor that could be useful for simulating a wide variety of membrane conductances and different types of action potentials. However, this model cannot be used to explain the role of ion channels whose opening and closing are initiated by the neurotransmitters binding with the specific receptor sites of the membrane. Neurotransmitters are diffused through the synaptic cleft and then bind with the receptors to open the channels. If a sufficient number of channels are open, then the membrane potential exceeds the threshold for initiating an action potential. Though it is established that field effect transistor (FET) is the ideal electronic element to simulate the axon membrane conductances, the neurotransmitter initiated conductances cannot be explained with the help of conventional FETs. This issue can be addressed by using biologically modified Field Effect transistors (BioFETs).

Referring to parameter estimation of neuron model, conductance based neuron models (e.g. H-H type models) are highly nonlinear and involve many electrophysiological variables and parameters. Among these parameters, some of them can be measured experimentally while other parameters can only be estimated with successful estimation technique. Parameter estimation of neuron model has mainly two purposes:

i. For finding the good set of model parameters required to reproduce a specific target signal.

ii. To compare the parameters of a developed model with a well established model say H-H model.

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 appropriate algorithm used.

It is stated that among all estimation algorithms, nature-inspired algorithms are the most powerful algorithms for optimizations. Three types of biologically inspired algorithms namely Genetic Algorithm (GA), Particle Swarm optimization (PSO) algorithm and Firefly algorithm (FA) have more often used in optimization. It is essential to investigate the best of these three algorithms that can be used for parameter estimation of conductance based model.

1.2 Objectives

In view of the above challenges and work plans, following objectives have been formulated in this research work:

i. To fabricate and characterize acetylcholine sensitive field effect transistor (AchFET) to use as an analog in a neuron circuit.
ii. To develop an electronic analog of excitable neuron membrane: The NEUROAchFET
iii. To estimate the parameters of the action potential generated by the NEUROAchFET and to compare it with standard output signal of neuron.

1.3 Thesis Outlines

To accomplish the above objectives the content of this thesis entitled "Development of NeuroAchFET: A Biologically Inspired Electronic Neuron Model" has been divided into the following chapters.

Chapter 1: Introduction

This Chapter presents the backgrounds of neuron modeling, followed by the motivations behind the pursue of research work in development of NEUROAchFET circuit, estimation of the parameters for the signals obtained from the NEUROAchFET circuit, challenges involved, objectives undertaken and the methodology used to meet the objectives.

Chapter 2: Literature Review

This chapter describes the development of neuron models in an historical setting. Based on the idea that the activity of neuron can be explained satisfactorily by conductance based neuron models, various conductance based neuron models with their limitations are discussed. In conformity with this, brief descriptions of the effect of parameters related to neuron models on the activity of neuron are also discussed. Later part of this chapter discusses several estimation techniques used for estimating the parameters involved in a neuron model. Several advantages and shortcomings of some remarkable estimation techniques implemented for estimating parameters in neuron models are highlighted.

Chapter 3: Fabrication and characterization of Acetylcholine sensitive field effect transistor (AchFET) to use as an analog in a neuron circuit.

The characteristics of certain types of Field Effect Transistors (FETs) have been found to be similar to that of the axon membrane conductances. In order that a biologically modified field effect transistor (BioFET) can be used in an electronic circuit to reproduce the potassium and sodium conductances satisfactorily, this chapter describes the fabrication and characterization of a compact n-type carbon nanotube (n-CNT) based junctionless acetylcholine sensitive field effect transistor (AchFET) 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 has been 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 has been found to be 8 month and 1s respectively. Its characteristics have been found to be similar to its metal oxide field effect transistor (MOSFET) that has facilitated to use AchFET as variable conductance in an electronic circuit for reproduction of potassium and sodium conductances of axon membrane.

Chapter 4: Study on the development of an Electronic analog of excitable neuron membrane: The NEUROAchFET

This chapter describes the development of an electronic circuit using AchFETs for reproduction of action potential produced by an excitable nerve axon. It is developed by replacing conventional FET used in Guy Roy circuit model with AchFET. This physiologic based circuit has been given the name NEUROAchFET. It is based on Hodgkin-Huxley model of neuron and their axon voltage clamp data. 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

Chapter 5: Parameter estimation of conductance model of neuron

To validate the NEUROAchFET model , the appropriate algorithm for parameter estimation is to be used. For this purpose, Genetic algorithm (GA), Particle Swarm Optimization (PSO) and firefly algorithm (FA) are tested for estimating the parameters of Hodgkin-Huxley conductance based model. 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. The algorithm which yields the parameters values close to the original H-H model has been found to be firefly algorithm (FA). This method is then used for estimating the parameters from the NEUROAchFET model. The estimated parameters by FA for NEUROAchFET model is found to be in good agreement with the values given by other models.

Chapter 6: Conclusion and Scopes for Future Work

This chapter gives the final conclusion of the research works along with the future direction in which the research work might be continued.

1.4 Methodologies Applied

The proposed research work is to proceed in the following phases:

Phase 1: Defining the Research problem through a detailed literature survey on neuron modeling that includes:

- Literature survey on various conductance based neuron models.

- Literature survey on electronic neuron models.
- Literature survey on Parameter estimation of neuron models.
- Literature survey on carbon nano tube based biologically modified field effect transistors CNTBioFETs)

Phase 2: Identifying the key steps for fabrication of high-k dielectric based CNTAchFET and its characterization. This includes the following:

- Preparation of chemicals/reagents and solutions: Preparation of Acetylcholine stock solution, Acetylcholine esterase solution, Phosphate buffer saline.
- Selection and cleaning of ITO coated glass as substrate for fabrication of AchFET
- Deposition of various layers using Electrochemical deposition (ECD) technique.
- Deposition of metal contacts for source and drain by physical vapor deposition (PVD) technique.
- Biasing of the device: Setting of drain source voltage and reference voltage.
- Determination of characteristics of the device
- Sensitivity determination
- Chemical testing : Characteristic curves for CNTAchFET between drain current(I_D) and drain to source voltage(V_{DS})for different concentration of acetylcholine, drain current for different reference voltage keeping V_{DS} and Acetylcholine concentration constant, drain current for different acetylcholine concentration at constant V_{DS} .

Phase 3: Development of an Electronic analog of excitable neuron membrane using AchFET: This includes:

- PSPICE simulation of proposed electronic model of neuron with AchFET counterpart, the MOSFET and its comparison with H-H voltage clamp data.

- Development of NEUROAchFET and the identification of procedural steps to be undertaken to perform the experiments for reproduction of sodium and potassium conductances.
- Study on the effects of sodium and potassium conductances on action potential.

Phase 4: Parameter estimation and Validation of the proposed model: The NEUROAchFET

- Identification of the best nature inspired algorithm for estimation of H-H model parameters.
- Application of the best nature inspired method for estimation of the parameters from the proposed model.
- Validation of the NEUROAchFET by comparing with other models.