MODELING AN EPILEPTIC BRAIN USING DISCRETE AND CONTINUOUS NEURAL NETWORK MODELS

by

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The work described in this thesis was carried out by me under the supervision of Dr. R.P.K.C. Malmini Ranasinghe and Prof. Asiri Nanayakkara and a report on this has not been submitted to any University or any other institution for another Degree/Diploma.

28/12/2005
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I/We certify that the above statement made by the candidate is true and that this thesis is suitable for submission to the University for the purpose of evaluation.

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LIST OF ABBREVIATION

McCulloch-Pitts	**MCP**
MCP with feedback	**MCPWF**
Biswal and Dasgupta	**BD**
Low-active patterns	**LAP**
Inter-spike interval	**ISI**
Inter-burst interval	**IBI**
Fixed sequential updating	**FSU**
Sub-pass updates	**SPU**
Hodgkin-Huxley	**HH**
Connor- Steven	**CS**
Huguenard-McCormick	**HM**
Random update with synaptic plasticity	**RUWSP**
Single compartment neuron model	**SCNM**

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ABSTRACT

Various neural network models on epileptic behavior of the human brain were investigated. Several experimental studies have been carried out to simulate behavior of human epileptic brain recently. One of such experiment is the study carried out by Schiff et. al. to study the firing behavior of neural networks in hippocampus slices of rat brain. In that study human epileptic brain activity was introduced using the high potassium concentration ($[K^{+}]_{o}$), where slices from the hippocampus of the temporal lobe of rat brain were exposed to artificial cerebrospinal fluid. Before introducing the high potassium concentration, it was observed that signals recorded from brain slices contained no spikes while with the introduction of high potassium concentration, spikes appeared in random intervals as in the case of brain having epilepsy.

The brain-slice experiment mentioned above has been examined using both discrete and continuous neural network models. This discrete model was based on the model developed by Biswal et. al. and Dasgupta et. al (BD model). In this model, the effect of high potassium medium was introduced through a Hebbian learning mechanism which is switched on during the simulation under reduced inhibition. The sub-passes which play a crucial role in reproducing experimental results in BD model are found to be not necessary when random weights at different stages of the simulation are introduced.

A continuous biophysical neural network model was also developed to describe the out-come of the brain-slice experiment mentioned above. In addition, effect of the input

current and the potassium concentration changes on dynamics of a single neuron and population of neurons were investigated.

It was found that the maps of network activities exhibits stable stationary states and bursting states like trajectories similar to those were found in experiments on hippocampus slices. The discrete and continuous neural network models developed in this work were able to successfully reproduced the experimental results.

CHAPTER 1

INTRODUCTION

The brain is a complex system, which evolves parallel to the environment and is very sensitive to time. That is, almost all processes in the brain are dynamic in nature. They are called dynamic because, under the influence of change in the environment, the state of the activities of the brain changes with time from their equilibrium state. To understand and model the brain, we need to know its structure and its functions. Several experimental studies [1-6] have been carried out in the past to understand brain functions such as memory, control of movements and higher mental functions. Several research projects on mathematical and computational neuroscience have been carried out in order to model human brain [7-11]. If there exist a universal (or very general) model for the brain then many functions of the living brain can be explained and predicted with it.

During the last ten years or so, there has been great interest in simulating brain activities using Neural Networks [1, 2]. It is well known today that neural networks can be used as universal approximates for unknown or complicated functions of dynamical systems such as the human brain [7-9]. A neural network consists of several processing units interconnected in a predetermined manner to accomplish a desired task. This processing unit named as artificial neuron is a model, based on biological neuron architecture and its activities. Most of the neural network models and their dynamics, developed so far, have been based on the results obtained from experimental work. Two of the most popular types of neural network models which mimic the biological phenomena of the central nervous system are the discrete neural network models governed by difference equations and the continuous neural network models governed by differential equations [1, 2, 7, 8].

Parallel to the above mentioned research work on modeling the normal human brain, there has been a growing interest in developing mathematical and computational models associated with brain disorders [2, 7, 8, 10]. Neural modeling research is currently a very active scientific field involving substantial work based on biological phenomena in the central nervous system [9, 11, 12]. Studies carried out on brain disorders include serious diseases such as Alzheimer's disease, Parkinson's disease and Epilepsy.

Epilepsy is a chronic medical condition produced by temporary changes in the electrical function of the brain, causing seizures which affect awareness, movement, or sensation. Epilepsy is thought to be a disease of pathological synchrony between the neurons affecting ~1% of the world's population. Although drug therapy is effective in many patients, 25% are not responsive to anticonvulsant drugs. In addition, up to 50% of those receiving regular medication suffer major side effects. Surgical treatment is another one associated with serious complications. An alternative method to control the disease is electrical stimulation. The key to a better life for hundreds of people with epilepsy depends on this type of research work.

One of the signatures of the human epileptic brain during periods of time in between seizures is the presence of brief burst of focal neuronal activity known as interictal spikes. Often such spikes emanate from the same region of the brain from which the seizures are generated but the relationship between the spike patterns and seizure onset remains unclear [1, 2, 8, 10]. There have been several *in vitro* and *in vivo* experimental studies [4-6, 13-19] carried out on healthy animal brain (Rat Brain) to understand epilepsy in the human brain. In order to introduce the epileptic behavior on healthy rats, a method called kindling has been used. Kindling is considered to be a very effective method for studying epilepsy and it is the mechanism used for generating epilepsy in brain tissues taken from laboratory healthy rats either by increasing the outside potassium concentration or by applying electrical stimulations to neurons in their brain tissues. In a high potassium medium, burst are generated, as collection of high amplitude spikes separated by regions with very low activity. In a neural network model, if these bursts occurred in a regular manner then the model represents normal brain behavior. On the other hand, if bursts occurred in an irregular manner, then the model represents epileptic brain activities. Therefore kindling is very important phenomenon when studying epilepsy [2, 4, 21, 22].

Recently, Schiff et al studied the firing behavior of neural networks in hippocampal slices of rat brain [4]. They made hippocampal slices produce interictal like spikes by using the high potassium concentration ($[K^+]_o$) (Chemical Kindling), where slices from the hippocampus of the temporal lobe of a rat brain were exposed to high potassium concentration to induce epilepsy. Before introducing the high potassium concentration, it was observed that signals recorded from brain slices contained no spikes or bursts, but