1 Introduction

Brain is one of the most complex organs in the human body. For a long period of time, neurophysics, scientists and researchers have been studying the functionality of human brain in order to understand the behaviour of brain or in search of groundbreaking computer architectures and techniques that can be utilized in various applications. The most important concept in brain science is the concept of a neuron, with its collective response to stimuli[1]. The nervous system provide sensing, processing and commands that control our bodily functionality. Dysfunction of any can cause loss of sensory systems or motor control or processing which in turn may lead to diseases like Parkinson's disease, Dystonia. Biomedical Engineers have been exploring methods for performing neurobionic replacement of lost functionality [2]. The biologically accurate stimulation of neural networks has three main implications. Firstly, it allows us to understand how the brain processes information without having to perform in vivo experiments. Secondly, it can lead to the design of brain implants capable of restoring damaged, destroyed, or even missing parts of the brain[3]. Lastly, it might lead to computer architectures, providing solutions to various complex engineering problems.

There has been a notable success in cochlear(hearing loss) prosthesis, heart pacemaker and deep brain stimulation. However, a retinal prosthesis have been particularly challenging and [2] proposes an opto-electric neural stimulation technique to address this problem. Patients with spinal cord injury may suffer from urinary tract dis-function and [4] discusses an electrical stimulation system dedicated for neural stimulation of bladder.[5] performed series of experiments on conditioning of eyelid responses in rabbit, they showed that conditioned eyelid responses were developed when unconditioned stimulus is electrically stimulated in nucleus of the inferior olive(IO). The IO works closely together with the Cerebellum to provide correct motor control. Although there exists a various dedicated work on implantable micro-systems in literature, a fully programmable and parameterised experimentation platform for IO neural stimulation, where stimulus pattern, type and number are re-configurable could lead to insight and development of neuro-prosthesis related to motor control(disease such as Parkinson's). In other words, it could serve as a research platform for IO neural stimulation.

In 1952, A.L Hodgkin and A.F.Huxley from the physiological laboratory, University of Cambridge proposed a set of mathematical equations after performing a series of experiments on gain squid axon. In order to model the analog behaviour of spikes, they proposed an electrical circuit representation of neuron membrane[6]. These mathematical equations also called as Hodgkin-Huxley(HH) equations can be used to simulate wide variety of neurons, as they can be tuned to behave like a preferred neuron. One of the most widely studied neuron type is the Inferior Olivary Nucleus(ION), because of its relation to brains response to reflexes.

A highly parallel architecture, such as a field programmable gate array (FPGA), provides sufficient hardware parallelism and performance for real-time and even hyperrealtime neuron simulations. The design model proposed in [7] maximizes amount of simulated neurons for a given FPGA family type. Although this model is capable enough to accurately model the behaviour of neurons with a scalable number of cell network it lacks “biologically realistic” configuration and real-time stimulation system. Currently, all cells are initialized with same parameters and all cells are excited with a discrete current(6pA) pulse using a non-real-time interrupt based hybrid technique. However, to be capable of performing neural stimulation experimentations each neuron should have a possibility to be stimulated with different stimulus patterns in real-time with a wide range of stimulus patterns to choose.

This thesis focuses on building a fully programmable and parameterised experimentation platform for IO neural stimulation where neural parameters, stimulus pattern, type and number are re-configurable. In other words, it includes configuration system that can configure static and dynamic parameters of Inferior Olive Nucleus network's(ION). The dynamic parameter being stimulus(I_{amp}) can also be configured with its wide range of re-configurable parameters which facilitates different pulse patterns. These stimulus parameters can depict all the stimulus patterns required to produce 20 prominent spiking behaviours of neurons as shown in Figure **??**(when properly selected and tuned). However, no model with same parameter values should depict all the 20 prominent spiking behaviours of neurons simply because some of the properties such as integrator and resonator are mutually exclusive[8]. In other words, it means that any neural model has to be tuned in order to observe all these spiking behaviours, particularly tuning HH model with its set of non-linear differential equations could be very challenging[9].

1.1 Problem statement

There exists a great need for miniature implantable micro-systems that can treat neurological disorders such as epilepsy, depression, Parkinson's disease, etc [10].

The HH based ION model used in this thesis simulates more number of neurons than the ones actually implemented on hardware. The cells actually present are referred to Physical Cells(Phyc) and ones simulated on the same hardware by means of time multiplexing are known as Simulated Cells(SimC)[7, 11]. To configure such a time shared network of SimC's each with a different set of parameters requires synchronisation of various signals at proper timings as discussed in Appendix D of [7]. In order to inject each SimC with a different stimulus at its run time also requires a similar set of constrains as discussed in Appendix D of [7].

In a bio-phisically meaningful system there can be continuously varying stream of pulses or spike patterns which poses a great need for re-configurable parameters as part of Stimulus Generator(StimG)[12].

In order to synchronize the stimulus generation and injection into the ION at specific time within a biological real-time(50us)[13] a reliable architecture which can satisfy the design requirements needs to be built.

With the existence of a large network of neuron cells and stimulus generators there exists a large set of parameters which needs to be specified before they can be initialized.

In other words, the system presents to user a great need of effort to configure, trigger and observe the response of ION network. Hence, there exists a need of a Graphical User Interface(GUI) which can be used to specify these parameters and display the response of ION network in a graphically meaningful way. This thesis work aims to solve all the above mentioned problems.

1.2 Goals

The main goals of this thesis work are:

- To build a real-time StimG in FPGA which provides a compact and low power solution.
- To build a reliable system-on-chip architecture which can integrate StimG and ION network with required synchronisation and provide the capability to configure both.
- To build a GUI which simplifies users effort in specifying the parameters, controlling the network of SimG's and ION's and displaying the response of the same in a graphical way.

As a whole, to build a fully programmable and parameterised experimentation platform for IO neural stimulation where neural parameter, stimulus pattern, type and number are re-configurable.

1.3 Contributions

- A Fully programmable and parameterised experimentation platform for IO neural stimulation where neural parameter, stimulus pattern, type and number are re-configurable and HH model is used to simulate neural behaviour.
- A Real-time StimG in FPGA which provides a compact and low power solution with a capability of stimulating 1000 neurons in real-time for ION machine built by [7].
- Classified 10/20 different prominent spiking behaviours by tuning HH-parameters and StimG parameters on FPGA.

1.4 Thesis Outline

Yet to be added after having a document flow.

Bibliography

[1] Eugene M. Izhikevich. *Dynamical Systems in Neuroscience: The Geometry of Excitability and Bursting.* The MIT Press Cambridge, Massachusetts London, England, 2007.

[2] Alex Bystrov Musa Al Yaman, Arfan Ghani and Patrick Degenaar. Fpga design of a pulse encoder for optoelectronic neural stimulation and recording arrays. *Biomedical Circuits and Systems Conference (BioCAS), 2013 IEEE.*

[3] Carlo Galuzzi Jaco Hofmann, Amir Zjajo and Rene van Leuken. Multi-chip dataflow architecture for massive scale biophysically accurate neuron simulation. *38th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC).*

[4] S. RobinM. SawanEmail authorM. Abdel-GawadT. M. Abdel-BakyM. M. Elhilali. Implantable stimulation system dedicated for neural selective stimulation. *Medical and Biological Engineering and Computing*, 36.

[5] JOSEPH E.STEINMETZ MICHAEL D. MAUK and RICHARD F. THOMPSON. Classical conditioning using stimulation of the inferior olive as the unconditioned stimulus. *Proc. Nati. Acad. Sci. USA*, 83.

[6] A.L. Hodgkin and A.F. Huxley. A quantitative description of membrane current and its application to conduction and excitation in nerve. *Journal of Physiology*, 117:500–544, 1952.

[7] G.J. Christiaanse. A real-time hybrid neuron network for highly parallel cognitive systems. masters thesis, Tu Delft.

[8] Eugene M. Izhikevich. Which model to use for cortical spiking neurons? *IEEE TRANSACTIONS ON NEURAL NETWORKS.*

[9] Xianyang Fei Jiang Wang, Liangquan Chen. Analysis and control of the bifurcation of hodgkin–huxley model. *Chaos, Solitons and Fractals.*

[10] IEEE Karim Abdelhalim Graduate Student Member IEEE Demitre Serletis Peter L. Carlen Farzaneh Shahrokhi, Member and IEEE Roman Genov, Member. The 128-channel fully differential digital integrated neural recording and stimulation interface. *IEEE TRANSACTIONS ON BIOMEDICAL CIRCUITS AND SYSTEMS.*

[11] C. Galuzzi R. van Leuken J. Christiaanse, A. Zjajo. A real-time hybrid neuron network for highly parallel cognitive systems. *Proceedings of International Conference of the IEEE Engineering in Medicine and Biology Society.*

[12] Francisco J. Pelayo, Samuel F. Romero, Christian A. Morillas, Antonio Martínez, Eduardo Ros Vidal, and Eduardo Fernández. Translating image sequences into

spike patterns for cortical neuro-stimulation. *Neurocomputing*, 58-60:885–892, 2004.

[13] Georgios Smaragdos, Sebastián Isaza, Martijn F. van Eijk, Ioannis Sourdis, and Christos Strydis. Fpga-based biophysically-meaningful modeling of olivocerebellar neurons. In *FPGA*, pages 89–98. ACM, 2014.