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NEURO-HYBRID SYSTEM WITH SPIKING NEURAL NETWORK AND BIOMIMETIC IONIC MICRO-STIMULATION

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ABSTRACT

Millions of people worldwide have neurodegenerative diseases that influence one's cognitive and/or motor functions. To bring neuroprosthesis into realization and for future long-term replacement of damaged brain areas with artificial devices, investigations on the interaction of neuronal cell assemblies are essential. To circumvent the limitations, we propose a new bio-hybrid system which includes a real-time Spiking Neural Network (SNN) and a biomimetic ionic micro-stimulation coupled to living *in vitro* neuron culture. This system characterizes the neural network and its evolution by using biomimetic spike-timing based ionic stimulation.

KEYWORDS: Neuro-hybrid, Spiking Neural Network, micro-stimulation, microfluidic, biomimetic

INTRODUCTION

Research on neurological disorder recently relies on alternative treatment using biomimetic and real-time hardware known as neuroprosthesis. Realization of such devices must follow several requirements including the knowledge on the relation between cells and machine or the neurons activities. This kind of neuromorphic engineering is called biomimetic artificial neural systems which are mostly *in silicon*-based [1], [2], [3]. The main goal of such systems is to design tools for biomedical applications including neuroprosthesis and to understand the human nervous system. This project reveals a new bio-hybrid system composed of a real-time Spiking Neural Network (SNN) and biomimetic ionic micro-stimulation coupled to living *in vitro* neuron culture. We describe here the three parts of this neuro-hybrid system (Figure 1). This system characterizes the neural network and its evolution by using biomimetic spike-timing based ionic stimulation.

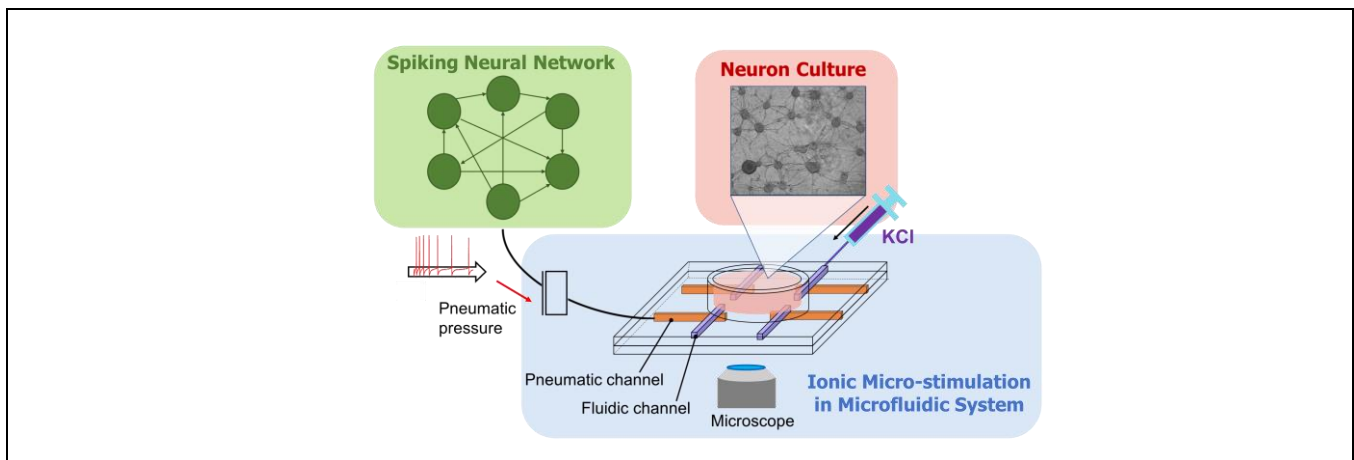


Figure 1. Neuro-hybrid system with real-time digital SNN (green), biomimetic ionic micro-stimulation in microfluidic system (blue) and biological neuron culture (pink). SNN electrical output is converted into air pulse

THEORY

The biomimetic SNN network is a neuromorphic system that is the closest detailed level of analogy to the nervous system [4]. A network of silicon neurons is connected via silicon synapses under plasticity rules. In bio-hybrid experiments, spike timing and shape of the action potential (AP) must reproduce the same dynamics of a real nerve impulse. This tunable biomimetic system works in real time and is based on Hodgkin-Huxley (HH) formalism [5] which is the most bio-plausible neuron model. We integrated the SNN in a digital platform (FPGA) (Figure 2). The

spike timing of our SNN is used for triggering the microfluidic ionic micro-stimulation to make the stimulation the closest to biological behavior.

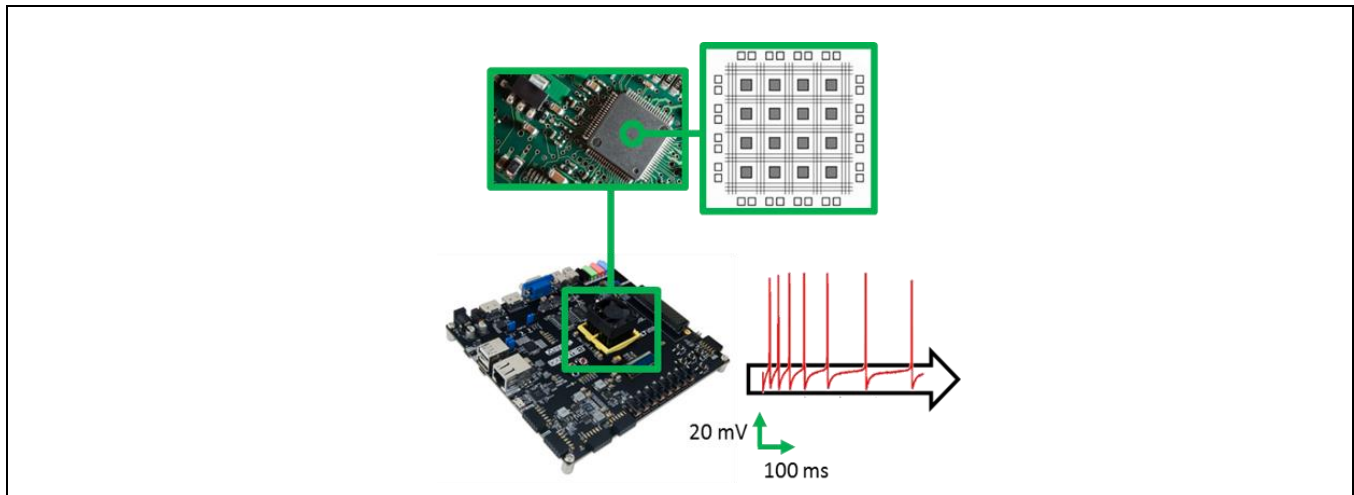


Figure 2. Real-time SNN. HH neuron model are implemented in a FPGA. Regular spiking neuron model parameters are: neuron surface area of $96 \mu\text{m}^2$, a K, Na and leakage conductance respectively at 5.00, 50.00, and 0.07 $\text{mS}\cdot\text{cm}^2$ and a K, Na and leakage reversal potential respectively at 50, 100, -70 mV. The SNN works in biological time and reproduces the spike timing of biological neural network.

Using silicon neurons bring some bio-compatibility issues (reject, power consumption). To simplify the interactions with biological neurons and to reduce the bio-compatibility issues keeping the same ionic currents (K^+) to the biologic ones, we designed a biomimetic ionic micro-stimulation using microfluidic techniques and ionic exchange. This microfluidic device [6] is made with Polydimethylsiloxane (PDMS) which is highly biocompatible and it is composed of two chambers intra- and extracellular modelling connected by channels with different KCl concentrations actuated by pneumatic microvalves [7] (Figure 3). The pneumatic valve-based technology requires multilayer soft lithography and an external air pressure controller. The latter air pressure system is triggered by the SNN to obtain biological like neuronal behavior. The channels are equipped with ion selective permeable membrane to mimic the chemical exchange of biological neurons.

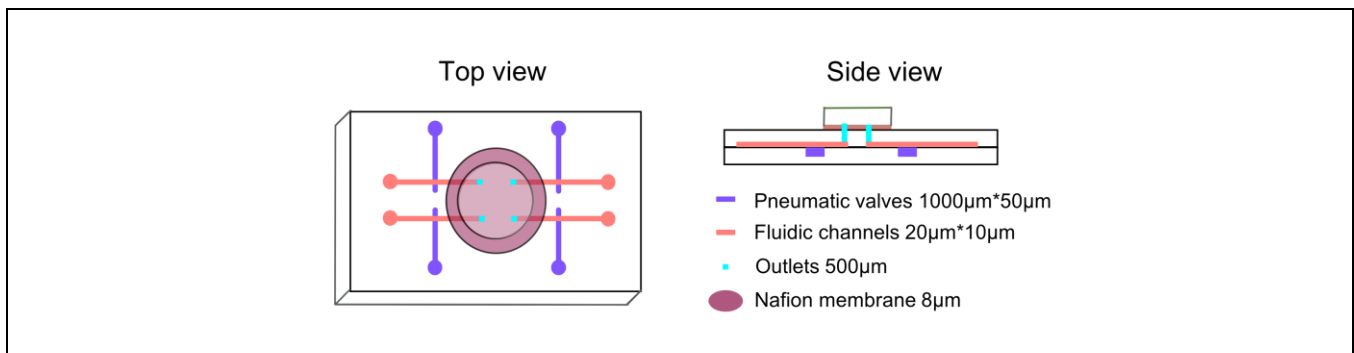


Figure 3. Different layers of ionic micro-stimulation device. In this example, four micro-stimulation holes are designed.

EXPERIMENTAL

This bio-hybrid system contains ‘in vitro’ primary cultures of mice hippocampal neurons. Neurons were carefully dissected from embryos and were prepared as described [8]. Neurons isolated from embryonic day 17 ICR mouse were plated in Neurobasal medium. The experiments were proceeded after two weeks of maturation inside the cell dish of the microfluidic device. Neuronal activities were visualized by calcium imaging with Fluo-4 AM. To visualize the spatial and temporal changes in calcium resulting from spontaneous activity, the raw sequences were processed to highlight changes in fluorescence intensity of when the biomimetic ionic micro-stimulation is activated (Figure 4).

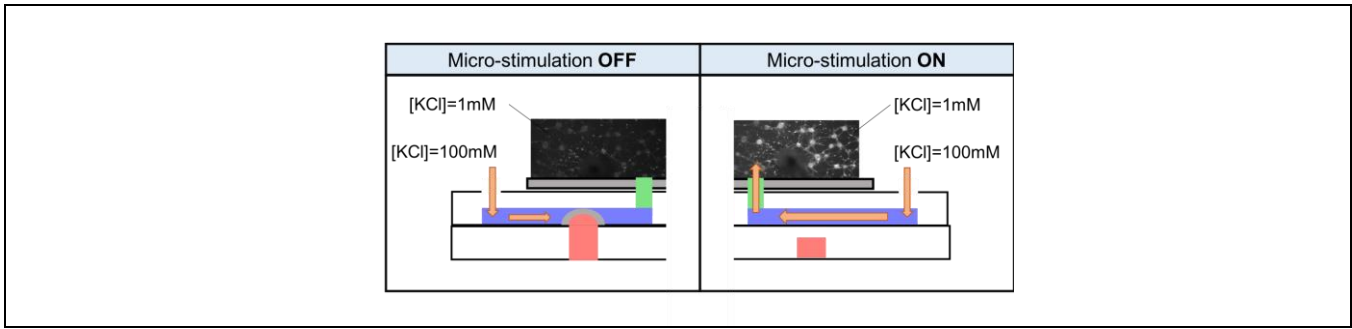


Figure 4. Bio-hybrid experiments using biomimetic ionic micro-stimulation. When micro-stimulation is ON, the neuron culture is active. Calcium imaging technique is used for detecting neuronal activity.

RESULTS

Regular and simplified equations of biomimetic SNN are implemented on a FPGA [9]. Electrical activities of different classes of cortical neurons can be simulated in biological time scale. Mathematical tools show strong correlation between hardware simulations and software simulations (Figure 5).

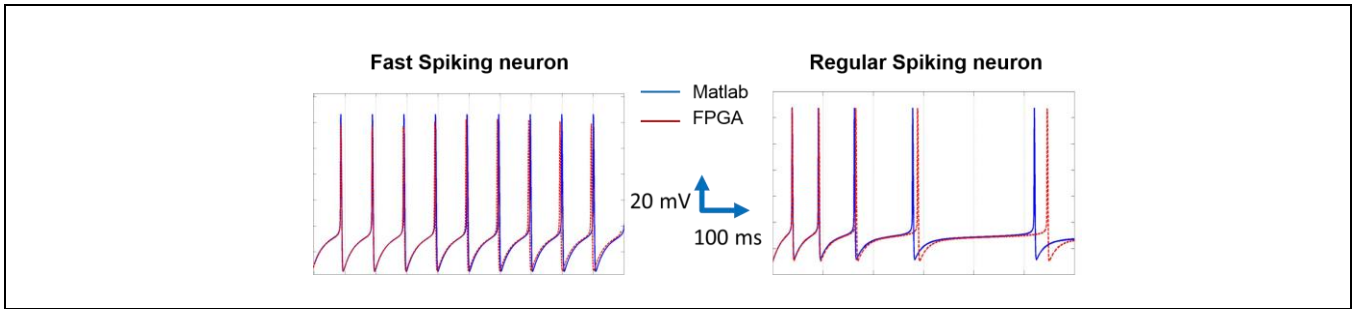


Figure 5. Real-time hardware implementation on FPGA of different neuron family. On the left panel, inhibitory neurons named Fast Spiking neuron. On the right panel, excitatory neurons named Regular Spiking neuron. FPGA implementation and Matlab software simulations are similar.

The device with integrated cell dish for the placement of living neurons has a thinness of less than 5mm allowing the observation through microscope during calcium imaging. Our device can generate a biomimetic stimulation [10] accordingly to the sequenced air pressure. The opening of the pneumatic microvalve was sequentially repeated after three pulses of 0.1s, 0.25s and 0.5s with each separated with 0.2s of closure. The matured neurons were stained with calcium specific fluorescence to observe the neural activity. Fluorescence response was successfully observed only during the opening of pneumatic microvalve.

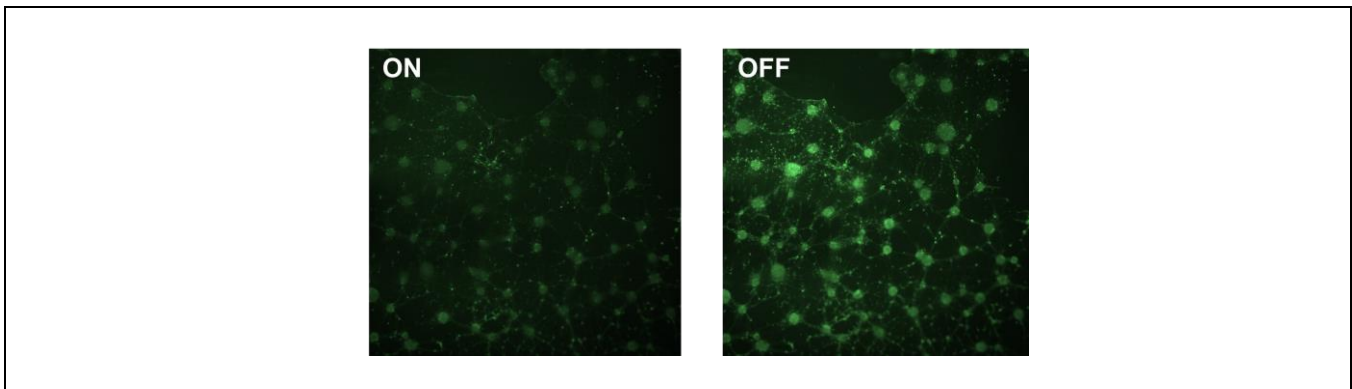


Figure 6. Calcium Imaging of opening (ON) and closing (OFF) of pneumatic microvalve

CONCLUSION

We demonstrated successful micro-stimulations of the neuron cells with potassium ions using microfluidic pneumatic microvalves operated by air pressure controller. The neural activities responded according to the programmed air pressure applied (0.1s, 0.25s and 0.5s), capable of generating a biomimetic behavior. Next step is to perform bio-hybrid experiments coupling all the modules. This system will investigate neural network dynamics and test new neuro-prosthesis [11], [12], [13], [14], [15].

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