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► **To cite this version:**

Stephany Mai Nishikawa, Soo Hyeon Kim, Yoshiho Ikeuchi, Teruo Fujii, Timothée Levi. BIOMIMETIC IONIC MICROSTIMULATION FOR NEURON CULTURE. 10th International Symposium on Microchemistry and Microsystems (ISMM2018), Jun 2018, Busan, South Korea. hal-02484018

HAL Id: hal-02484018

<https://hal.science/hal-02484018>

Submitted on 19 Feb 2020

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BIOMIMETIC IONIC MICROSTIMULATION FOR NEURON CULTURE

Stephany Mai Nishikawa¹, Soo Hyeon Kim¹, Yoshiho Ikeuchi¹, Teruo Fujii¹
and Timothée Levi^{1,2}

¹Institute of Industrial Science, The University of Tokyo, Japan

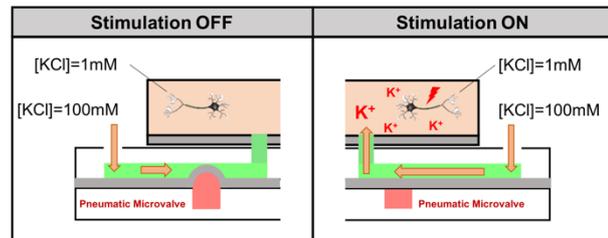
²IMS Lab, University of Bordeaux, France

INTRODUCTION

Neurodegenerative diseases are incurable and debilitating conditions that influence cognitive and/or motor functions in millions of people worldwide. Neuroprosthesis are used today to support the quality of life but have yet to improve in their power consumption and biocompatibility issues. For the future realization of neuroprosthesis, understanding the neurophysiological behaviors and the investigations on the interaction of neuronal cell assemblies is therefore essential. Here, we propose a novel microfluidic system to investigate the response of the neurons directly stimulated by the potassium ions *in vitro*. Unlike the conventional way of stimulating neurons by pipetting or sending electrical stimulus, this biomimetic stimulation system enables precise and rapid control of ion concentration by utilizing microfluidic pneumatic valves, which mimics physiological stimulation in a body. By using the system, we demonstrated stimulations of the neuron cells with potassium ions and monitored neural activities with a calcium-specific fluorescence indicator.

CONCEPT OF THE DEVICE

The device was inspired by nervous system which is a network of neurons. Each neuron is connected through synapses, to a large number of other neurons, through dendrites and axons. The axon transmits electrochemical pulses (including KCl, NaCl) to communicate between neighboring neurons by transmitting electrical signals based on ionic flow between intracellular and extracellular environments. To simulate this physiological behavior, a device made with Polydimethylsiloxane (PDMS) has two chambers intra- and extracellular chambers connected by channels with high and low concentrations of potassium chloride actuated by pneumatic microvalves. An ion selective permeable membrane (Sigma-Aldrich, Nafion® perfluorinated resin solution 5wt.%) is used for and the concentration of potassium ions can be changed.



Stimulation OFF and ON controlled by pneumatic microvalve

RESULTS

The device with integrated cell dish for placing living neurons has a thinness of less than 5mm allowing the observation through microscope during calcium imaging. Our device can generate a biomimetic stimulation 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.

CONCLUSIONS

We successfully demonstrated stimulations of the neuron cells with potassium ions using microfluidic pneumatic microvalves operated by air pressure controller. The neural activities were visible according to the programmed air pressure applied, capable of generating a biomimetic behavior. We believe that our novel system can be utilized for the fundamental investigation of the response of the neurons stimulated by well-modulated ion stimulus to understand the neurophysiological behaviors.

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KEYWORDS: Ionic stimulation, Biomimetic activity, Microfluidic neuron.