Alterations in Neuronal Action Potential Shape and Spiking Rate Caused by Pulsed 60 GHz Millimeter Wave Radiation

Sergii Romanenko[abc]*, Peter H. Siegel[a], Victor Pikov[b], Vincent Wallace[c]
[a]California Institute of Technology, Pasadena, CA 91125 USA
[b]Huntington Medical Research Institutes, Pasadena, CA 91105 USA
[c]University of Western Australia, Perth, 6009 Australia
*sergii.romanenko@uwa.edu.au

***Abstract* — This study demonstrates effect of 60 GHz radiation applied in a pulsed mode to the finite neuronal network. Short powerful pulses of 50 to 300 msec duration were applied to leech neuronal ganglion and electrophysiological activity of the Retzius cells were recorded via sharp electrodes. Pulses were applied with respect to the natural activity of the tested cell and preconditioned every recorded action potential. Despite fairly low increase of sample's temperature caused by radiation's heating, clear and instant alteration in action potential parameters occurred. Along with that the prolonged utilization of this mode resulted into decrease of action potential spiking rate. Obtained results demonstrate the potential use of sub-terahertz radiation for wireless modulation of neuronal activity.**

I. INTRODUCTION

The utilization of long wave electromagnetic radiation of sub-infrared and terahertz range for cell function stimulation is currently experiencing expansion of interest among biomedical community, and neuroscience is one of the fields which may potentially benefit from this technology.

Some good examples already have demonstrated the use of THz radiation for detection of inhomogeneous structure of biological tissues in normal and pathological conditions[1]. Good contrast based on water content of the tissue was observed with 90 -150 GHz CW radiation to detect superficial skin defects.

Despite high absorption level by water, with an appropriate design terahertz radiation could be sensitive to different molecules in media. Some examples of blood glucose level detection have been demonstrated both *in vitro* [2] and, most importantly, *in vivo*[3]. Another example is the detection of nitrous oxide release due to the neuronal tissue damage in *ex vivo* preparation with sensor operating on 140-220 GHz [4].

Beside of detection and imaging features, it was shown that with relatively low power exposure levels the radiation in terahertz range could modulate electrophysiological activity of neurons in *in vitro* and *ex vitro* preparation by suppressing action potential's firing rate[5-7].

In recent years a new approach based on the use of single electromagnetic pulse in THz range and proved to be advantageous by means of power applied to the tested sample and amount of information delivered from the single test [8]. Pulsed terahertz radiation have been successfully used for detection of the human breast tumor, skin cancer and basal cell carcinoma in *ex vivo* preparation [9].

Due to importance of minimization of deposited energy within a living tissue at a single act of interaction with a radiation, we investigated how short pulses of millimeter wave (MMW) radiation could affect natural activity of neuronal tissue.

II. RESULTS

In order to reduce the effect of live tissues vitality artifacts in *ex vivo* experiment we selected a freshly-dissected segmental ganglion in the medicinal leech (*Hirudo verbana*) as our test object and well established experimental model in neuroscience. Electrophysiological recordings were done by using the sharp electrode technique. In all experiments data were collected from the Retzius cells without of desheathing of the ganglia and natural activity of probed neurons were recorded with Axoclamp 900A amplifier-electrometer in current-clamp mode with zero current clamped during acquisition.

The MMW exposure system consisted of a synthesized microwave source for 17-23 GHz (HP 83650L, Agilent Technologies, Santa Clara, CA), a 4x frequency-multiplying stage (HP 83557A, Agilent Technologies) followed by a 20dB amplifier (AMP-15, Millitech, Northampton, MA, USA) to generate continuous wave power between 4 and 64 mW at 60 GHz.

Monitoring of the ganglion temperature during MMW irradiation was done using a fiber-optic spectrophotometric temperature sensing device (OTG-M360 sensor with PicoM spectrophotometer, Opsens Inc), which is insensitive to MMW irradiation and mechanical vibration due to its optical mode of measuring the GaAs crystal bandgap (accuracy 0.05°C, response time <100 ms).

Short pulses of 50 to 300 msec duration and instant power at the output of the rectangular waveguide ranging from 64 to 550 mW were applied to the tested ganglion through 3.2 mm thick paraffin padding (used as a ganglion attachment base). Pulses were applied on somewhat irregular basis corresponding to the natural activity of the neuron which was done via feedback control of the MMW source from recording amplifier. This way the radiation was applied at moments of similar electrophysiological events ongoing on a cellular level (fig. 1).

978-1-4673-8485-8/16/$31.00 ©2016 IEEE

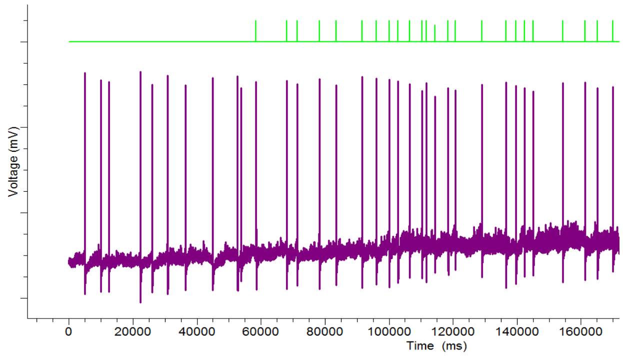

Fig. 1. The effect of stimulation of the Retzius cell in leech neuronal ganglia with MMW 60 GHz, 550 mW, 50 msec pulses driven by positive going slope of action potential: record of the natural and affected neuronal activity of Retzius cells (purple) and moments of MMW stimulus application (green).

Within several seconds after start of the stimulation the affected action potentials demonstrated decrease in its amplitude, half-width, depolarization and repolarization phases. This phenomena was somewhat similar to the results observed in our previous study conducted with 60 GHz radiation in CW mode. Although, in contrast to our previous results, observed alterations appeared with a much smaller changes in sample temperature (fig. 2). Within less than 2 min of stimulus application (with average spiking rate 1-0.2 Hz) the temperature of sample stabilized and did not exceed 0.3 °C. Thus, in average and within one act of stimulation temperature alterations of the sample were less than 0.1 °C which is within usual fluctuations.

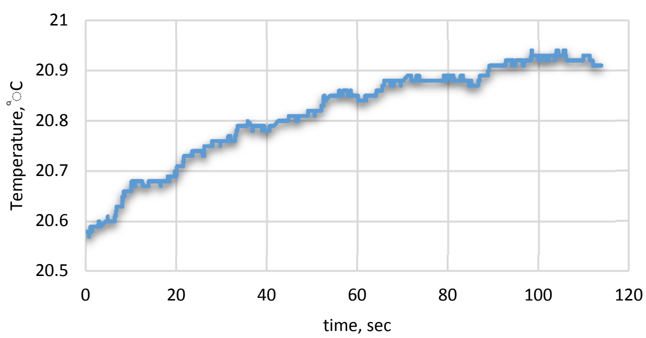

Fig. 2. The record of MMW radiation mediated heating of leech neuronal ganglia. The stimuli of 50 msec pulses with carrier frequency of 60 GHz and 550 mW instant power were driven by positive going slope of action potential.

To investigate the effect of MMW pulses on membrane excitability of the Retzius neurons, we compared cell's responses to steps of injected current (step-protocol) under control and test conditions. Neurons were exposed to the MMW radiation (64 mW, 65 msec) and effect was characterized by maximal slope of action potential rise phase (fig. 3) because this phase determines the ability of the neuron to be excited from the resting state. As it well seen, for a relatively weak injected currents application of the MMW causes suppression of cell excitability by decreasing its speed of depolarization, whereas for stronger protocol's stimulus, cell excitability is completely dominated by injected current and MMW effect is diminished up to insignificant level.

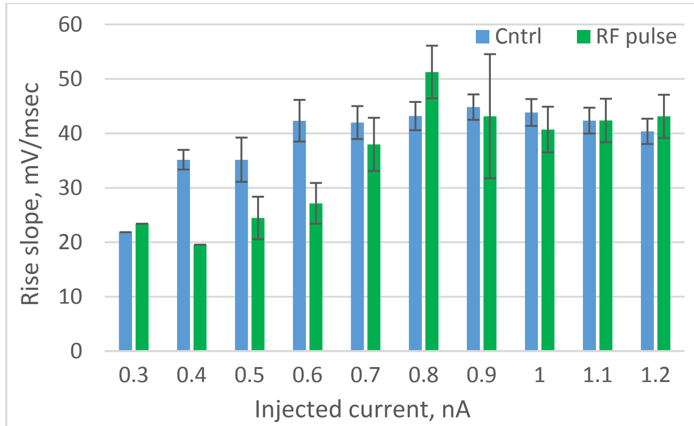

Fig. 3. The bar graph of Retzius cell Action Potential's maximal rise slope for different strengths of injected current stimulus (step protocol) presenting data for control measurement (blue; Cntrl) and measurement conducted during exposure to MMW 60 GHz, 64 mW, 65 msec pulses (green; RF pulse) applied to the sample during 70 msec run of the protocol's step.

III. Summary

This study demonstrates possibility of neuronal activity control by pulsed MMW mediated stimulation with irregular mode of stimulus application based on feedback from tested sample.

References

[1] E. Pickwell, and V. P. Wallace, "Biomedical applications of terahertz technology," *Journal of Physics D: Applied Physics,* vol. 39, no. 17, pp. R301, 2006.

[2] H. Choi, J. Naylon, S. Luzio, J. Beutler, J. Birchall, C. Martin, and A. Porch, "Design and Interference Test of Microwave Noninvasive Blood Glucose Monitoring Sensor," *IEEE Trans Microw Theory Tech,* vol. 63, no. 10 Pt 1, pp. 3016-3025, Oct 1, 2015.

[3] P. H. Siegel, A. Tang, G. Virbila, Y. Kim, M. C. F. Chang, and V. Pikov, "Compact non-invasive millimeter-wave glucose sensor." pp. 1-3.

[4] A. D. Abbas, Thomas; Croix, Dominique; Salzet, Michel; Bocquet, Bertrand, "Ex-vivo detection of neural events using THz BioMEMS," *Med Sci Monit*, (9), 2009, pp. 121-5

[5] V. Pikov, X. Arakaki, M. Harrington, S. E. Fraser, and P. H. Siegel, "Modulation of neuronal activity and plasma membrane properties with low-power millimeter waves in organotypic cortical slices," *Journal of Neural Engineering,* vol. 7, no. 4, Aug, 2010.

[6] S. Romanenko, P. H. Siegel, D. A. Wagenaar, and V. Pikov, "Effects of millimeter wave irradiation and equivalent thermal heating on the activity of individual neurons in the leech ganglion," *Journal of Neurophysiology,* vol. 112, no. 10, pp. 2423-2431, Nov 15, 2014.

[7] S. Romanenko, P. H. Siegel, D. A. Wagenaar, and V. Pikov, "Comparison of the effects of millimeter wave irradiation, general bath heating, and localized heating on neuronal activity in the leech ganglion," *Terahertz and Ultrashort Electromagnetic Pulses for Biomedical Applications,* vol. 8585, 2013.

[8] A. J. Fitzgerald, V. P. Wallace, M. Jimenez-Linan, L. Bobrow, R. J. Pye, A. D. Purushotham, and D. D. Arnone, "Terahertz Pulsed Imaging of Human Breast Tumors," *Radiology,* vol. 239, no. 2, pp. 533-540, 2006.

[9] R. M. Woodward, V. P. Wallace, D. D. Arnone, E. H. Linfield, and M. Pepper, "Terahertz Pulsed Imaging of Skin Cancer in the Time and Frequency Domain," *Journal of Biological Physics,* vol. 29, no. 2, pp. 257-259.