33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

# Optical Stimulation of Visual Cortex with Pulsed 620-nm RED Light

Wen S. Hou, Zong X. Mou, Wei W. Shi, Xiao L. Zheng, Jun P. Yao, Guan B. Shang, and Zheng Q. Yin

*Abstract*-**To explore the optical neural stimulation with visible light, 620-nm red light pulse emitted by LED was used to stimulate the left primary visual cortex of adult rat. The neural response in right primary visual cortex was recorded with a flexible microelectrode. By synchronized averaging the raw signal, optical evoked potentials (OEPs) were observed a negative wave and positive wave after optical stimuli. Furthermore, the amplitude and occurrence of the negative and positive wave were modulated by the strength and pulse width of the optical stimulus. The preliminary experiment suggested that, beyond the infrared laser, the pulse of visible light (e.g. red light) can modulate the neural activity in central nervous system.**

## I. Introduction

NEURAL stimulation is an engineering method by which the ion channel of neuron can be activated and the action potential can be evoked by various physical stimulus. Electrical stimulation, which injects a current or change in voltage to neural tissue and generates neural action potentials by activation of voltage-gated ion channels of neurons [1], has been widely used for the neural stimulation of central nervous system (CNS) and peripheral nervous system (PNS). Although the electrical neural stimulation has been successfully applied in motor [2], visual [3]-[4], and auditory [5] functional rehabilitation, the cross-talking resulted from spread current around the electrode and tissue damage induced by electro-chemical changes at the electrode-tissue interface are the stumbling blocks for clinical application all the time.

Optical stimulation is an alternative approach to evoke the action potential of neuron with optical radiation [6]-[8]. As the stimulus is the irradiated light in neural tissue, the optical neural stimulation has the unique advantages of high spatial resolution and low damage to the neural tissue due to no physical contact of stimulator. Infrared laser has been used to effectively stimulate the sciatic nerve [6]-[8], facial nerve [10], and auditory nerve [11]-[15]. Recently, optical stimulation has been introduced to stimulate CNS, and the excited and inhibited neural responses have been recorded in thalamocortical brain slices [17] and somatosensory cortex [16], respectively.

In the reported experiments, infrared laser has been widely explored for the optical neural stimulation [6]-[11], [17], however, the feasibility of neural stimulation with visible light has never been attempted. This work is to test whether the optical stimulation with LED 620-nm red light can activate the cortical neural activity in vivo.

## II. Materials and Methods

### A. Surgical Procedure

The procedures performed in our study met the "Laboratory Animal Management Regulations" instituted by the State Science and Technology Commission. Rats (200g-400g) used in the study were initially anesthetized using 20% urethane solution (1.33 g/kg) by intramuscular injection. The rat was fixed in a stereotactic frame and a medical electric bone drill was used to open the skull until to expose the primary visual cortex (Brodmann area 17). Body temperature was monitored and kept at approximately 38°C by a heating pad (HSS-1, Chengdu Instrument Manufactory, Chengdu, China).

### B. 620-nm LED Stimulation

620±20 nm red light was produced by CLS-150, a high brightness LED light (Nanjing Chunhui Science and Technology Industrial Co.Ltd, Nanjing, China). The intensity, width and repetition rate of the pulse can be controlled between 0-1.22mW, 50μs-20ms and 1-250Hz, respectively. The optical power was delivered to a 500-μm-diameter optical fiber positioned 1 mm above the exposed left primary visual cortex of anesthetized rat (Fig. 1).

### C. Electrophysiological recordings

The cortical responses to pulsed red light stimulation were recorded using a custom-made flexible microelectrode array located on the surface of right primary visual cortex of the rat. The microelectrode was stabilized by the dental cement with bone wax. Recording signal was connected to an 8-channle physiological signal recording instrument (Rm6280C, Chengdu Instrument Manufactory, Chengdu, China). Band-pass filtered 0.2 to 100 Hz and sampled at 2000Hz. The synchronous signal of the optical stimulus, collected by a photistor (3DU33), was recorded simultaneously by the 8-channel physiological signal recording instrument. Heart

This work was supported by the National High Technology and Development Program of China (863 Program) (Vo. 2007AA04Z324) and the Nature Science Foundation of China Grant (No. NSFC31070882).

W. S. Hou is with the Bioengineering college of Chongqing University, Chongqing 400044 China (Tel: 86-23-65111931; fax: 86-23-65111931; e-mail: w.s.hou@cqu.edu.cn).

Z. X. Mou is with the Bioengineering college of Chongqing University, Chongqing 400044 China (e-mail:mouzongxia@163.com).

W. W. Shi is with the Bioengineering college of Chongqing University, Chongqing 400044 China (e-mail: juandewei410@163. com).

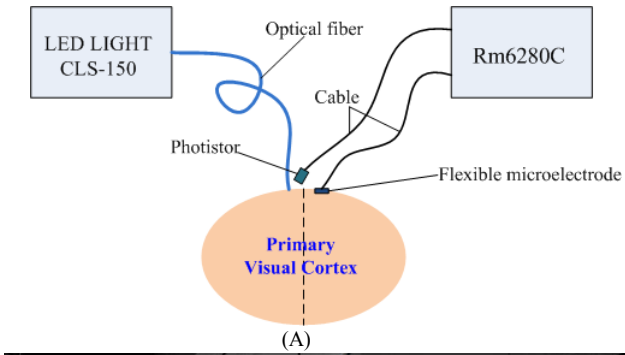
X. L. Zheng is with the Bioengineering college of Chongqing University, Chongqing 400044 China (e-mail: zxl@cqu.edu.cn).

J. P. Yao is with the Bioengineering college of Chongqing University, Chongqing 400044 China.

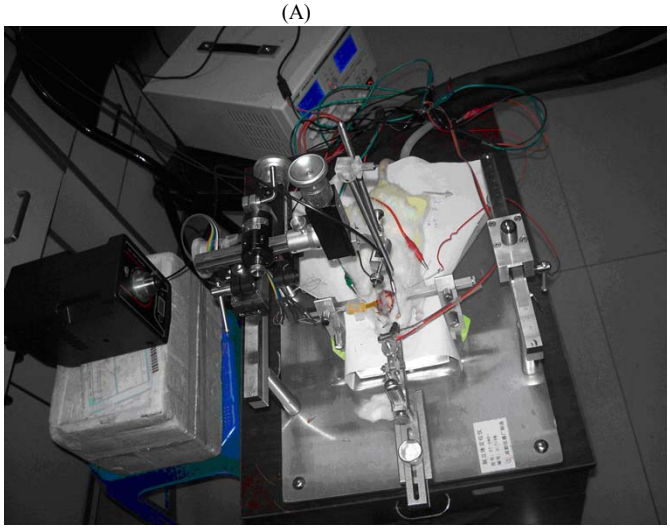
G. B. Shang is with the Bioengineering college of Chongqing University, Chongqing 400044 China.

Z. Q. Yin is with Department of Ophthalmology, Third Military Medical University, Chongqing 400038, China.

rate and electrocardiogram (ECG) were monitored throughout the experiments (see Fig. 1).




(A)



(B)

Fig. 1 Conceptual illustration (A) and experiment scene (B) of the 620-nm optical stimulation and its cortical response recording in primary visual cortex.

### *D. Data Analysis*

The recordings collected in individual sessions were analyzed offline in MATLAB 7.0. Each session of the raw signals was segmented according to the recorded synchronous signal of the optical stimulus. The synchronized averaging, a conventional process for ERP signal, were employed to process the recorded neural response of optical stimulation until the averaged noise level is less than 10 μV.

## III. Results and Discussion

After 100-trial averaging, the optical evoked potentials (OEPs) were observed in the averaged neural electrical activities recorded on the primary visual cortex, and illustrated in Fig.2. It showed that, with a certain level of pulsed optical stimulation, 620-nm red light of LED evoked an event-related neural activities consisting of a negative wave (N1) and a positive wave (P1). With the stimulation of 60mW/cm$^2$, latencies of the negative wave (N1) and positive wave (P1) were around 100ms and 150ms, respectively. Furthermore, the amplitude of the negative wave is much bigger than the positive wave.

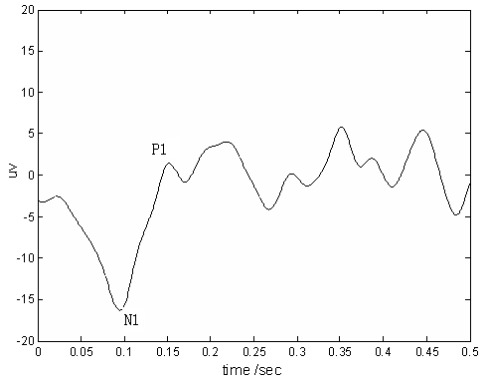
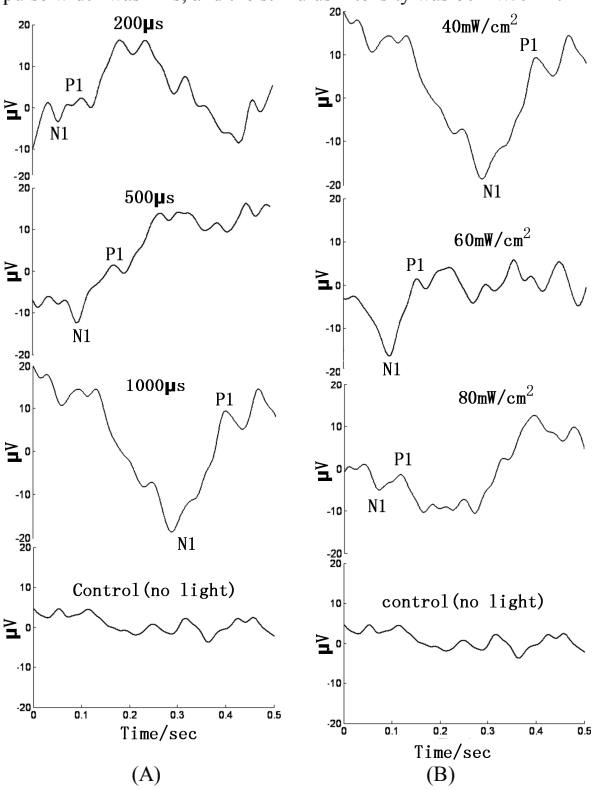



Fig. 2 An individual representative OEPs. An obvious negative wave followed by a positive wave. Here the pulse repetition rate was set at 1Hz, the pulse width was 1ms, and the stimulus intensity was 60mW/cm$^2$ .




(A) (B)

Fig. 3 OEPs elicited by varying pulse durations (A) and stimulus intensity (B) in one rat after synchronized averaging 100 trials. The stimulus intensity of the pulsed red light is all 40mW/cm$^2$ in left panel (A), while the pulse width is all 1ms in right panel (B).

To evaluate the effect of the parameters of optical pulse on the evoked neural response in primary visual cortex, the characteristics of the OEPs were further examined by varying stimulus intensity and pulse width. The Fig.3 showed the OEPs resulted from varied pulse width (A, left panel) and intensity (B, right panel) of optical stimulation. It could be observed that, the amplitude of the negative wave (N1) and its peak latency increased with the pulse durations. However, the power of optical pulse affects the OEPs in different trends; the amplitude of N1 and latency decrease with the increase of the stimulus intensity.

Compared to the base-line neural activities (bottom panel in Fig.3.), stimulation of optical pulse to primary visual cortex induced event-related neural response. Unlike the electrical stimulation of visual cortex, the OEPs prolong for

hundreds milliseconds, whereas the neural response of electrical pulse is about 10ms [4]. The possible reason relies on the different mechanisms, the current injection of electrical stimulation lead short term neural activation by activation of voltage-gated ion channels of neurons abruptly [1], but the optical stimulation needs to create a temporally and spatially mediated temperature gradient to activate the neurons [9]. The effects of pulse duration and stimulation intensity on neural response were explored in vestibular [18] and thalamocortical brain slices [17], the latency and amplitude of N1 varied with pulse duration and stimulation intensity may manifest the optical-induced inhibition [17].

## IV. SUMMARY

As an extension of Infrared neural stimulation (INS), our work showed that the neurons in visual cortex can be activated with a pulsed stimulation of visible 620-nm LED-light, and different intensities of pulsed red light induced different neural responses in primary visual cortex.

To our knowledge, this is the first attempt to use pulsed 620-nm LED light stimulating the primary visual cortex. The preliminary experiment showed that the neural activities can be modulated by the local stimulation of pulsed red light. Since the Infrared light was employed to stimulate the neural tissue by Well in 2005 [7], the optical neural stimulation has been an attractive research field. However, only the near infrared [6]-[11] or mid-infrared [17] was selected as the light source by the transient deposition of infrared energy into neural tissue, and the visible light (e.g. red light) has never been accessed. Our work indicated that, beyond infrared light, pulsed visible light can be a potential stimulus to activate the neuron. Because of the shorter wavelength, the proposed red light can stimulate the neural tissue with more spatial resolution than infrared.

Currently, the optical neural stimulation of infrared laser has been extensively studied in the sciatic nerve [6]-[9] and auditory nerve [11]-[15]. For the central nervous system (CNS), mid-infrared with the wavelength of 2.5-5.3 μm evoked neural response in thalamocortical brain slices [17], whereas near infrared with wavelength of 1.875-1.94 μm evoked inhibitory responses in rat somatosensory [16]. Our experiment put further light on the optical neural stimulation, which revealed that the pulsed stimulation of visible red light can modulate the neural activities in visual cortex. Compared to PNS, CNS owns different geometry, physiology, and more complex neuronal networks. Although the optical stimulus to CNS tissue will activate a pool of neurons rather than the axon of neuron in PNS, the latest reports [16]-[17] and present work indicated that the transient energy of infrared or red light can be absorbed by neuron and induce neural responses. However, the mechanism behind the optical energy and the change of the transmembrane potential of neurons need to be investigated.

## ACKNOWLEDGMENT

This work was supported by the National High Technology and Development Program of China (863 Program) (Vo. 2007AA04Z324) and by the Nature Science Foundation of China Grant (No. NSFC31070882). The authors would like to thank Nan Xia for providing assistance.

## REFERENCES

[1] C. Huang, "Characterization of voltage-gated sodium channel blockers by electrical stimulation and fluorescence detection of membrane potential," *Nat. Biotechnology*, vol. 24, pp. 439-446, 2006.

[2] M. Tinazzi, S. Zarattini, M. Valeriani, C. Stanzani, G. Moretto, N. Smania, et al., "Effects of transcutaneous electrical nerve stimulation on motor cortex excitability in writer's cramp: neurophysiological and clinical correlations," *Mov Disord.*, Vol. 21, no. 11, pp. 1908-1913, 2006.

[3] D. C. Bradley, P. R. Troyk, J. A. Berg, M. Bak, S. Cogan, R. Erickson, et al., "Visuotopic mapping through a multichannel stimulating implant in primate V1," *J. Neurophysiol*., vol. 93, pp. 1659-1670, 2005.

[4] D. K. Chelvanayagam, R. M. Vickery, M. T. K. Kirkcaldie, M. T. Coroneo, J. WMorley, "Multichannel surface recordings on the visual cortex: implications for a neuroprosthesis," *J. Neural. Eng.*, vol. 5, pp. 125–132,2008..

[5] F. G. Zeng, S. Rebscher, W. Harrison, X. A. Sun, and H. H. Feng, "Cochlear Implants: System Design, Integration, and Evaluation," *IEEE Reviews in Biomedical Engineering*, vol. 1, pp. 115-148, Dec. 2008.

[6] J. Wells, P. Konrad, C. Kao, E. D. Jansen, and A. Mahadevan-Jansen, "Pulsed laser versus electrical energy for peripheral nerve stimulation," *Journal of Neuroscience Methods*, vol.163, pp. 326-337, 2007.

[7] J. Wells, C. Kao, K. Mariappan, J. Albea, E. D. Jansen, P. Konrad, and A. Mahadevan-Jansen, "Optical stimulation of neural tissue in vivo," *Opt. Lett.*, vol. 31, pp. 235-238, 2005.

[8] J. D. Wells, S. Thomsen, P. Whitaker, E. D. Jansen, C. C. Kao, P. E. Konrad, et al., "Optically Mediated Nerve Stimulation: Identification of Injury Thresholds," *Lasers in Surgery and Medicine*, vol. 39, pp. 513-526, 2007.

[9] J.Wells, C. Kao, P. Konrad, T.Milner, J. Kim, A.Mahadevan-Jansen, E. D. Jansen, "Biophysical mechanisms of transient optical stimulation of peripheral nerve," *J. Biophys*..vol. 93, pp. 2567–2580, 2007.

[10] I. U. Teudt, A. E. Nevel, A. D. Izzo, J. T. Walsh, Jr, and C. P. Richter, "Optical Stimulation of the Facial Nerve: A New Monitoring Technique," *Laryngoscope*, vol. 117, pp. 1641-1647, 2007.

[11] C. P. Richter, R. Bayon, A. D. Izzo, M. Otting, E. Suh, S. Goyal, et al., "Optical stimulation of auditory neurons: Effects of acute and chronic deafening," *Hearing Research*, vol. 242, pp. 42-51, 2008.

[12] A. D. Izzo, J. T. Walsh Jr., E. D. Jansen, M. Bendett, J. Webb, H. Ralph, et al., "Optical Parameter Variability in Laser Nerve Stimulation: A Study of Pulse Duration, Repetition Rate, and Wavelength," *IEEE Transactions on Biomedical Engineering*, vol. 54, no. 6, pp. 1108-1114, 2007.

[13] A. D. Izzzo, C. P. Richter, E. D. Jansen, and J. T. Walsh Jr., "Laser Stimulation of the Auditory Nerve," *Laser in Surgery and Medicine*, vol. 38, pp. 745-753, 2006.

[14] A. D. Izzo, J. T. Walsh Jr., H. Ralph, J. Webb, M. Bendett, J. Wells, et al., "Laser Stimulation of Auditory Neurons: Effect of Shorter Pulse Duration and Penetration Depth," *Biophysical Journal*, vol. 94, pp. 3159-3166, 2008.

[15] A. D. Izzo, E. Suh, J. Pathria, J. T. Walsh Jr., D. S. Whitlon, and C. P. Richter, "Selectivity of neural stimulation in the auditory system: a comparison of optic and electric stimuli," *Journal of Biomedical Optics*, vol. 12, no. 2, pp. 1-7, 2007.

[16] J. M. Cayce, R. M Friedman., A. W. Roe, P. E. Konrad, E. D. Jansen, and A. Mahadevan-Jansen, "Relating Optical Signals Induced by Infrared Neural Stimulation to Electrophysiology," in *2010 Biomedical Science and Engineering Conference - Biomedical Research and Analysis in Neuroscience (BRAiN)*, Oakridge, TN, 2010.

[17] J. M. Cayce, C. C. Kao, J. D. Malphrus, P. E. Konrad, A. Mahadevan-Jansen, and E. D. Jansen, "Infrared Neural Stimulation of Thalamocortical Brain Slices," *IEEE Joural of Selected Topics in Quantum Electronics*, vol. 16, no. 3, pp. 565-572, 2010.

[18] D. M. Harris, S. M. Bierer, J. D. Wells, J. O. Phillips, "Optical nerve stimulation for a vestibular prosthesis," *in conference on Pphotons and Neurons*, San Jose CA, 2009.