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Optogenetics: Optical Methods for Cellular Control

Samarendra K. Mohanty
Nitish V. Thakor
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Anna W. Roe, Vanderbilt University (United States)

Introduction

By combining genetic and optical methods, "optogenetics" has allowed control (stimulation or silencing) of electrically activatable, genetically targeted cells with high temporal precision. This has heavily impacted neuroscience research by allowing dissection of neuronal circuitry function. Since its first in-vivo demonstration, optogenetics technology has been applied to freely moving mammals and could eventually form the basis for vision restoration, psychiatric treatment and pain control. Optogenetic technology is also impacting other biomedical research areas such as control of cardiac function, stem cell differentiation and reprogramming of metabolic activities in mammalian cells. Topics of interest for this conference included new therapeutic applications, including control of central and peripheral nervous system, cardiac system, as well as control of metabolic activities of cancer cells. In these therapeutic settings, optics is playing a crucial role in both delivering light for cellular control, and, in some cases, for imaging the consequences of this control.

The conference was divided into five major sessions, namely (1) Optogenetics: Technology, (2) In-vivo Optogenetics, (3) Cellular optogenetics, (4) Hybrid Optical control of cells-I, and (5) Hybrid Optical control of cells-II, along with the poster session. Prof. Karl Deisseroth (Stanford University) described advancement of optogenetics technology and applications carried out in his laboratory as part of the opening keynote lecture. Prof. George Augustine (KIST and Duke) presented an invited talk on the use of optogentics in probing functioning of specific neuronal circuitry in a high-throughput manner. Use of combinatorial optogenetic approach to understand the functioning of medial habenula, as well as theta and gamma oscillations from cerebellum and pre-frontal cortex respectively, was presented by several researchers. The second keynote lecture by Prof. Ernst Bamberg (Max Planck Institute) was related to advancement in the development of optogenetics probes, their characterization, and applications. He also gave a lecture titled "Optogenetics and Hybrid Optical control of cells" as part of BiOS Hot Topics. Prof. Richard Kramer (UC Berkeley) gave the third Keynote lecture on photochemical tools for manipulation of endogenous ion channels and neuronal firing for applications in pain inhibition and vision restoration.

Optical microscopy, spectroscopy, and imaging techniques hold significant promise for characterizing optogenetic probes and the invited talk by Prof. Klaus Gerwert (Ruhr-Univ. Bochum) precisely highlighted the use of FTIR in understanding the functioning of light-activated proteins. While use of crystallography and spectroscopic methods will enhance the understanding of the interaction processes between light and optogenetic molecules, a detailed understanding of tissue optics is essential for delivery of stimulation light. Innovative schemes for delivery and control of light irradiation, including miniaturized light sources, fiber optics, waveguides and special beams can potentially improve optogenetic therapy. In-vivo optical stimulation and electrical read-out from neural circuits in non-human primates and rodents by chronically implanted devices was presented. The invited talk by Prof. Arto Nurmikko (Brown University), as well as other talks (e.g. micro-LED array

and Bessel beam), depicted the role of nanophotonics and understanding of tissue optics in successful implementation of optogenetic technologies. Development of optics with micro-LED arrays, micro-mirror arrays and glass-optrode arrays were presented for stimulation of cells with high spatial resolution. The use of micro-LED arrays on flexible substrates was demonstrated for optical cochlear implants. Optogenetic stimulation of the auditory nerve for cochlear implants provides increased number of frequency channels and dynamic range.

The introduction of non-linear optics has further allowed very precise and in-depth spatial control of optogenetic stimulation. The talks on in-vivo near-infrared stimulation and use of two-photon for precise activation were presented highlighting the better penetration depth and functional mapping of neural circuitry. Though fiber optic and waveguide technology is enabling delivery of light to targeted tissue regions, other photonic imaging technologies have the potential to significantly contribute to imaging read-outs of neural/cellular activities during optogenetic stimulation. Interesting talks on label-free speckle imaging and quantitative phase imaging, as well as bioluminescence and calcium-fluorescence imaging were presented as non-invasive optical modalities for detection of optogenetically activated processes. These optical readout methods can provide complementary information to electrical recordings for better evaluation of the physiological changes in the whole tissue-system during optogenetic stimulation. Further, a new multifractal detrended fluctuation analysis method was presented for monitoring optogenetic modulation of neural activity.

Notably, several talks on other emerging hybrid optical technologies, such as optomechanical, photothermal, optoelectronic, and photochemical modulation of cells, were presented. In one of the talks, application of light with genetic manipulations in cells was used to target spatial regulation of actin-regulating proteins in dendritic spines to intervene Alzheimer's disease. Photothermal, as well as optofluidic control of cells, especially axonal guidance was also presented. While looking forward, we believe applications of optogenetic and other hybrid-optical modulation of cells will have wide-variety of biomedical applications including neural modulation for restoration of audio-visual systems, and inhibition of pain and psychiatric disorders, to name a few. Therefore, one-to-one interaction and dialogue between optical engineers, molecular biologists and medicos is required in a platform such as this conference.

While molecular biology researchers will continue to engineer more efficient opsins having unique temporal, functional, and spectral characteristics, there is also a need to develop new molecular probes for imaging cellular activation. With development of near-infrared light controllable proteins, cellular systems can be modulated in a minimally invasive manner. While lasers have been used to deliver genes (encoding for the opsins) to targeted cells/tissue by a process called optoporation, and for monitoring expression of marker fluorescent proteins (and opsins) in a minimally invasive manner, new optical methods are emerging to control the expression of genes-of-interest. For the optics community, there is a big opportunity, as well as challenge, to first deliver the light efficiently to tissues of interest, and also to develop and/or implement functional optical imaging methods for high-throughput detection of cellular stimulation. The role of the

photonics industry in developing novel source and imaging platforms for stimulation and detection will be crucial for the successful development of this area.

We hope that reading the articles provided in this volume will convey the knowledge and excitement of the first annual Optogenetics and Hybrid Optical control of cells conference. We look forward to your participation as authors and presenters in this conference next year. Besides the travel support provided by SPIE to selected students, we are proud to announce that travel grants will be available to support graduate and under-graduate students who are first authors, provide oral or poster presentations for this conference, and submit the full paper to the proceedings. We believe that we will be able to support a large number of students next year with support from the sponsors.

We would like to thank BiOS symposium chairs Prof. Rox Anderson (Harvard) and Prof. Jim Fujimoto (MIT) for allowing us to organize the first conference on Optogenetics and Hybrid Optical control of cells as part of the BiOS symposium during Photonics West 2013. We would also like to thank Prof. Anna Roe (Vanderbilt University), Prof. Elizabeth Hillman (Columbia University), Prof. George Augustine (KIST and Duke University), Dr. Isaac Clements (Plexon Inc.), Prof. John Welsh (University of Washington-Seattle), Prof. Rafael Yuste (Columbia University), Prof. Richard Kramer (UC Berkeley), Prof. Xue Han (Boston University), Prof. Klaus Gerwert (Ruhr-Univ. Bochum), Prof. Alfred L. Nuttall (Oregon Health & Science Univ) for their valuable input as members of the Program Committee. We would like to thank all keynote and invited speakers, session chairs, and participants for their important contributions. We would like to thank our sponsors, SPIE and Plexon Inc. (Mr. Harvey Wiggins) for their support.

Samarendra K. Mohanty
Nitish V. Thakor