Optogenetics

Optogenetics is a biological technique which involves the use of light to control cells in living tissue, typically neurons, that have been genetically modified to express light-sensitive ion channels. It is a neuromodulation method employed in neuroscience that uses a combination of techniques from optics and genetics to control and monitor the activities of individual neurons in living tissue—even within freely-moving animals—and to precisely measure the effects of those manipulations in real-time.

The key reagents used in optogenetics are light-sensitive proteins. Neuronal control is achieved using optogenetic actuators like channelrhodopsin, halorhodopsin, and archaerhodopsin, while optical recording of neuronal activities can be made with the help of optogenetic sensors for calcium (GCaMP), vesicular release (synaptopHluorin), neurotransmitter (GluSnFRs), or membrane voltage (Arclightning, ASAP1).

Control or recording is confined to genetically defined neurons and performed in a spatiotemporally precise manner by light.

The earliest approaches for optogenetic control were developed and applied by Boris Zemelman and Gero Miesenböck, at the Sloan-Kettering Cancer Center in New York City, and Dirk Trauner, Richard Kramer and Ehud Isacoff at the University of California, Berkeley; these methods conferred light sensitivity but were never reported to be useful by other laboratories due to the multiple components these approaches required. A distinct single-component approach involving microbial opsin genes introduced in 2005 turned out to be widely applied, as described below. Optogenetics is known for the high spatial and temporal resolution that it provides in altering the activity of specific types of neurons to control a subject's behaviour.

In 2010, optogenetics was chosen as the “Method of the Year” across all fields of science and engineering by the interdisciplinary research journal Nature Methods. At the same time, optogenetics was highlighted in the article on “Breakthroughs of the Decade” in the academic research journal Science.

Wireless optogenetics based on the photon upconversion technique has recently provided an effective and interference-free alternative for remote brain stimulation and inhibition in behaving animals, which is of great promise for neuroscience research. However, more versatile upconversion devices are yet to be implemented for neural tissues other than the brain. In this study, a flexible and fully implantable upconversion device was developed for epidural spinal cord stimulation. The upconversion device was fabricated via a straightforward, two-step, heat-pulling process using biocompatible thermoplastic polypropylene as a backbone, which is mixed with upconversion nanoparticles (UCNPs) to form a flexible optrode device that converts near-infrared (NIR) irradiation to visible light for the optogenetic manipulation of spinal cord tissues. In this system, the flexible upconversion device is fully implantable within the rigid spine structure and shows excellent long-term biocompatibility even after a four-month experiment. In anesthetized mice, the UCNP device implanted at the L4 vertebra can be used to reliably evoke hindlimb muscular activity upon NIR triggering. In behaving mice, neural modulation by the same UCNP devices effectively inhibits the animals' movement as a result of remote spinal cord stimulation. We believe that the flexible upconversion device provides new possibilities for wireless neural modulation in spinal cord tissues, and will become a valuable supplement to the current toolsets of upconversion based wireless

optogenetics [1].

Optogenetics provide a potential alternative approach to the treatment of chronic pain, in which complex pathology often hampers efficacy of standard pharmacological approaches. Technological advancements in the development of thin, wireless, and mechanically flexible optoelectronic implants offer new routes to control the activity of subsets of neurons and nerve fibers in vivo. This study reports a novel and advanced design of battery-free, flexible, and lightweight devices equipped with one or two miniaturized LEDs, which can be individually controlled in real-time. Two proof-of-concept experiments in mice demonstrate the feasibility of these devices. First, we show that blue-light devices implanted on top of the lumbar spinal cord can excite channelrhodopsin expressing nociceptors to induce place aversion. Second, we show that nocifensive withdrawal responses can be suppressed by green-light optogenetic (Archaerhodopsin-mediated) inhibition of action potential propagation along the sciatic nerve. One salient feature of these devices is that they can be operated via modern tablets and smartphones without bulky and complex lab instrumentation. In addition to the optical stimulation, the design enables the simultaneously wireless recording of the temperature in proximity of the stimulation area. As such, these devices are primed for translation to human patients with implications in the treatment of neurological and psychiatric conditions far beyond chronic pain syndromes [2].

Fifteen rats received injections of engineered AAV with NpHR-YFP gene into the substantia nigra. They were then subjected to illumination of 590-nm light wavelengths with 3 optical stimulation conditions, i.e., frequency-width: 5 Hz-10 ms (n = 5), 5 Hz-100 ms (n = 5), and 50 Hz-10 ms (n = 5). Eleven rats received 6-hydroxydopamine injections to establish the conventional PD model.

The optogenetic models showed characteristic PD manifestations, similar to those of the conventional models; the severity of forelimb akinesia correlated with the total illumination value (frequency × width). The group with a low illumination value (5 Hz-10 ms) was comparable to the conventional partial model whereas the groups with high illumination values (5 Hz-100 ms and 50 Hz-10 ms) were similar to the conventional complete model.

An optogenetic PD model has the advantage of more appropriately representing various PD stages by controlling illumination parameters [3].

Optogenetics makes possible highly precise spatial and temporal control of specific neuronal populations. This technique has already provided several new insights relevant to clinical neuroscience, from the physiological substrate of functional magnetic resonance imaging to the mechanism of deep brain stimulation in Parkinson's disease. The increased precision of optogenetic techniques also raises the possibility of eventual human use. Translational efforts have begun in primates, with success reported from multiple labs in rhesus macaques. These developments will remain of ongoing interest to neurologists and neurosurgeons [4].

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