HIJACKING THE BRAIN

BY YIZHEN ZHANG

EXPLORING THE BACKGROUND AND IMPACTS OF OPTOGENETICS

You're using light at the moment to read this. I am using light to write this. Although we use light on an everyday basis, we often take it for granted and do not fully appreciate its power. As a matter of fact, light can control the brain.

Optogenetics is a new hot biotech technique that uses light to control cells in living tissue, usually neurons. Neurons are cells that process and transmit chemical or electrical signals. As its name implies, optogenetics is a combination of optics and genetics. The technique is composed of three major steps. The first step is genetically modifying neurons to become responsive to light. A light source is then implanted to turn neurons "on and off," correlating it with behavioral or physiological changes. The last part, which is occasionally skipped, is recording the brain's resulting electrical activity. These intricate yet invasive procedures have limited optogenetics to animal models only.

Despite the current limitation on recipients, there is no limit on potential applications. Optogenetics has been highlighted as a "Breakthrough of the Decade" and "Method of the Year" by renowned scientific journals such as Science and Nature, respectively. Thus far, optogenetics has been used to directly treat diseases and to better understand the neuroscience.

The concept for optogenetics was first conceived in the 1970s when Francis Crick, also co-discoverer of the structure of DNA, noted that cell stimuli cannot distinguish cell types1. Therefore, a stimulus must be precise enough to control the activity of one cell type. Crick later casually speculated that light could potentially be a tool for this. A few years before this, the basis for the tool, initially unrelated, was identified—bacteriorhodopsin, a light sensitive microbial protein that captures light energy and converts it to chemical energy that stimulates the cell. This discovery soon led to the identification of channelrhodopsin, which is the protein commonly used now for optogenetics. However, it took decades for neuroscientists to link these two concepts. Only in the summer of 2005 the insertion of channelrhodopsin gene into mammalian neurons was reported.

The full potential of optogenetics is still being discovered. The applications seem to be limitless and can only be bound by ethics. Most application has been used to treat diseases including Parkinson's disease, addiction, depression, and many more. The basis of these relies on 'hijacking' specific neuronal circuits that are genetically modified to have the light sensitive protein, like channelrhodopsin. These neurons are then selectively controlled by a laser to activate specific regions of the brain or body. It is almost like a light switch but

> "..the idea of controlling the brain with light moves away from fantasy."

reversed. Light can turn the switch on or off which leads to a behavioral or physiological change.

Beyond application, the use of optogenetics also sheds significant light on basic research and understanding the functions of neurons in our body. One particular research at New York University has been able to help clarify how the hippocampus, part of the brain responsible for long term memory, works.2 Prior, the function of the hippocampus had been identified for a long time but linking it to the structure of circuits has been weak. Optogenetics allowed the researchers to better understand which other brain regions responded to an activation or inactivation of the hippocampus. Parallel research is performed to better understand other portions of the brain, muscles, and stem cells.

The primary drawback of optogenetics is the genetic mutation part. It has been found that not all desired cells may express the light sensitive protein gene, thus not representing the full functions. At the same time, these genetic mutations have also been known to accidentally alter undesired cells. This technique, nevertheless, is still relatively young and more research is required.

This technique seems like it came straight out of a science fiction story, and the possibilities are truly endless. The current advancements in neuroscience and genetics are promoting the development of optogenetics at an increasingly faster rate. The full realm of possibilities is becoming clearer as the idea of controlling the brain with light moves away from fantasy.

1. Crick, F.H. (1979). Thinking about the brain. Sci. Am. 241, 219-232
2. Suzuki, W., & Naya, Y. (2011). Two Routes for Remembering the Past. Cell,147(3), 493-495. doi:10.1016/j.cell.2011.10.005
3. Ferenczi, E., & Deisseroth, K. (2016). Illuminating next-generation brain therapies. Nature Neuroscience, 19(3), 414-416. doi:10.1038/nn.4232
4. Yizhar O, Fenno LE, Davidson TJ, Mogri M, Deisseroth K. Optogenetics in neural systems. Neuron. 2011 Jul 14;71(1):9-34. doi: 10.1016/j.neuron.2011.06.004. PubMed PMID: 21745635.
5. Cho, Y. K., & Li, D. (2016). Optogenetics: Basic Concepts and Their Development. Methods in Molecular Biology Optogenetics, 1-17. doi:10.1007/978-1-4939-3512-3_1