Light in Biology: From Fundamental Life-Giver to Brain-Modulator

Theresa Lückner[1]
Department of Systems Physiology of Learning, Leibniz-Institute for Neurobiology, Magdeburg, Germany

Photosynthesis: The Fundament of Life on Earth

When relating light to biology, the first thing that pops into one's mind is photosynthesis. The sunlight shines onto the leaves, photons excite the light-sensitive molecule chlorophyll and with the use of several cascades, nature produces carbohydrates and oxygen out of carbon dioxide and water. The usage of light is the fundament of eukaryotic life on earth and there is only little life that can exist without it. Even life in the deep sea relies on organic sediments produced by photosynthesis in upper sea levels.[1] The oxygen produced by photosynthesis is used in aerobic metabolic pathways and the produced carbohydrates make up the basis of the food chain with animals on the top of it.

The Visual System – Sensing Light

Animals do not only benefit from the supply of nutrients and oxygen, but also have several light-sensitive systems. The most obvious one is the visual system. In vertebrates, the photons affect the protein opsin which is coupled to the molecule retinal located in the photoreceptors of the retina. Subsequent events generate signals to the brain relaying information about color, contrast, object movement and shapes.[2] Vision is considered to be the most dominant sense in humans and without light, sighted people would surely miss seeing the beauty of a sunset, the colorful Times Square or the face of our loved ones.

Light Influencing Wakefulness and Mood

In addition to the photoreceptors, there are light-sensitive cells in the retina containing melanopsin whose activity does not yield information relevant for vision. These cells send signals to brain nuclei, such as the suprachiasmatic nuclei, to maintain the circadian rhythm. On this basis, the release of e.g. the hormone melatonin and the neuropeptide orexin is synchronized.[3] Both substances influence wakefulness in humans. Humans frequently experience the importance of the balance provided by the circadian rhythm upon disharmonizing it while on long-distance flights, commonly known as jet lag.[4] However, not only the circadian rhythm relies on the regular presence and absence of light. A specific form of depression is predominantly found in northern countries that characteristically have long and dark winters or even polar nights. Seasonal depression is expressed in wintry bad mood and negative habit changes. So we should not wonder why we are less happy during winter and there even is a tendency that the suicide rate increases in the winter months, especially in Scandinavian countries.[5]

Applying Light to the Brain

All the above-mentioned systems demonstrate that light is fundamentally important for life on Earth and especially for humans. Our visual system and our brain are naturally influenced by photons and their absence makes our life colorless, sleepy and sad. However, this is not the end of the story. Late developments in neuroscience demonstrate that what we know about the fundamental mechanisms of how light is used in biology can be applied to further study the function of the brain by shining light on it.

It has been known before that there are certain algal proteins that are light-sensitive but do not contribute to photosynthesis. Primarily, these are light-gated ion channels that enable the organism to orient and to move towards light by creating photocurrents (i.e. electrical currents induced by photons).[6] In the beginning of the 21st century, the structure of these channels was artificially modified and reconstructed in order to integrate them into other organisms. In the brain, they were firstly used in flies and the roundworm *Caenorhabditis elegans*. They were genetically expressed in dopaminergic cells and light was shone onto these animals. As a result, their behavior changed in response to light stimulation, just as if someone had switched the light on in this brain region.[7,8] Not long after, the first successful experiments in mammals were reported.[9] Specific brain cells were transduced with light-gated ion-channels and their stimulation induced activity in the region's neurons. So, how does this magic work?

The most frequently used light-gated ion-channel is channelrhodopsin. Just like in the photoreceptors of the eye, the light-sensitive molecule is retinal and it is coupled to a 7-transmembrane protein. Without light of a channel-

[1] e-mail: tlueckne@lin-magdeburg.de

typical wavelength, the channel is closed but once it is stimulated, the channel opens for cations.[10] In neurons, the most relevant ones are sodium, potassium and calcium ions and protons. Once a cation channel is opened, the sodium-influx into and the potassium-efflux out of the cell results in electrical currents. These currents are signals that are passed on to other neurons. Once channelrhodopsin is integrated into neurons, the experimenter can decide when and where these processes occur.

Beforehand, it has been possible to arbitrarily manipulate neurons using electrical currents. The novelty using the light technique is, that it can be specified which cells are supposed to respond to stimulation. Using electrodes, all cells in the vicinity could basically respond to an electrical stimulus.[11] However, if only specific cells are equipped with a light-sensitive cation channel, selective stimulation can be achieved. So how is specificity in cells determined? In genetics! Every cell type has its very own cluster of expressed genes. The developments of modern genetics allow using cell-type-specific genetic promotors to express genes that have been smuggled into the cell. Hence, the channelrhodopsin lying on a DNA plasmid contains a special code that can only be read in cells that have the encryption key. Because the light technique uses optics and genetics, it was termed optogenetics.

In the past years, this method has been used to study the function of specific cell populations in the brain and the neurotransmitter systems. Furthermore, it is possible that optogenetics can be applied to recover vision[12] or to treat neurological diseases such as Parkinson's disease[13] and epilepsy.[14] However, to accomplish clinical application, some open questions need to be answered. For example, more research has to be conducted on the method itself and light delivery. All in all, the importance of light for our life in general and for our well-being in particular is very prominent. Light is fundamentally necessary. More and more applications arise that make use of light, such as optogenetics. Still, we might not yet be at the tip of the iceberg when it comes to exploring the full potential that light has to offer in biology.

References

[1] T. Fenchel, *Annu. Rev. Ecol. Evol. Syst.* **1988**, *19*, 19–38.

[2] J. T. McIlwain, *An Introduction to the Biology of Vision*, Cambridge University Press, Cambridge - New York - Melbourne, **1996**.

[3] P. Fuller, J. Gooley, C. Saper, *J. Biol. Rhythms* **2006**, *21*, 482–493.

[4] J. Waterhouse, T. Reilly, G. Atkinson, *Lancet* **1997**, *350 (9091)*, 1611–1616.

[5] H. Hakko, P. Räsänen, J. Tiihonen, *J. Affect. Disord.* **1998**, *50*, 49–54.

[6] K. Foster, R. Smyth, *Microbiol. Rev.* **1980**, *44*, 572–630.

[7] S. Lima, G. Misenböck, *Cell* **2005**, *121*, 141–152.

[8] G. Nagel, M. Brauner, J. Liewald, N. Adeishvili, E. Bamberg, A. Gottschalk, *Curr. Biol.* **2005**, *15*, 2279–2284.

[9] E. Boyden, F. Zhang, E. Bamberg, K. Deisseroth, *Nature Neurosci.* **2005**, *8*, 1263–1268.

[10] G. Nagel, T. Szellas, W. Huhn, S. Kateriya, N. Adeishvili, P. Berthold, D. Ollig, P. Hegemann, E. Bamberg, *Proc. Natl. Acad. Sci.* **2003**, *100*, 13940–13945.

[11] J. Ranck, *Brain Res.* **1975**, *98*, 417–440.

[12] V. Busskamp, B. Roska, *Curr. Opin. Neurobiol.* **2011**, *21*, 942–946.

[13] V. Gradinaru, M. Mogri, K. Thompson, H. Henderson, K. Deisseroth, *Science* **2009**, *324*, 354–359.

[14] J. Tønnesen, A. Sørensen, K. Deisseroth, C. Lundberg, M. Kokaia, *Proc. Natl. Acad. Sci.* **2009**, *106*, 12162–12167.