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Illuminating the brain for Nobel: a brief journey of optogenetics

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Read about discovery of light-activated molecular switches that have provided the much-needed tools for taking neuroscience and biology research to the next level.

This year's Nobel Prize in Physiology or Medicine started with the discovery of a special light-sensing protein and engineered it into a tool that has moved our understanding of our own brain and biology by leaps and bounds. On 10 December 2026, Karl Deisseroth, Peter Hegemann and Georg Nagel will be presented with the most prestigious award in science for their development of optogenetics.[1] As they are preparing for their flight to Stockholm, we get to learn more about what it means to use light as a switch for cells.

Opsin: the light-sensing protein

Light is all around us, and sometimes we forget how cool it is that we can detect it. The retina in our eyes is filled with cells that are activated in response to light, aptly called photoreceptor cells. Photoreceptor cells can do this because their cell membranes have special proteins called opsins. When hit by light, an opsin protein changes its shape and triggers a chain reaction in a cell.[2] The chain reaction causes the cell to generate an electrical signal, which is sent to the brain, *et voilà* – you can read this article.

Being fascinated by their ability to change shape in response to light, scientists have been studying opsins since the 1970s. There are many different opsins found in nature.[3] In addition to our eyes, many unicellular organisms, such as bacteria and algae, have opsins, which they use to guide their movements in response to light or to produce energy. The details of cellular changes depend on the opsin type and the organism, but bacterial opsins share a basic mechanism with those in our eyes. Opsins change their shape in response to incident light, opening channels that let many charged particles enter the cell. Changes in the cell's electric potential signal it to move in a specific direction. The movement of charged particles can also be linked to the energy-producing reactions in the cell.[4,5] Nevertheless, the opsins found in these unicellular organisms differ from the opsins in our eye in a very fundamental way, which proved to be pivotal in the discovery of optogenetics.

From algae to neurons

In the 1990s, Peter Hegemann's team showed that opsins drive light-directed movement in *Chlamydomonas*, a unicellular alga (figure 1).[6] This specific opsin, called channelrhodopsin-2, is different from the ones found in our eyes.

Channelrhodopsin-2 is not only a light detector, but also a gate that opens in response to light. When light falls on the protein, it opens its channel and lets positively charged particles (protons or cations) into the cell. The change in concentration of electrically charged particles causes the cell to activate.[4,5] This reaction is very fast and precise, making it highly relevant for quick changes in response to light.
Following this discovery, Hegemann established a collaboration with Georg Nagel, who had experience in studying ion channels such as channelrhodopsins. Utilising the power of genetic engineering, Georg Nagel and his colleagues expressed channelrhodopsin-2 in frog egg cells and then in human kidney cells in the early 2000s.[7] These initial studies established that genetically engineered channelrhodopsins can indeed be expressed in other cell types, allowing scientists to develop a system that can change the cellular electric potential within milliseconds using light. Given that electrical signals are the basis of our brain function, these findings inspired Karl Deisseroth to develop the same system to work in neurons.

But why neurons?

Simply because we know very little about our brain. Neurons are the cells that transmit signals and process all the information inside our brains. The interaction between neurons is how we learn, feel, move and experience the world around us. For years, neuroscientists have tried to figure out the details of these interactions, but their understanding has remained vague because they did not have the tools to capture them.[8] Peeking into an active brain to look at a specific neuronal circuit is tricky because a lot is going on in the brain at the same time. To establish proof that specific neurons in a region cause specific behaviour, we need to observe the effect of rapidly activating and silencing them.
The challenge of activating neurons using an opsin from a completely different organism was a big one for Karl Diesseroth and his team.[9] After much trial and error, tweaking methods, and optimising the molecule itself, Karl and his colleagues were able to express channelrhodopsin-2 in neurons grown on a petri dish.[10] Their study showed that light-based modulation of channelrhodopsin-2 can activate neurons and

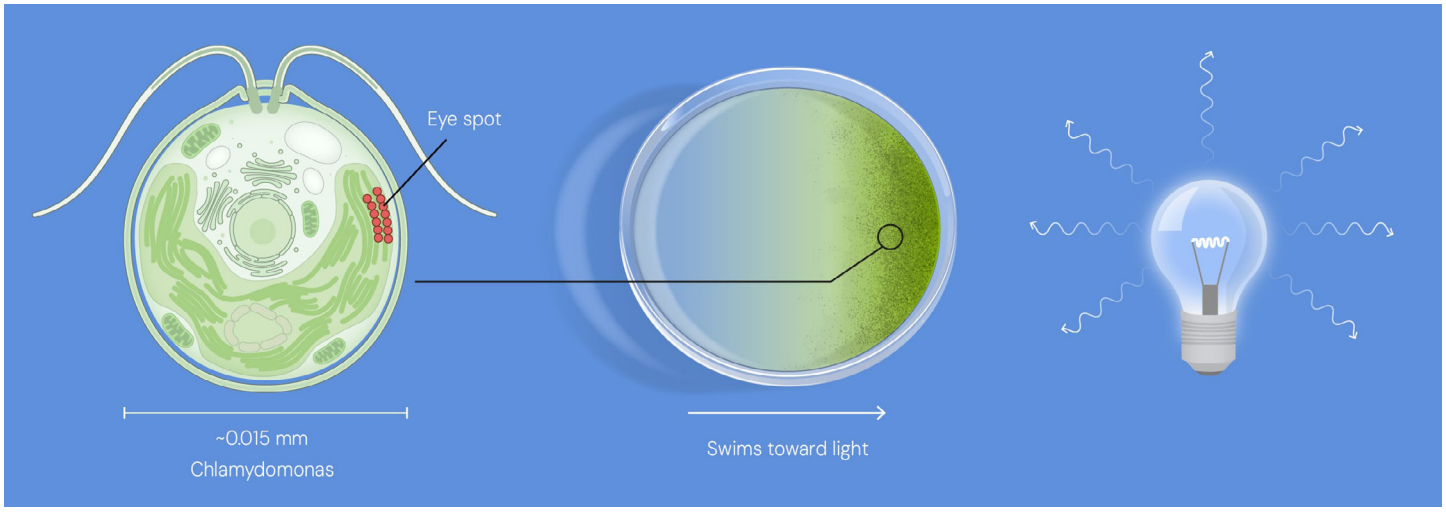


Figure 1: Light-directed movement in *Chlamydomonas*
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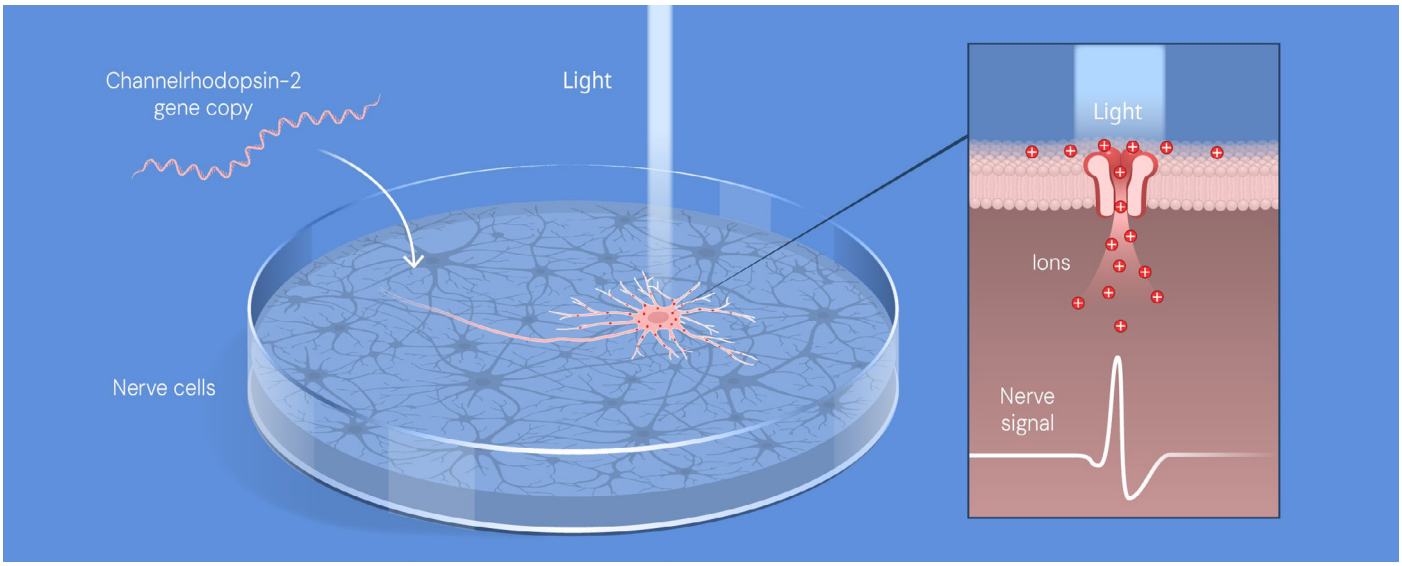


Figure 2: Neurons in a Petri dish expressing channelrhodopsin-2 are activated in response to light

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established the field of 'optogenetics', which uses genetically modified proteins that can be switched on or off using light to control cells (figure 2).

Eventually, many other neuroscientists around the world placed channelrhodopsin-2 in the neurons of different model organisms, including chickens,[11] worms[12] and flies,[13] to show that they could control specific behaviours in animals by switching neurons on and off with light (figure 3).

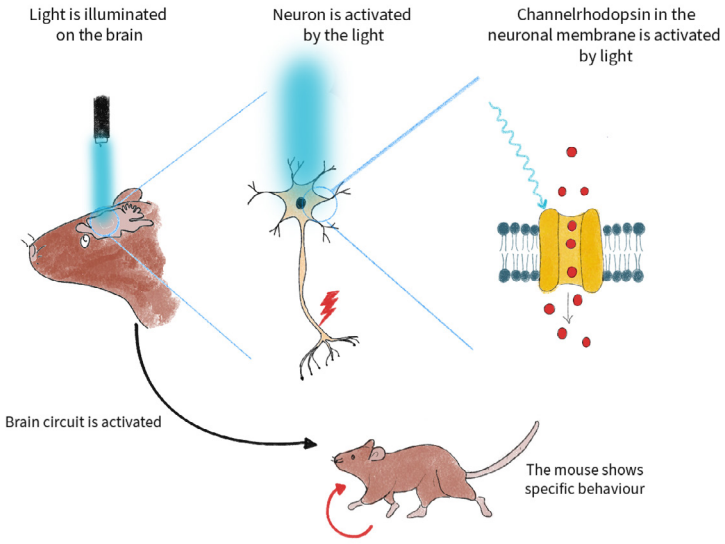


Figure 3: The illustration shoes optogenetics in a mouse model. The mouse is genetically engineered to express channelrhodopsin-2 in specific neurons. An optical fibre is inserted into the skull. The mouse behaves completely normally when the light is switched off. When the light is switched on, the channelrhodopsins open and the neurons expressing them depolarise. They activate the downstream neuronal circuit, and the mouse shows specific behaviour. When the light is switched off, the mouse resumes normal behaviour.

Image courtesy of the author, based on Ref. [19]

Scientists have also discovered and designed different variants of opsins to target specific types of neurons, brain regions and functions, enabling them to study these areas more effectively.[14–16] Within the first three years of inserting channelrhodopsin-2 into neurons, scientists began to unravel the neuronal mechanisms behind complex functions such as learning, sensations, sight, breathing and movement. These findings fed directly into the study of psychological disorders, including depression, schizophrenia and anxiety, as well as neurodegenerative disorders such as Parkinson's disease.[17]

Optogenetics beyond neuroscience

While neuroscience remains at the forefront of optogenetics, it has also benefited the study of heart muscle cells, advancing possible interventions for cardiac arrest and heart failure.[18] The ability to exert highly precise control at molecular-scale and at milliseconds rates allows optogenetics to be a multifaceted tool that is also used in immunology, metabolism, plant biology, development and cancer research.[19,20]

One of the biggest achievements in clinical application of optogenetics emerged in 2021. Optogenetics was used to partially restore vision for a patient with retinitis pigmentosa, an eye disease in which loss of light-sensing receptors can cause vision loss.[21] Within two decades, optogenetics went from briefly activating some neurons in a petri plate to restoring vision. This exemplifies how curiosity-driven interdisciplinary research forms the basis for advanced applications that can improve lives.[17]

Optogenetics is now moving towards the development of more precision, integration with newer genetic advancements such as the gene editing technique CRISPR and diversification of applications in plant biology, cancer research

and larger-scale clinical trials. The field also needs to overcome many challenges that are inherent in using light and genetics. In animal models, optogenetics can only be used for organs that can be penetrated by light, unless invasive surgery is involved. Moreover, the introduction of foreign proteins and genes can trigger immune responses and off target effects.[17] Yet we can rest assured that through the sheer desire to solve problems and answer fundamental questions, the field of optogenetics will keep moving forward.

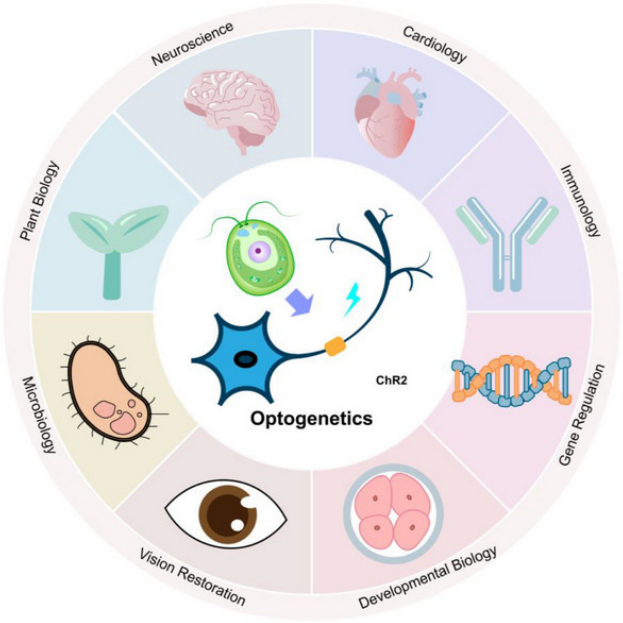


Image taken from Ref. [17]

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Resources

- Read this popular science article released by the Nobel Assembly for a brief explanation of optogenetics.
- Deep dive into the scientific background of optogenetics and the specific milestones in its discovery.
- Watch Edward Boyden, one of the pioneering scientists in the field of optogenetics and a professor at MIT, explanation on optogenetics.
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