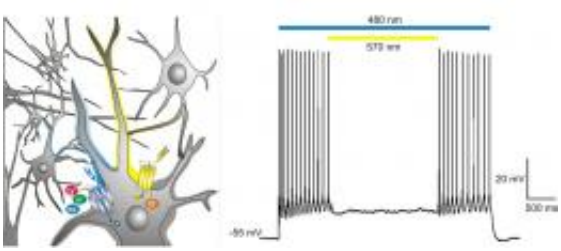
# Light switches for nerve cells

April 6 2010



Left: Schematic diagram of channelrhodopsin-2 and halorhodopsin in nerve cells. Right: Triggering of spikes by channelrhodopsin-2 (blue light) and their repression by halorhodopsin (yellow light) in cultivated hippocampus cells. Image: MPI of Biophysics

(PhysOrg.com) -- It sounds like a neurobiologist's dream: a light-switch that allows nerve cells to be switched on and off at will. Three scientists have found just such a light switch and are now being honoured for their work.

Ernst Bamberg, Director at the Max Planck Institute of Biophysics, Georg Nagel of the Würzburg University and Peter Hegemann of the Humboldt University Berlin have won this year's Wiley Prize for Biomedical Sciences for their discovery of the light-gated ion channel channelrhodopsin. The prize has been presented annually since 2001 for outstanding research in medicine and biosciences. The award ceremony is to take place on April 9th at Rockefeller University in New York.

The Wiley Prize jury is honouring the three researchers for their

discovery of channelrhodopsins, a family of light-activated ion channels. The use of these proteins has opened up new opportunities for investigating nerve cells and networks in culture, and also in the brain of live animals and has established the research field of optogenetics. Light can be used specifically to switch individual nerve cells or nerve networks on and off without electrodes. Apart from the importance of this discovery for basic research, in the future it might benefit patients with neurodegenerative diseases, such as macular degeneration, Parkinson's disease and epilepsy.

## Light switches nerve cells on and off

Channelrhodopsins are channel proteins in the cell membrane and occur in the eye spot of the green algae Chlamydomonas reinhardtii. They enable the algae to move towards or away from the light. When illuminated the proteins become permeable to positively charged ions. The ion flow through the open channels into the cells triggers an electric signal. The negative electric potentiall inside the cell becomes more positive, meaning that the cell is depolarized.and swiched on: the nerve begins to fire action potentials. Until this discovery in 2002 and 2003, naturally occurring light-activated ion channels were unknown. On the basis of this ground-breaking work, in collaboration with other laboratories the scientists succeeded ,to express these channels into nerve and muscle cells in culture and also in living animals. Again in collaboration with other scientists Bamberg and Nagel also managed to transfer the light-activated chloride pump halorhodopsin from salt loving bacteria nerve and muscle cells . After activation of the pump the potential is shifted towards more negative values, which leads to the inactivation of the cells, the firing of action potentials stops. This made it possible to switch cells on using blue light (absorption maximum of channelrhodopsin: 480 nm) and to switch off using yellow light (absorption maximum of halorhodopsin: 570 nm). By this not only cells in culture could be studied but also behaviour of the animals The

discovery of channelrhodopsins and its application together with halorhodopsin paved the way for the fast-moving field of optogenetics., which means worldwide many research groups are now successfully using optogenetic tools in different areas of neurobiological research.

The story of the discovery of light-activated ion channels is one example of how basic research can give rise to new techniques and treatments for humans. These channels open up a large potential for applications. "Optogenetics is currently revolutionizing neuro- and cell-biological research," explains Ernst Bamberg. "Now for the first time, without electrodes or any chemical modification, we can easily use light to control the activity of neurons and muscle cells, reliably and with a high spatial resolution that has never been achieved before."

Optogenetics could also produce medical benefits in the future. In 2006 and 2008 for instance, Swiss and US researchers enabled mice to recover from blindness. They injected channelrhodopsin into nerve cells in the retina of mice with a genetic defect that prevented the development of photoreceptor cells. Following this treatment, the animals were able to distinguish between light and dark. Scientists hope that patients with a eye disease - macular degeneration - will also regain at least partial vision as a result of gene therapy based on channelrhodopsins. Possibly optogenetic methods could also be used to treat neurodegenerative diseases in the brain. For example, nerve cells in the brain of patients with epilepsy or Parkinson's could be "switched on or off" as necessary in a controlled manner using light conducting glass fibres, in order to eliminate the corresponding symptoms of the disease.

**More information:** Publications:

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Nagel, G., M. Brauner, J.F. Liewald, N. Adeishvili, E. Bamberg, A. Gottschalk, Light-activation of Channelrhodopsin-2 in excitable cells of Caenorhabditis elegans triggers rapid behavioral responses. Current Biology 15(24):2279-84 (2005)

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Provided by Max-Planck-Gesellschaft

Citation: Light switches for nerve cells (2010, April 6) retrieved 16 April 2024 from https://medicalxpress.com/news/2010-04-nerve-cells.html

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