

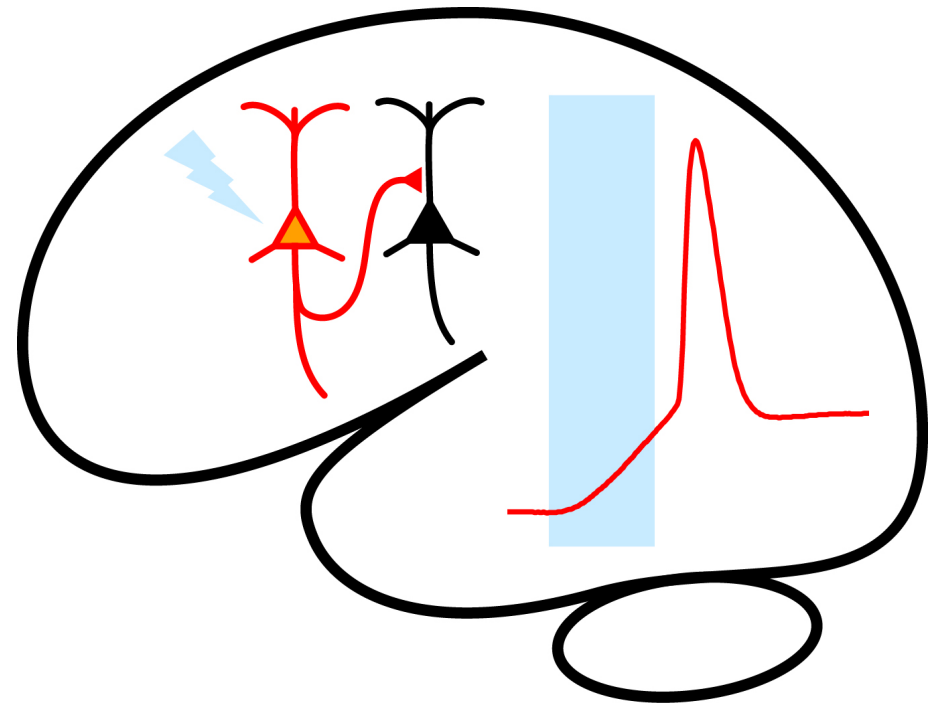
6.5 Controlling brain function

Cellular Mechanisms of Brain Function

Prof. Carl Petersen

Controlling brain function

Optogenetics

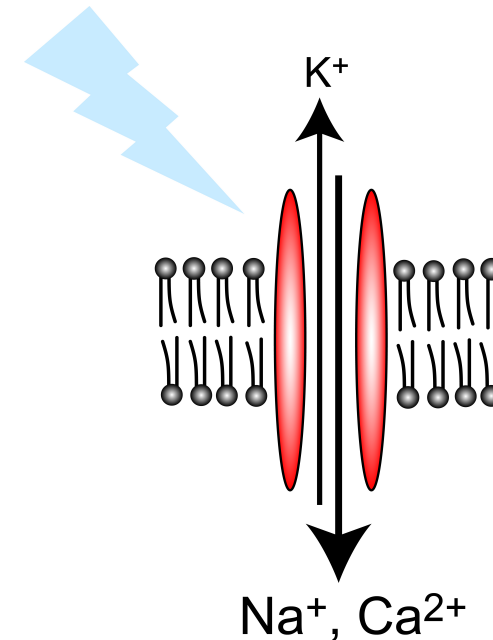


A light-activated cation channel

Channelrhodopsin-2 (ChR2) is a light-activated cation channel, cloned from the green algae *Chlamydomonas reinhardtii*.

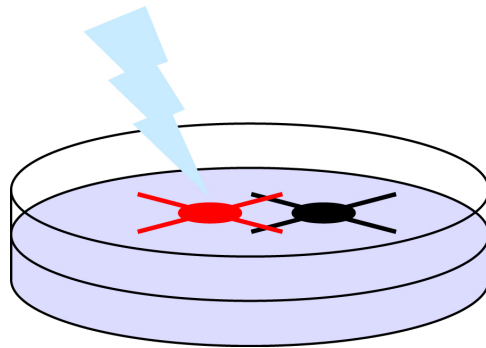
Retinal is bound to ChR2 and changes conformation from all-*trans* to 13-*cis* upon photon absorption.

Nagel, Szellas, Huhn, Kateriya, Adeishvili, Berthold, Ollig, Hegemann, Bamberg (2003)
Channelrhodopsin-2, a directly light-gated cation-selective membrane channel.
Proc Natl Acad Sci USA 100: 13940-13945.

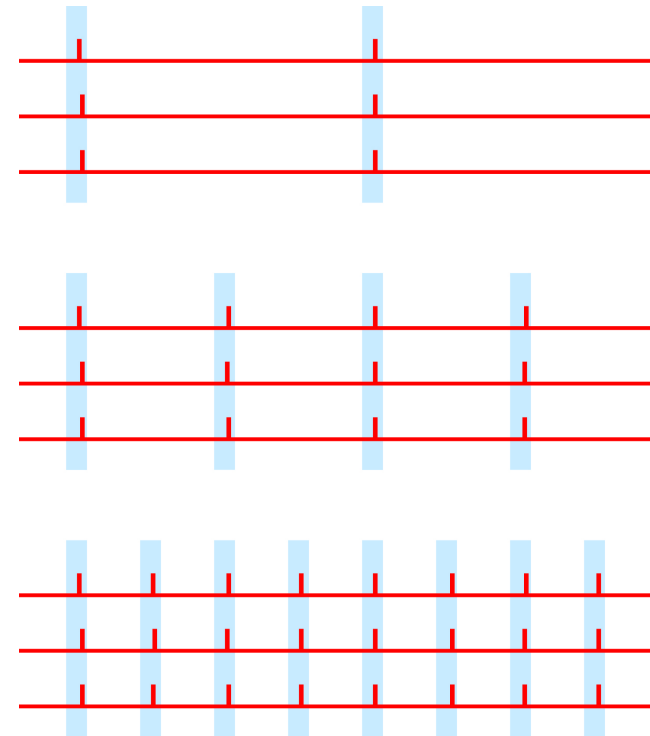


Neuronal stimulation with channelrhodopsin-2

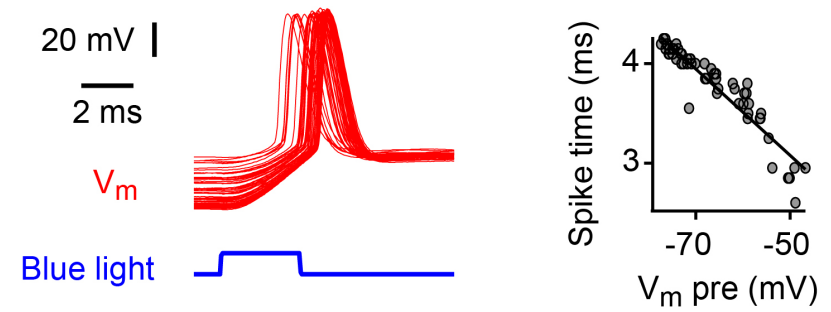
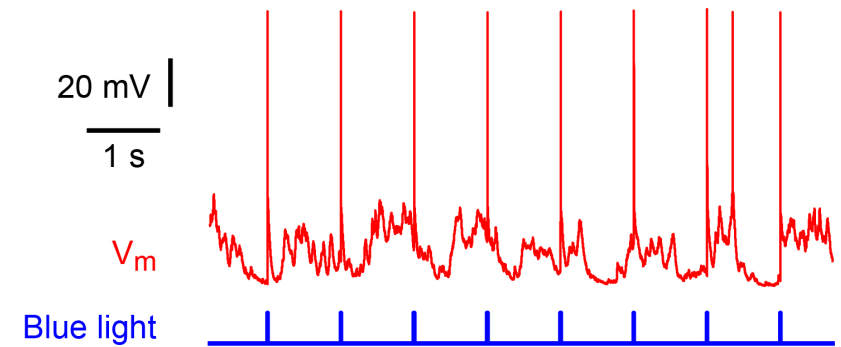
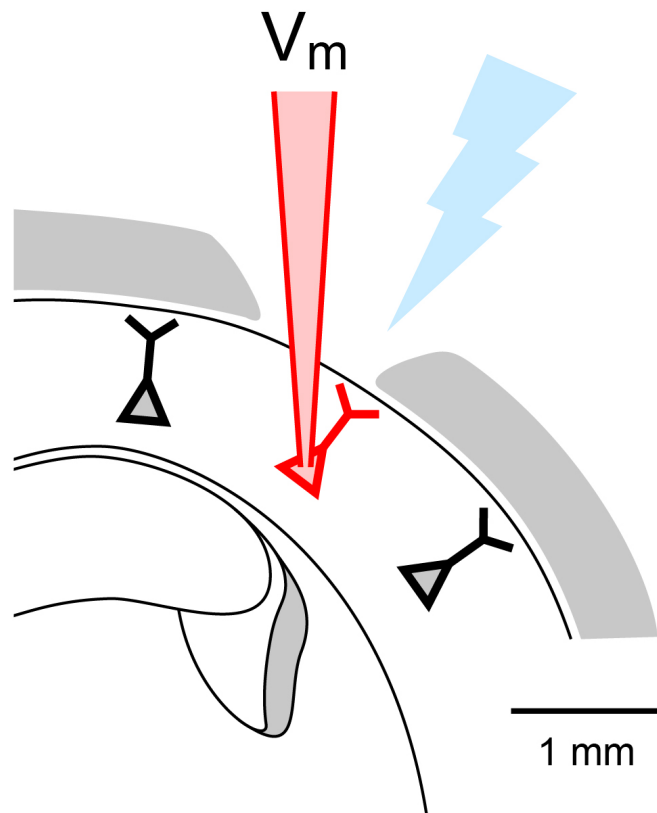
ChR2 can be used to stimulate neurons with millisecond precision.



Boyden ES, Zhang F, Bamberg E, Nagel G, Deisseroth K (2006) *Millisecond-timescale, genetically targeted optical control of neural activity*. Nature Neuroscience 8: 1263-1268.

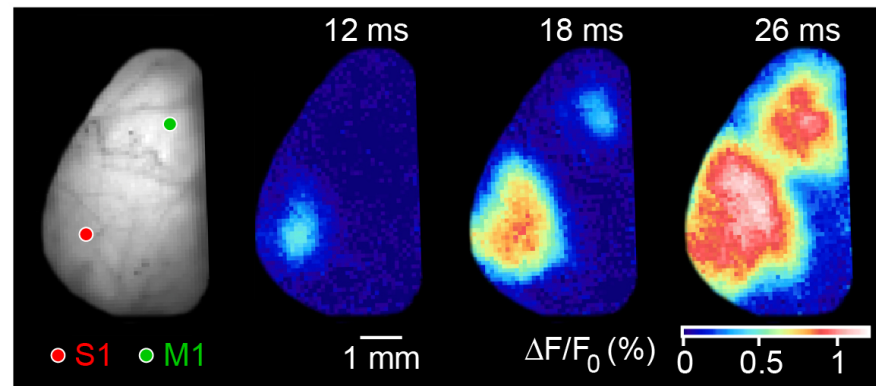
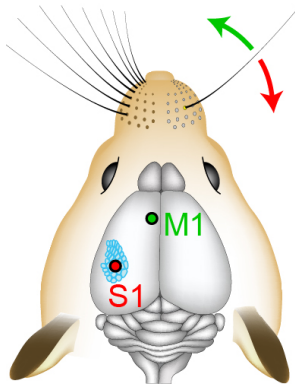


Channelrhodopsin-2 *in vivo*



Mateo, Avermann, Gentet, Zhang, Deisseroth and Petersen, 2011

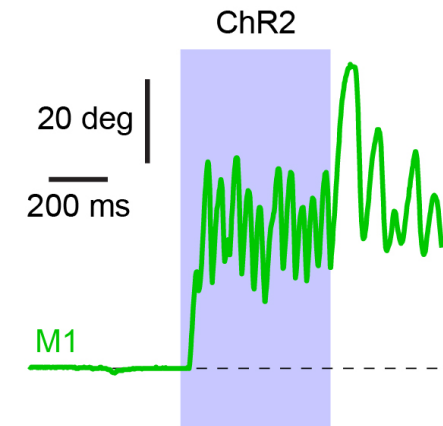
Channelrhodopsin-2 can drive behavior



Matyas, Sreenivasan, Marbach, Wacogne, Barsy, Mateo, Aronoff and Petersen, 2010

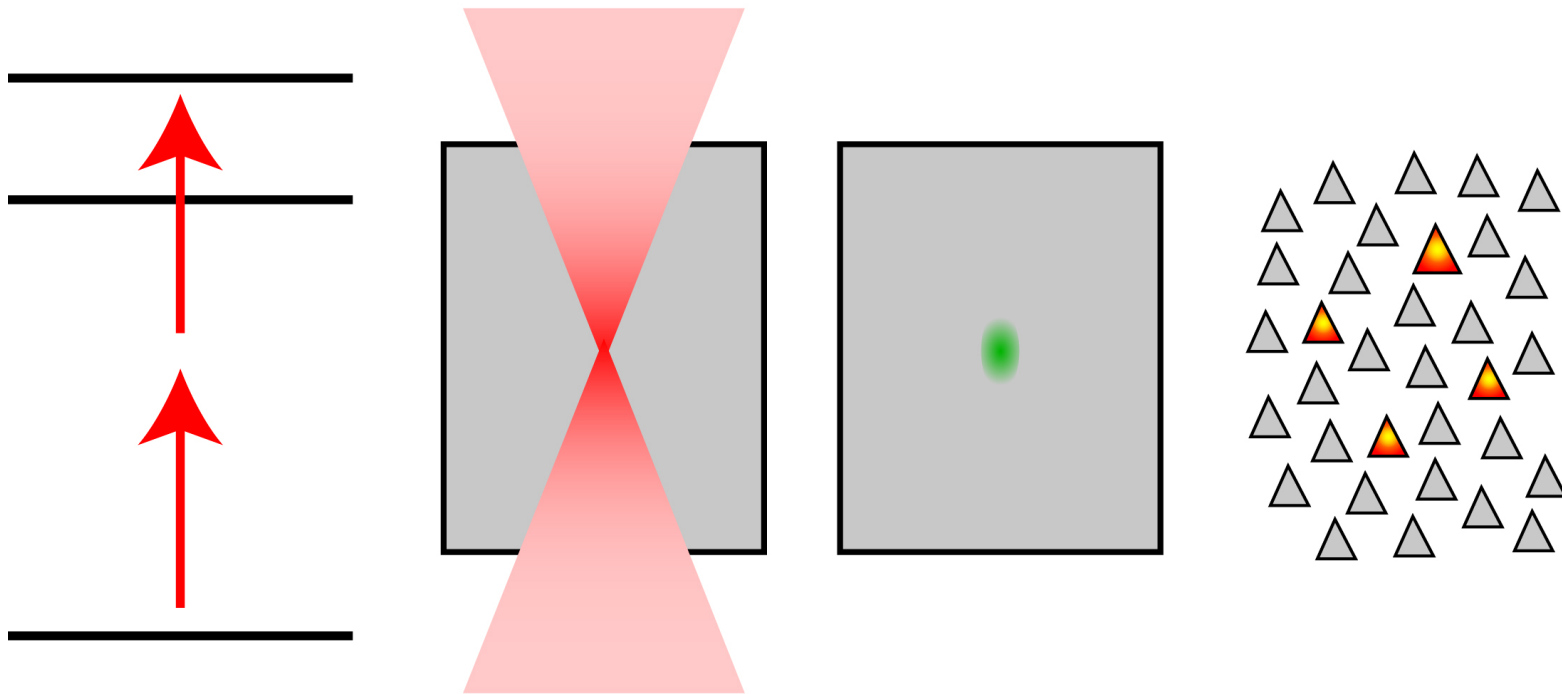
S1 – primary somatosensory cortex

M1 – primary motor cortex



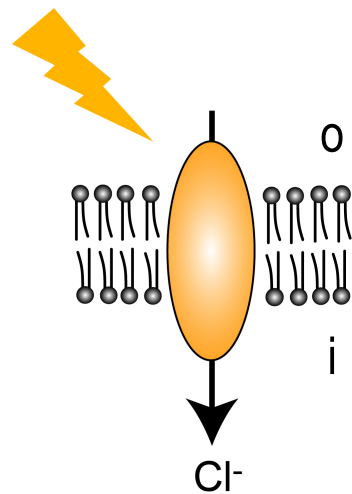
Single-cell stimulation

Two-photon excitation of ChR2 allows control at single-cell level.



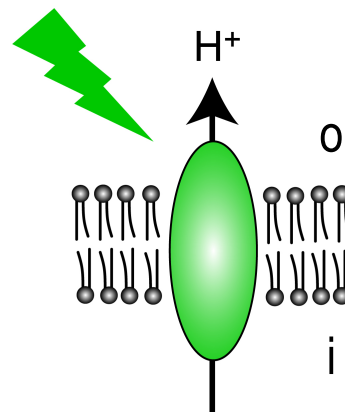
Optogenetic inhibition

NpHR



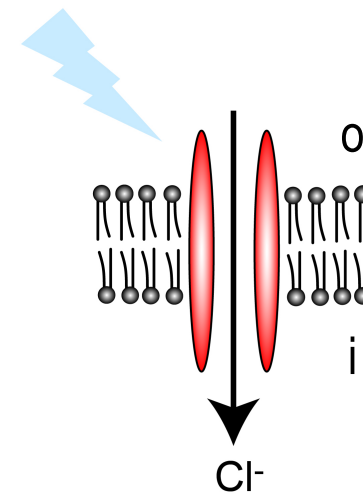
Zhang et al. (2007)

Arch



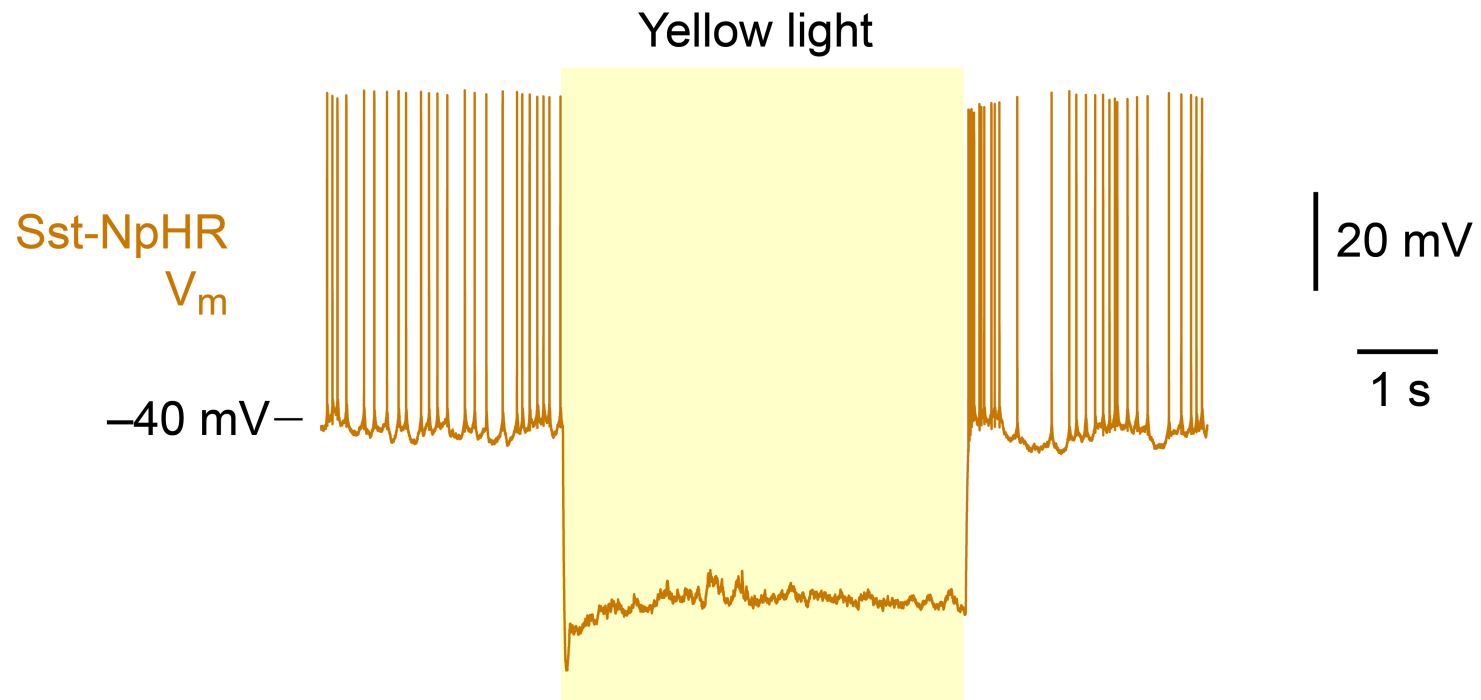
Chow et al. (2010)

iC1C2



Berndt et al. (2014)
Wietek et al. (2014)

Cell-type specific optogenetic inhibition



Gentet, Kremer, Taniguchi, Huang, Staiger and Petersen, 2012

Optogenetic tool development

Higher conductance, ion selectivity

Faster, slower, switching

Spectral variants

Dendrite, soma, axon

+ optogenetic tools are being developed for controlling many other cellular and molecular processes.

Optical control of neuronal activity

- Channelrhodopsin-2 (ChR2) encodes a light-activated cation channel, that can be used to drive action potential firing in genetically-defined neurons with millisecond precision.
- Optogenetic actuators are being developed to inhibit neurons and to control many other processes.