

## 6.5 Controlling brain function

Cellular Mechanisms of Brain Function

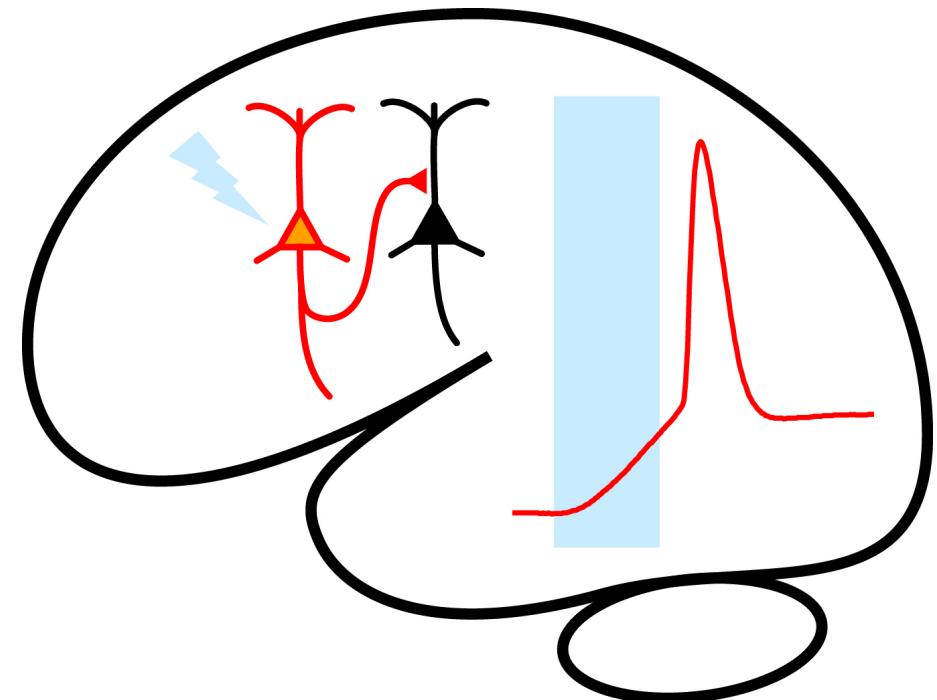
Prof. Carl Petersen

# Controlling brain function



Cellular Mechanisms of Brain Function

# Optogenetics



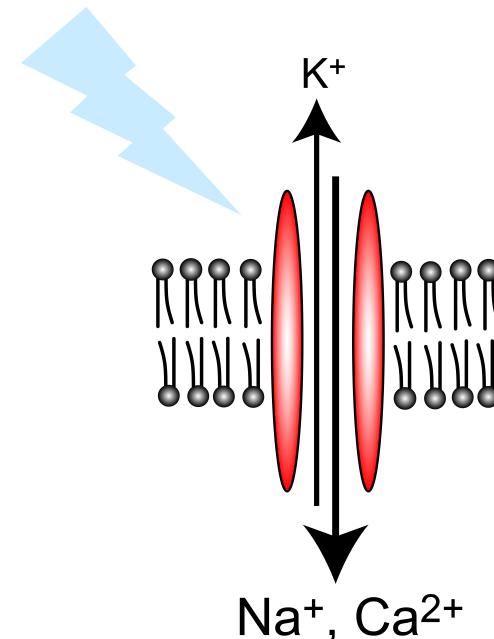
Cellular Mechanisms of Brain Function

# 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.

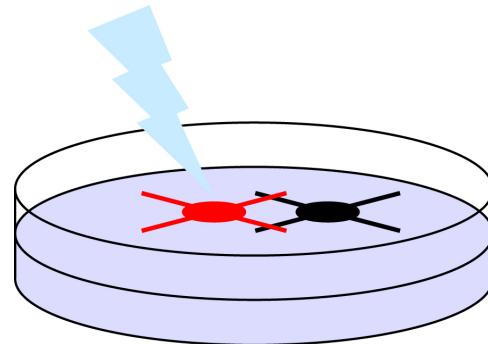
Nagel, Szellas, Huhn, Kateriya, Adeishvili,  
Berthold, Ollig, Hegemann, Bamberg (2003)  
*Channelrhodopsin-2, a directly light-gated  
cation-selective membrane channel.*  
Proc Natl Acad Sci USA 100: 13940-13945.



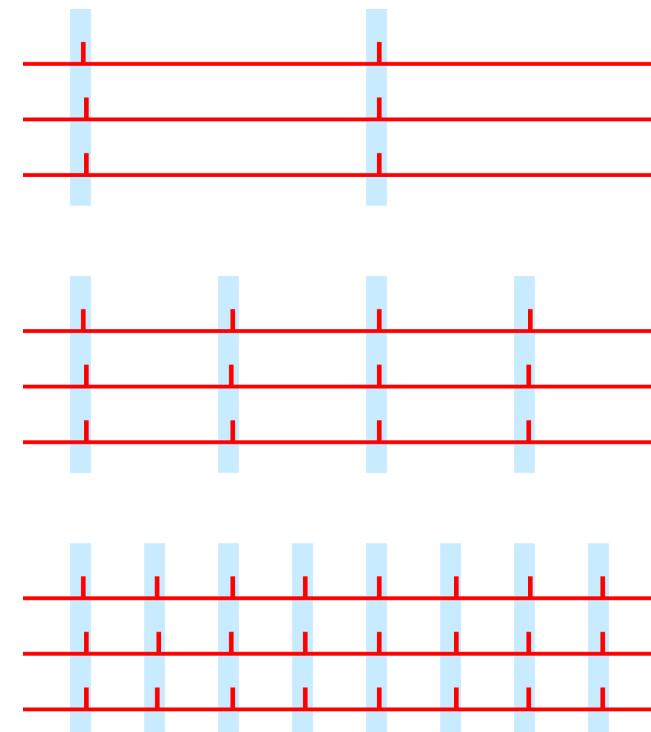
# Neuronal stimulation with channelrhodopsin-2



ChR2 can be used to stimulate neurons with millisecond precision.

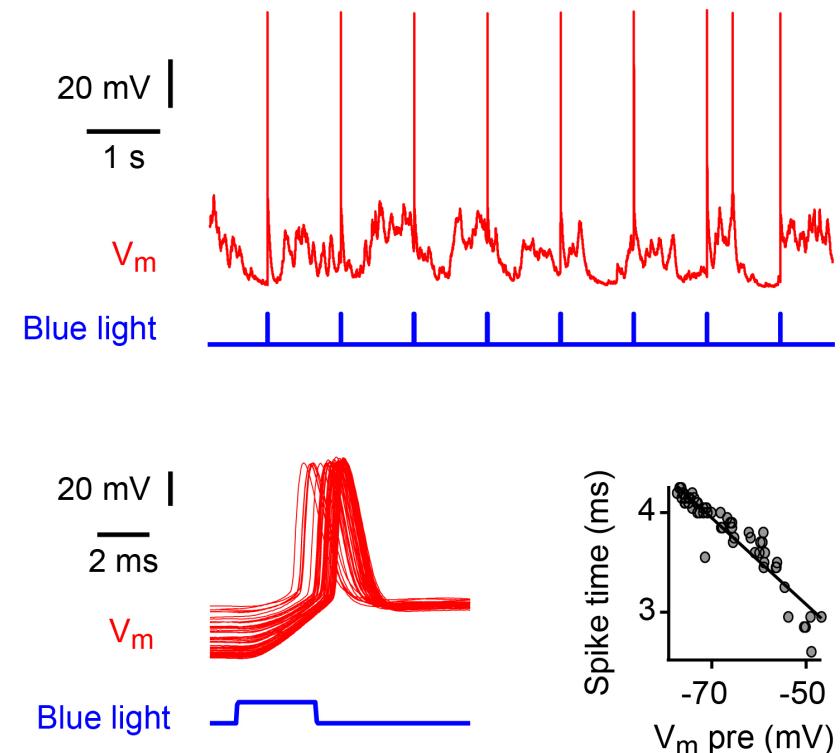
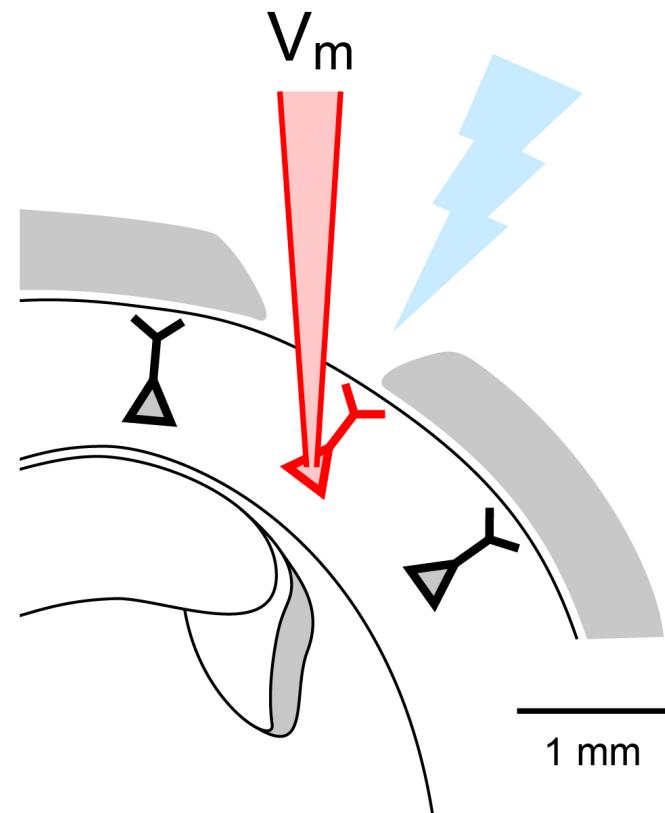


Boyden ES, Zhang F, Bamberg E, Nagel G, Deisseroth K (2006) *Millisecond-timescale, genetically targeted optical control of neural activity*. Nature Neuroscience 8: 1263-1268.



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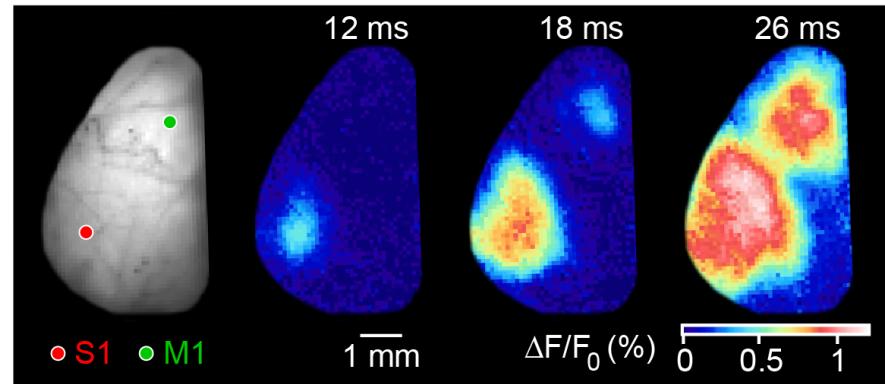
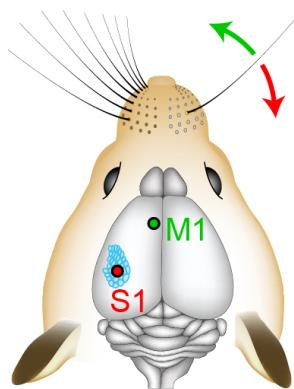
# Channelrhodopsin-2 *in vivo*



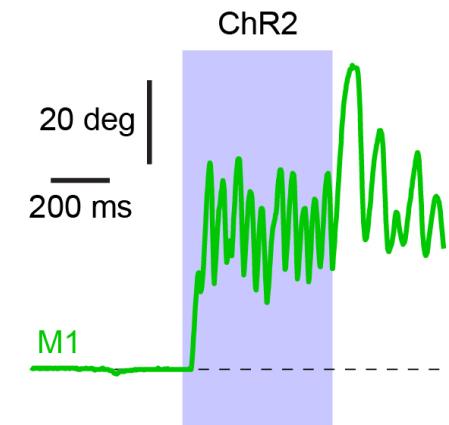
Mateo, Avermann, Gentet, Zhang, Deisseroth and Petersen, 2011

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# Channelrhodopsin-2 can drive behavior



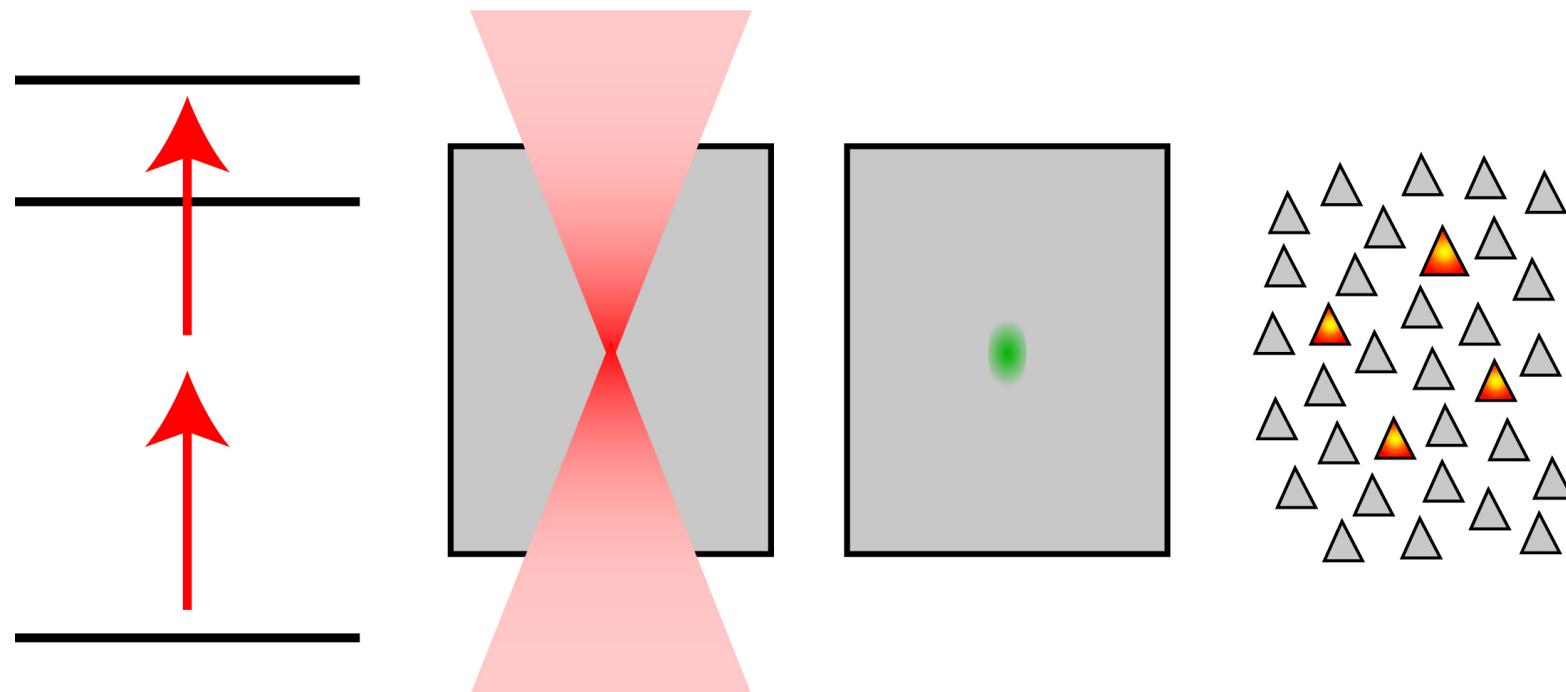
Matyas, Sreenivasan, Marbach, Wacongne, Barsy, Mateo, Aronoff and Petersen, 2010



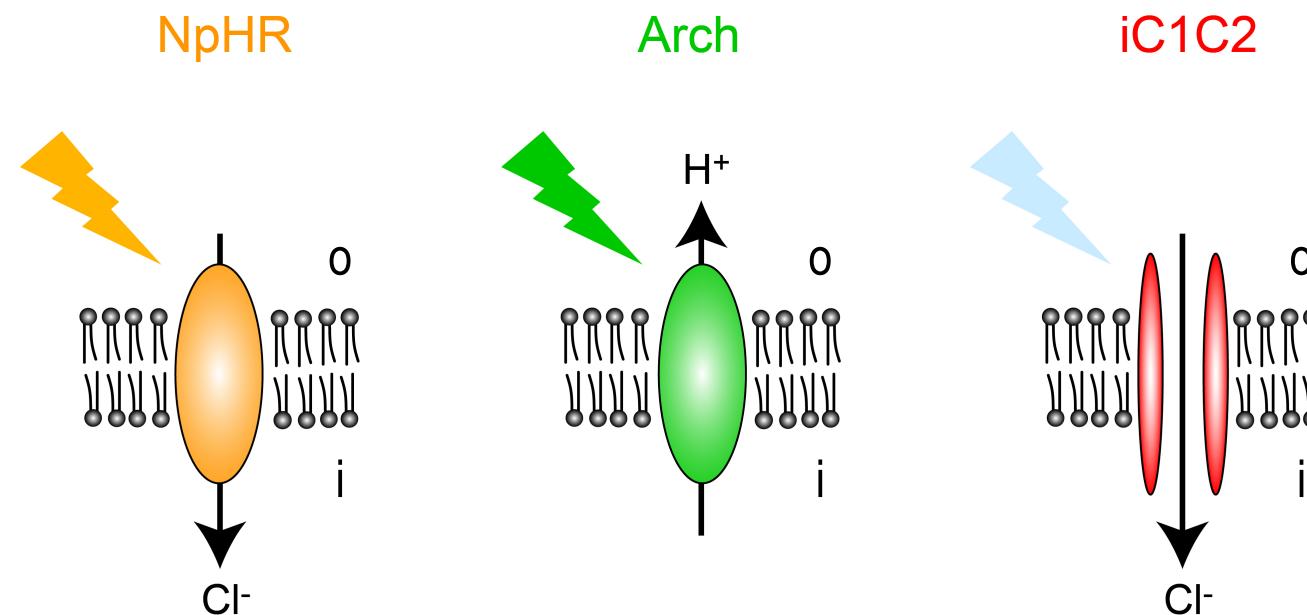
S1 – primary somatosensory cortex  
M1 – primary motor cortex

# Single-cell stimulation

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



# Optogenetic inhibition

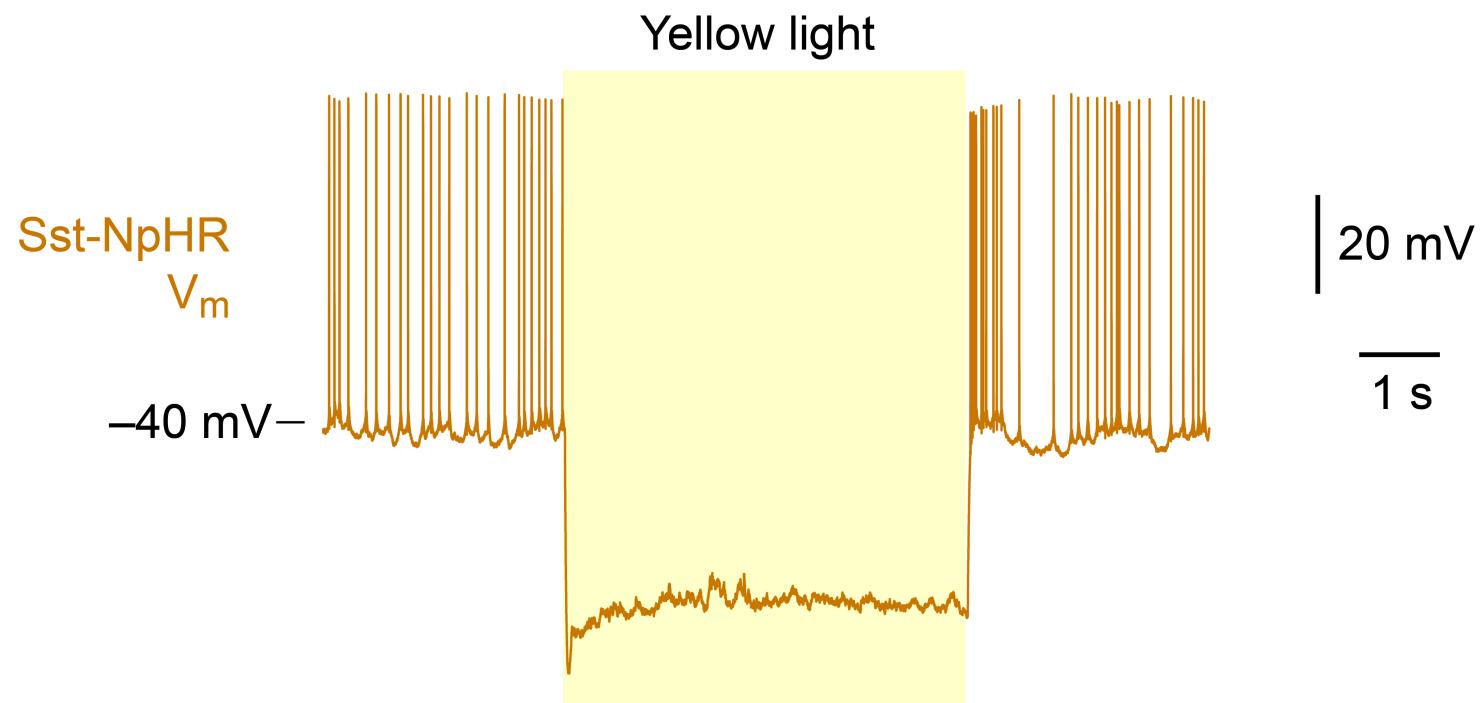


Zhang et al. (2007)

Chow et al. (2010)

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

# Cell-type specific optogenetic inhibition



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

Cellular Mechanisms of Brain Function

# 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.