Optogenetics update

A brief story about the past, present, and future of opsins in Neuroscience

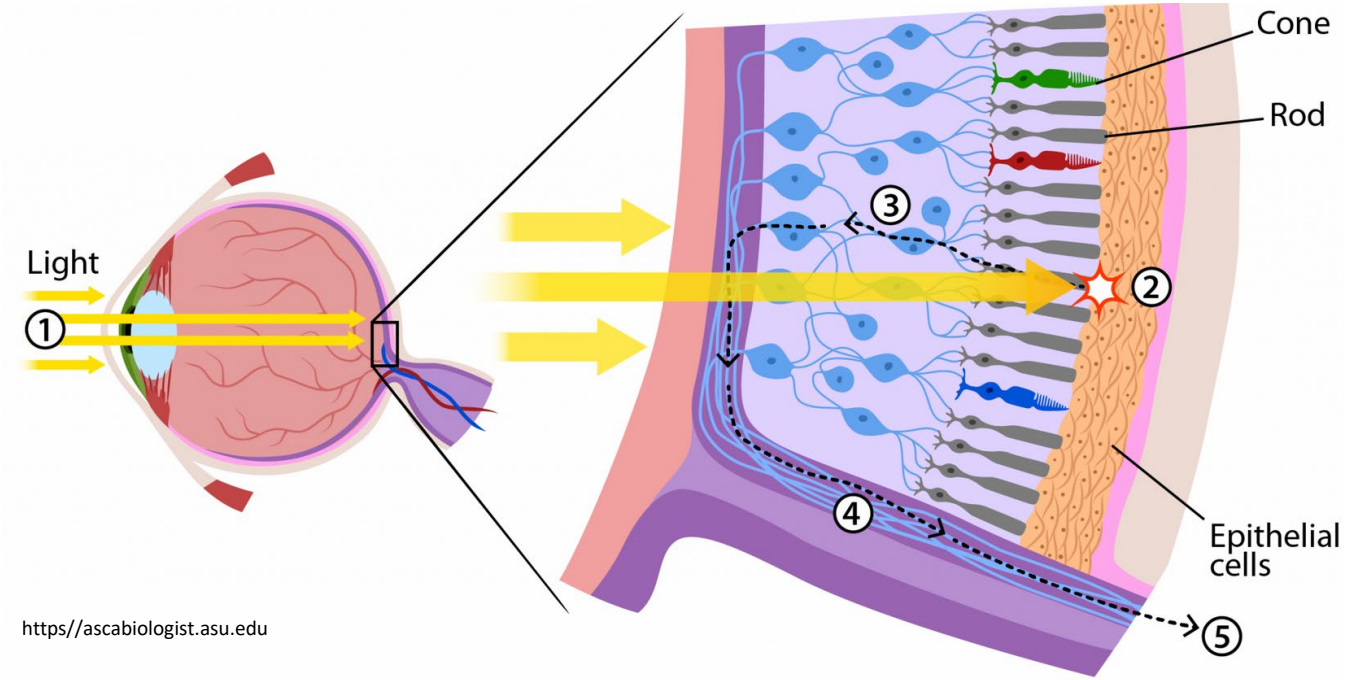
Overview

- Historical milestones in Neuroscience Optogenetics
- Optogenetic applications in Neuroscience
- Recent advances in the optogenetic toolbox

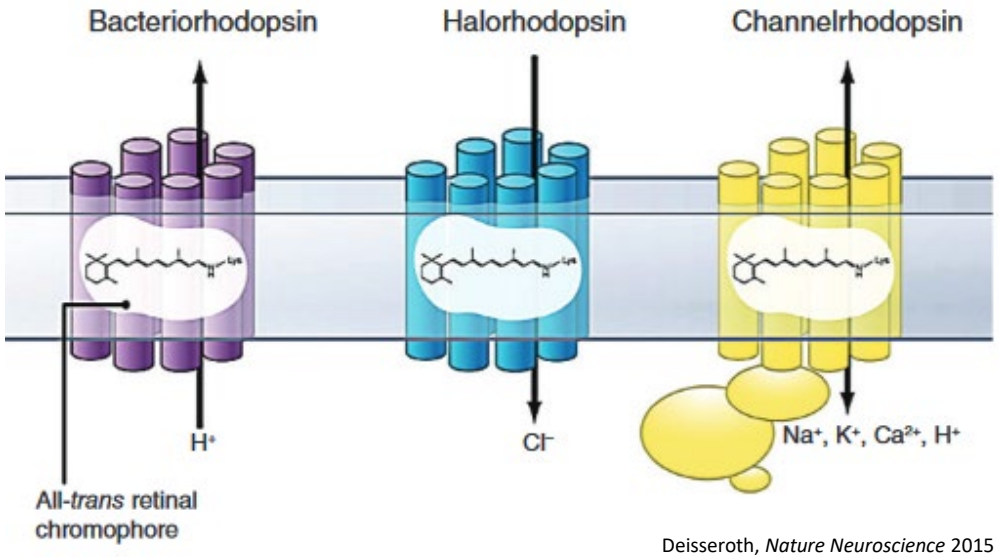
Definition

Optogenetics uses light to control neurons which have been genetically modified to express light-sensitive receptors/ion channels.

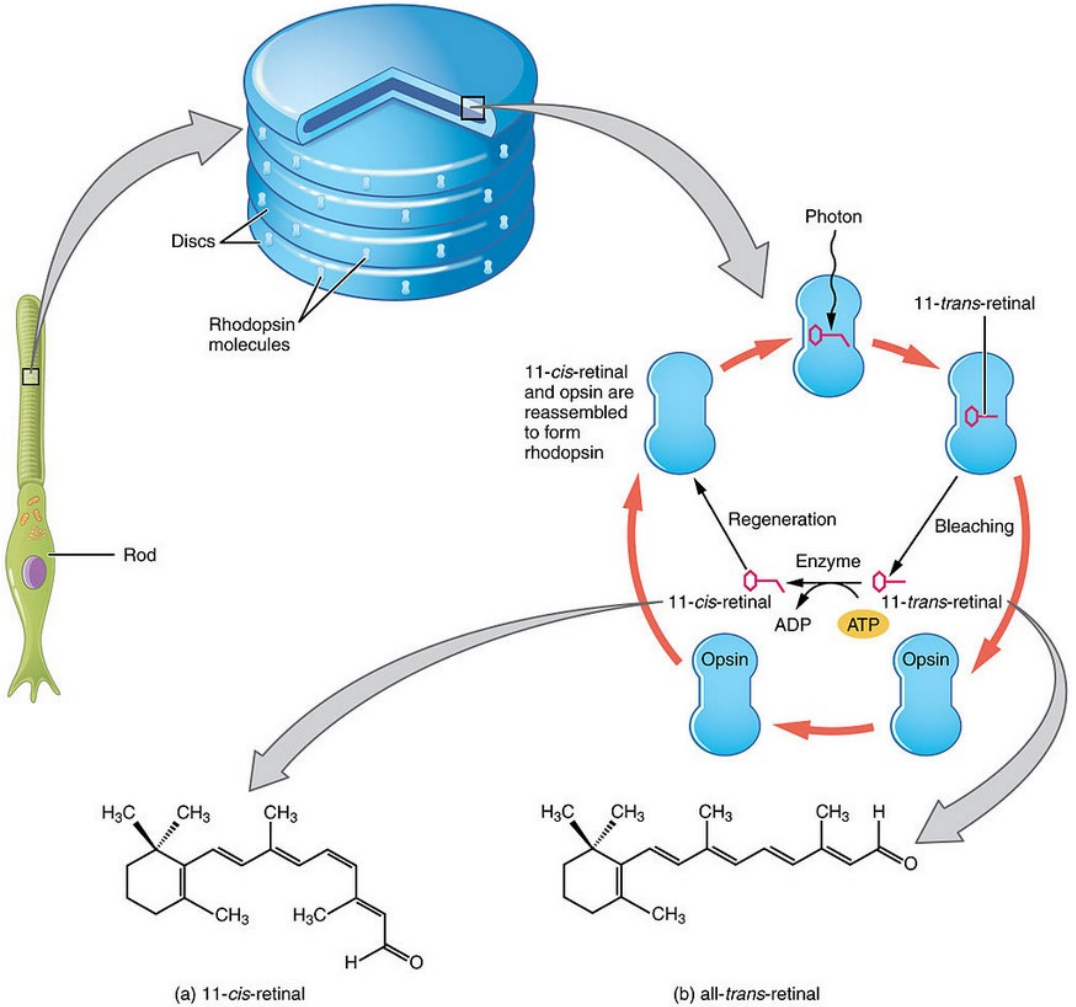
Opsins and where to find them…



https//ascabiologist.asu.edu



Deisseroth, *Nature Neuroscience* 2015



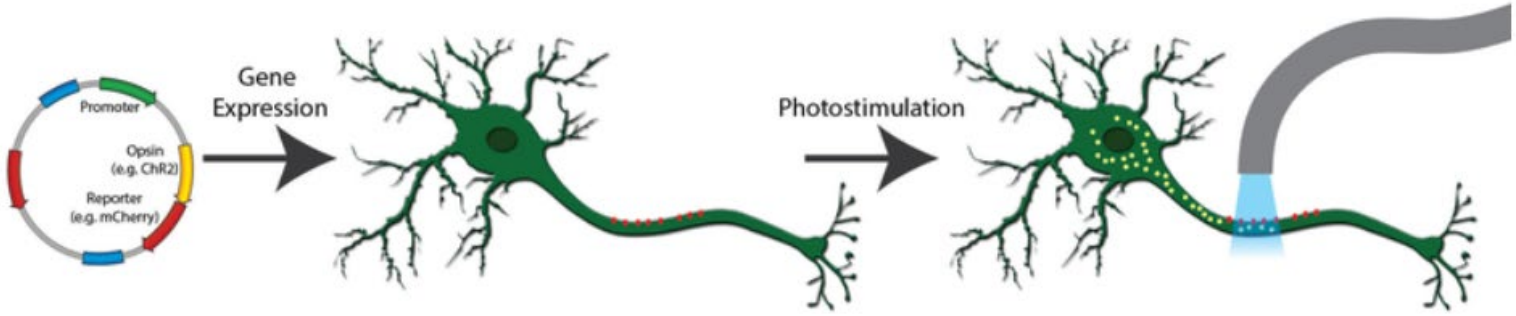
Anatomy and Physiology Connexionx Web site http://cnx.org

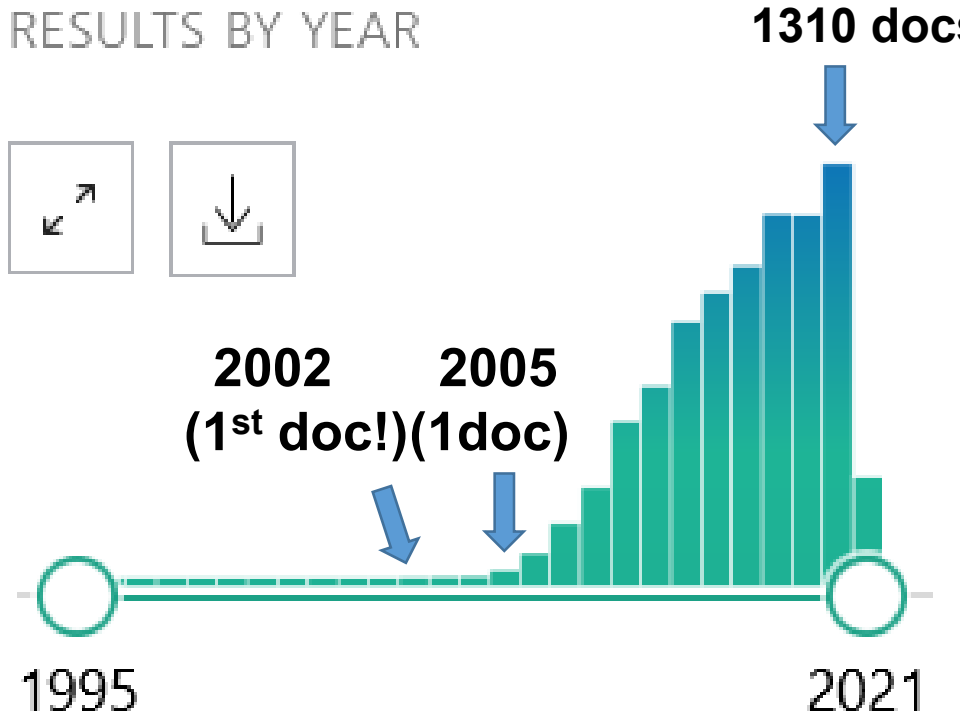
Optogenetics and their impact on Neuroscience

HISTORY

- The "far-fetched" possibility of using light for selectively controlling precise neural activity (action potential) patterns within subtypes of cells in the brain was articulated by Francis Crick in his Kuffler Lectures at the University of California in San Diego in 1999.

By Aksha Goyal https://www.slideshare.net





Pubmed NCBI

https://www.addgene.org

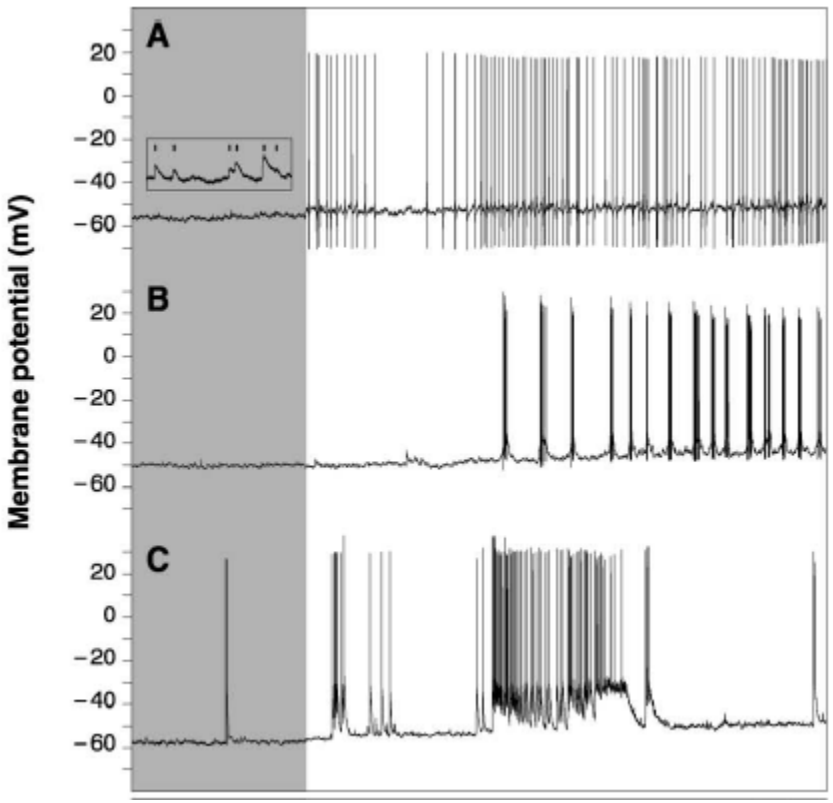
Neuron, Vol. 33, 15–22, January 3, 2002, Copyright ©2002 by Cell Press

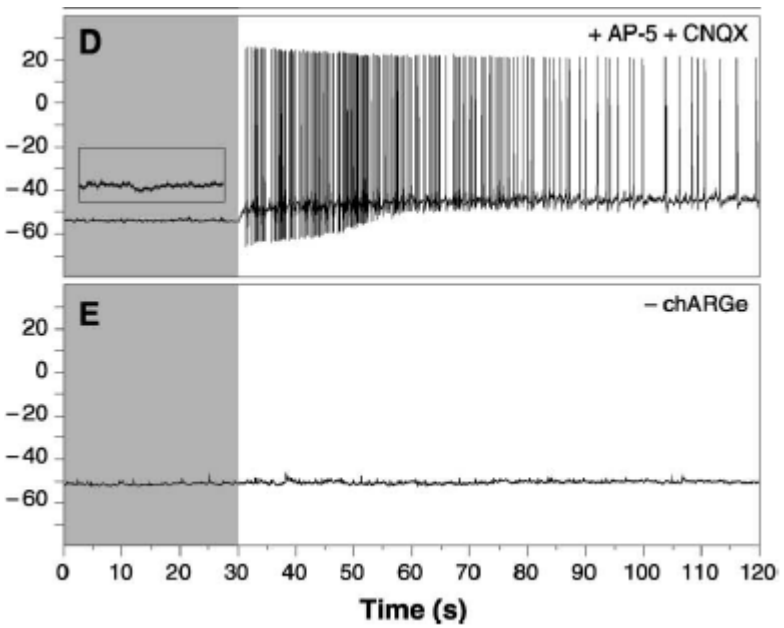
Selective Photostimulation of Genetically ChARGed Neurons

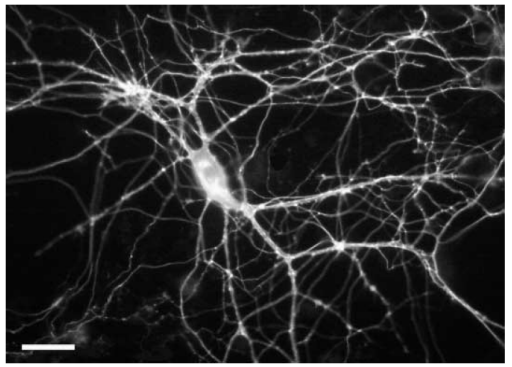
Neurotechnique

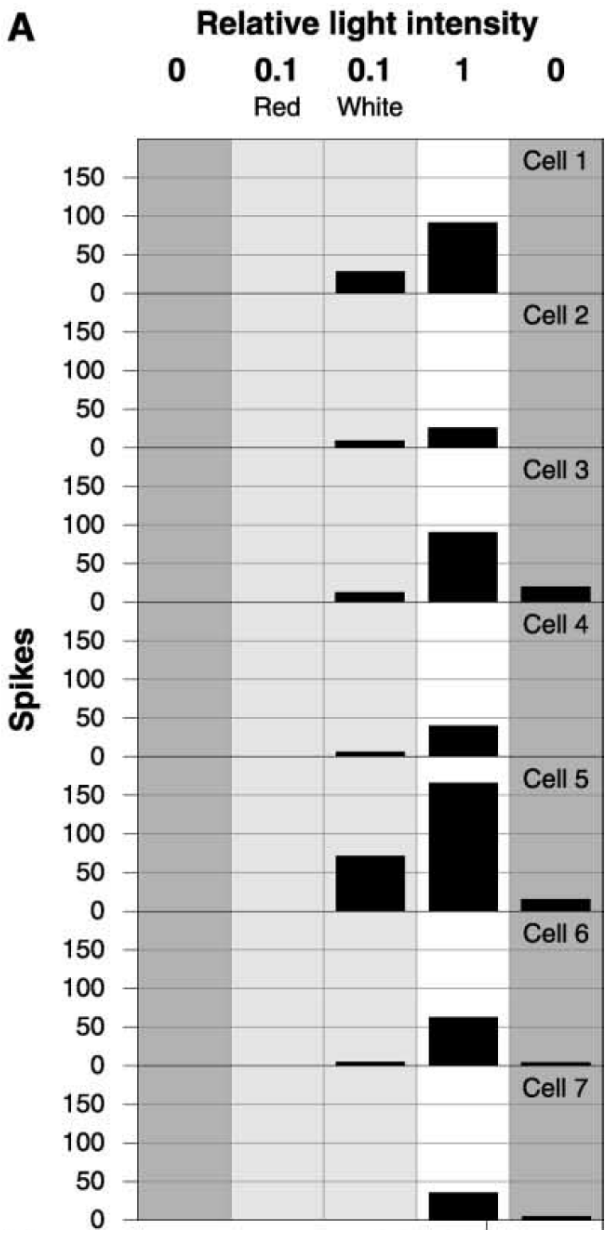
Boris V. Zemelman, Georgia A. Lee, Minna Ng, and Gero Miesenböck[1]
Laboratory of Neural Systems
Cellular Biochemistry and Biophysics Program
Memorial Sloan-Kettering Cancer Center
1275 York Avenue
New York, New York 10021

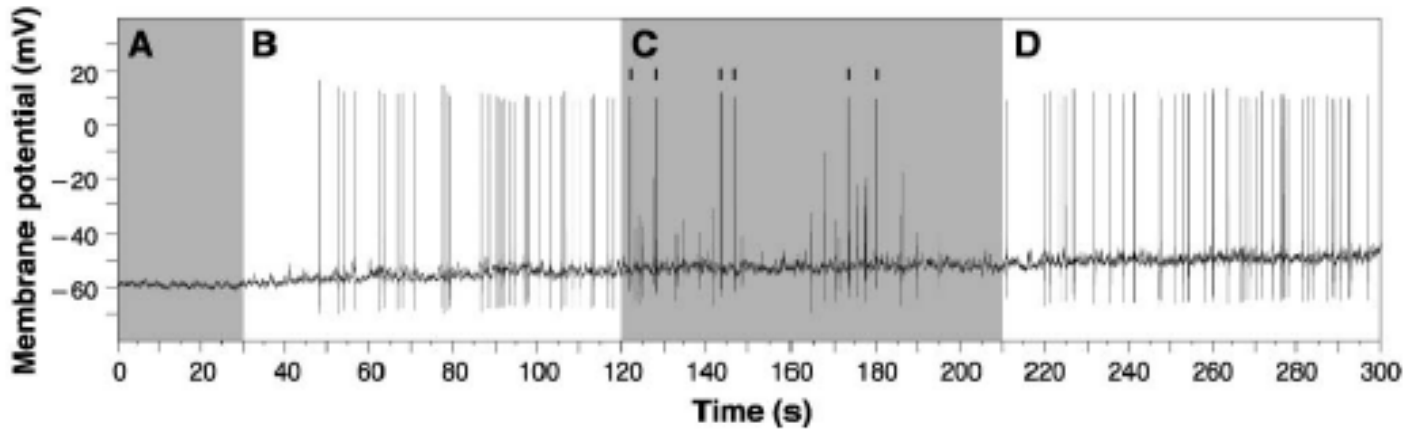
Drosophila **photoreceptor genes encoding arrestin-2, rhodopsin (formed by liganding opsin with retinal) and the subunit of the cognate heterotrimeric G protein - an explosive combination we termed "charge"**








A
Relative light intensity
0
0.1
Red
0.1
White
1
0
Cell 1
Cell 2
Cell 3
Cell 4
Cell 5
Cell 6
Cell 7
Spikes
150
100
50
0


A
B
C
D
Membrane potential (mV)
20
0
−20
−40
−60
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
Time (s)

nature neuroscience

TECHNICAL REPORT

Millisecond-timescale, genetically targeted optical control of neural activity

Edward S Boyden[1], Feng Zhang[1], Ernst Bamberg[2,3], Georg Nagel[2,5] & Karl Deisseroth[1,4]

IOP Publishing — Journal of Neural Engineering

J. Neural Eng. 4 (2007) S143–S156 — doi:10.1088/1741-2560/4/3/S02

An optical neural interface: *in vivo* control of rodent motor cortex with integrated fiberoptic and optogenetic technology

Alexander M Aravanis[1,5], Li-Ping Wang[1,5], Feng Zhang[1,3], Leslie A Meltzer[1], Murtaza Z Mogri[1], M Bret Schneider[2,4] and Karl Deisseroth[1,2]

[1] Department of Bioengineering, Stanford University Medical Center, Stanford, CA 94305, USA
[2] Department of Psychiatry and Behavioral Sciences, Stanford University Medical Center, Stanford, CA 94305, USA
[3] Department of Chemistry, Stanford University, Stanford, CA 94305, USA
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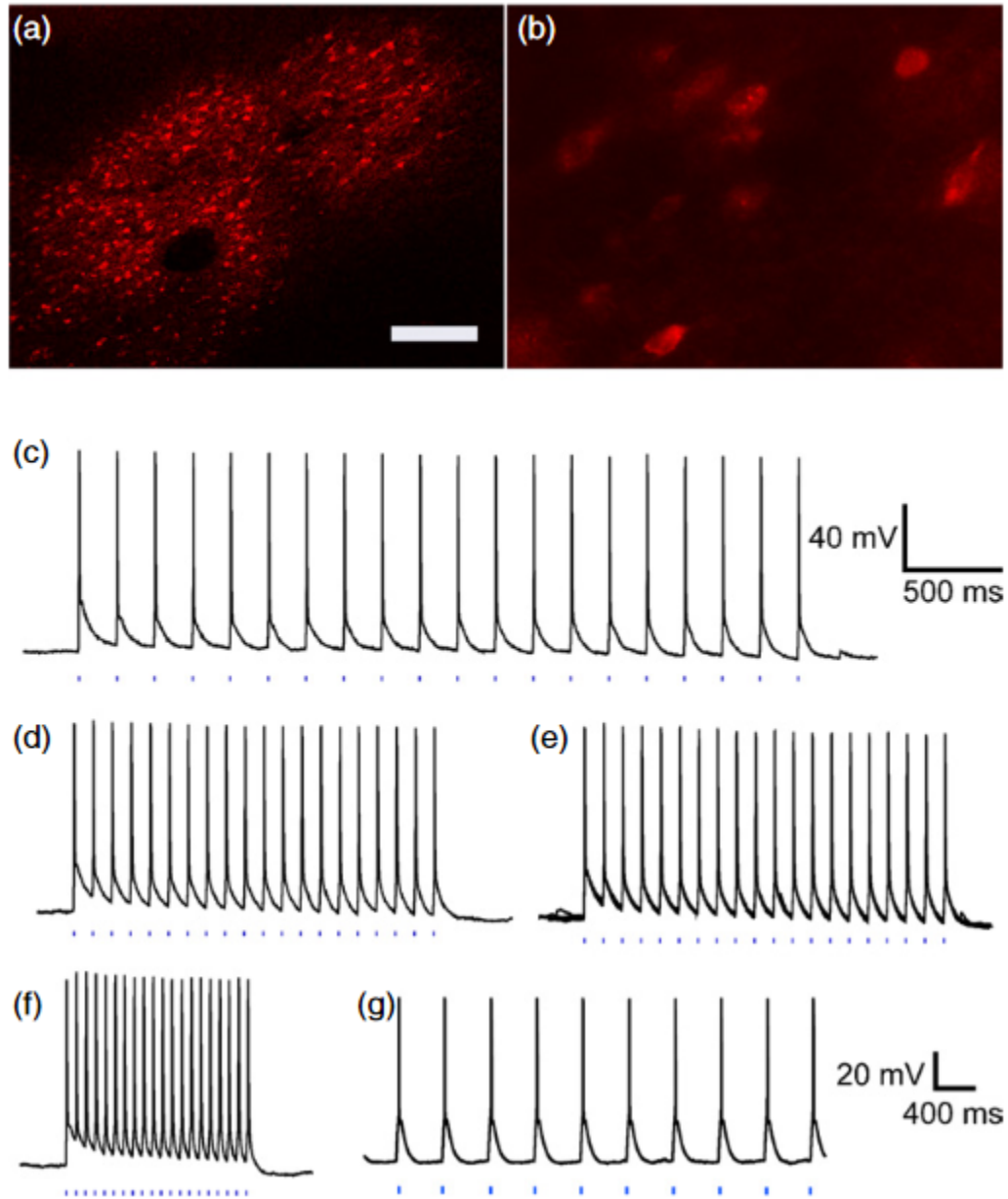
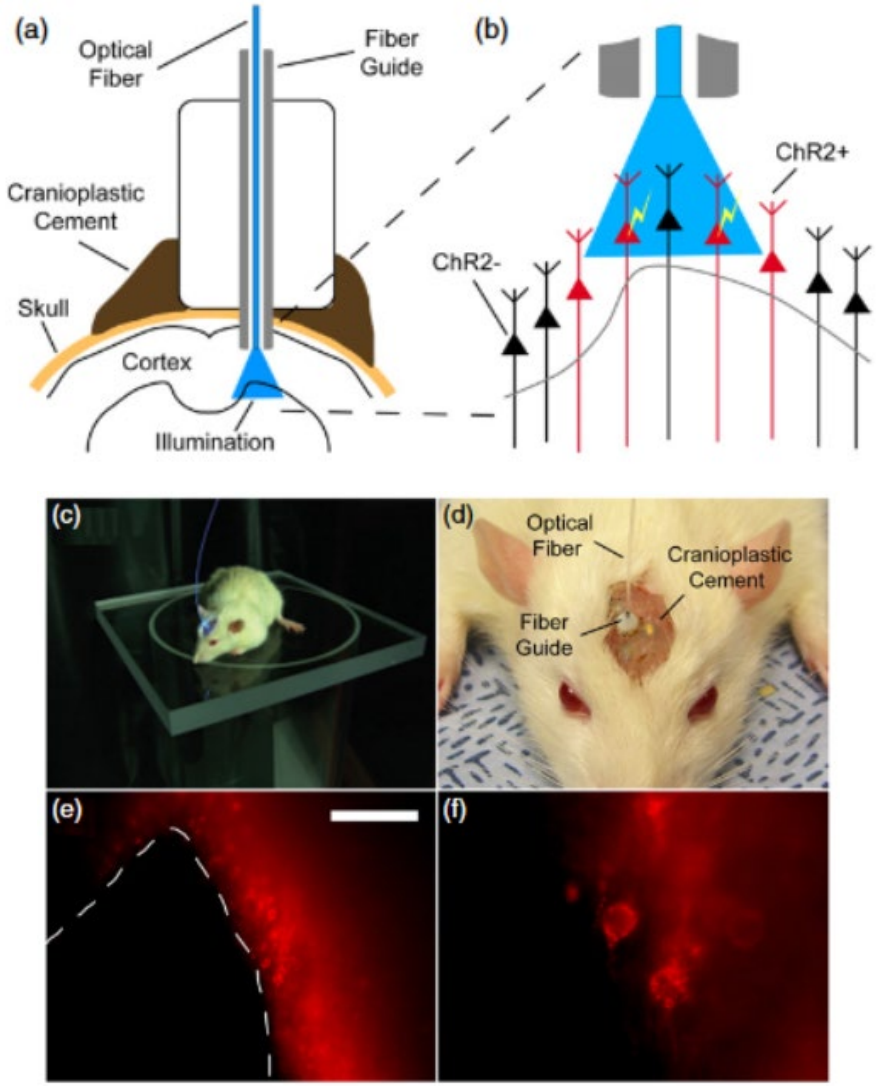
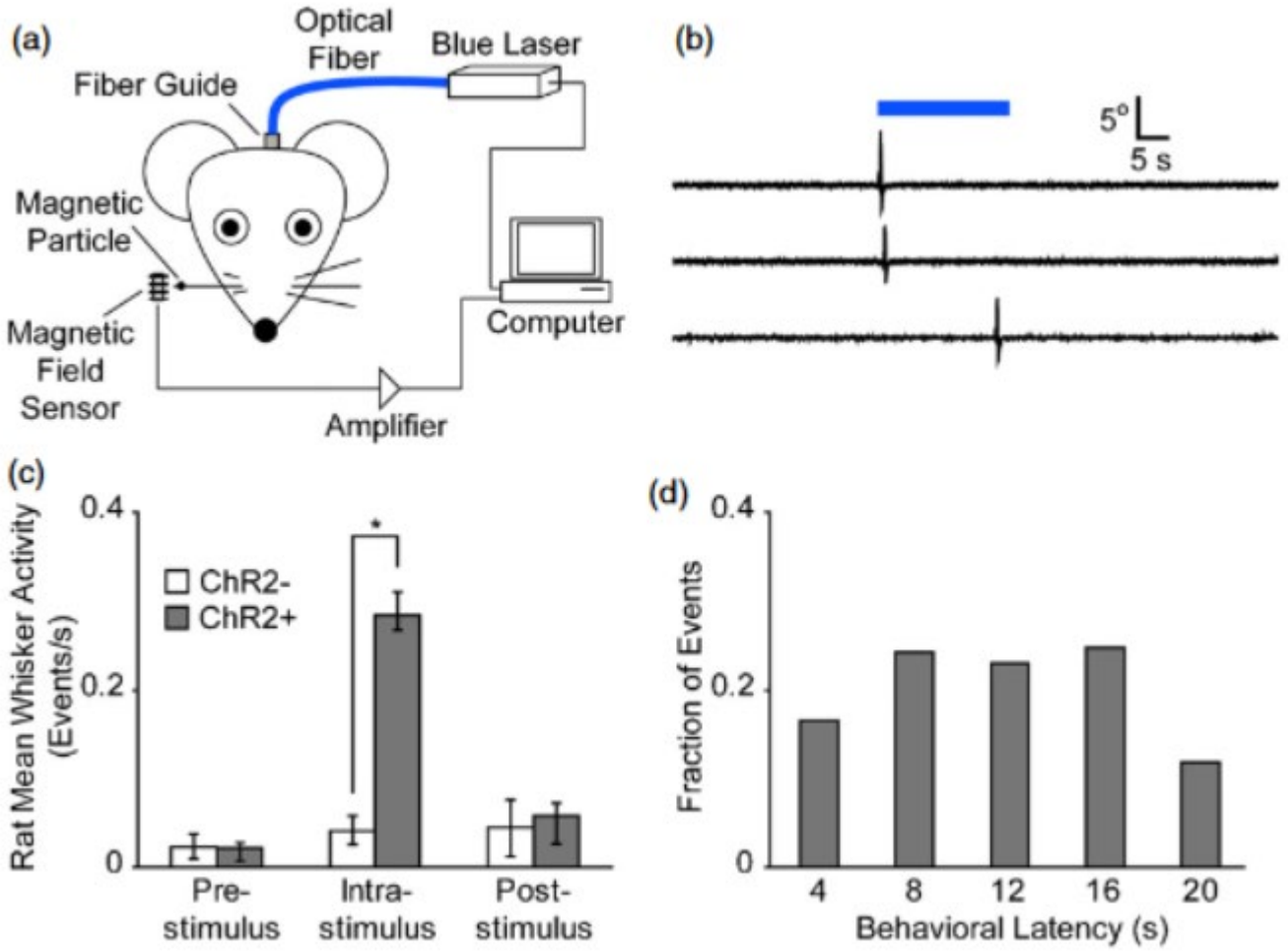

(a)
(b)
(c)
40 mV
500 ms
(d)
(e)
(f)
(g)
20 mV
400 ms

1st in vivo application of optogenetics in mammals



Motor cortex stimulation to move whiskers
(based on electrical stimulation knowledge)



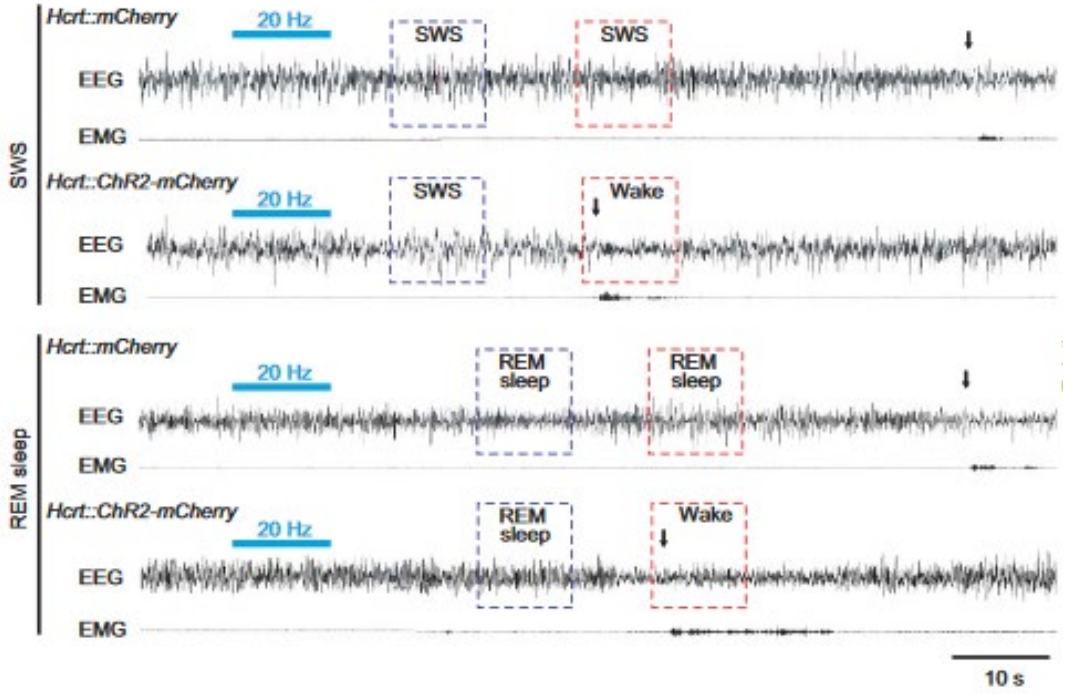
1st biological question addressed by optogenetics

nature Vol 450|15 November 2007|doi:10.1038/nature06310

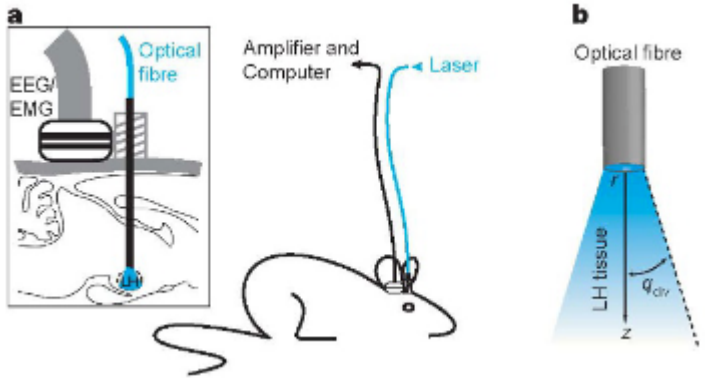
LETTERS

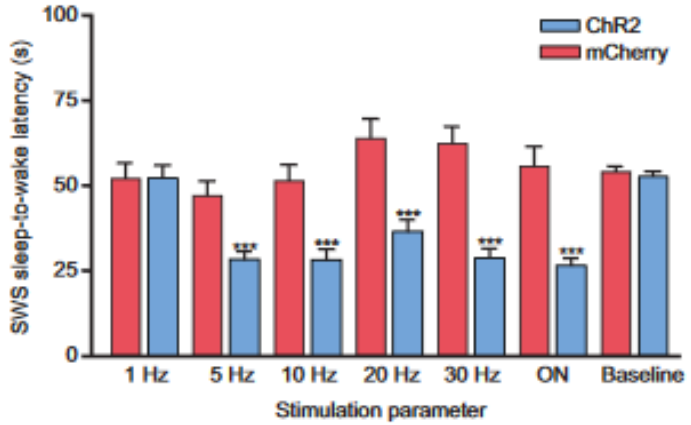
Neural substrates of awakening probed with optogenetic control of hypocretin neurons

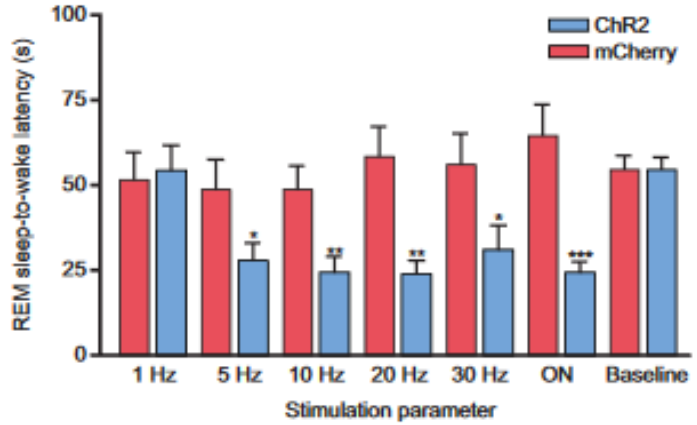
Antoine R. Adamantidis[1]*, Feng Zhang[2]*, Alexander M. Aravanis[2], Karl Deisseroth[1,2] & Luis de Lecea[1]



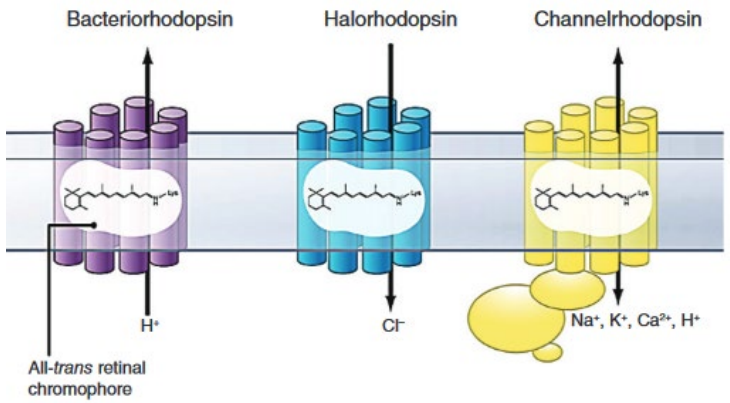
Activation of lateral hypothalamus orexin neurons

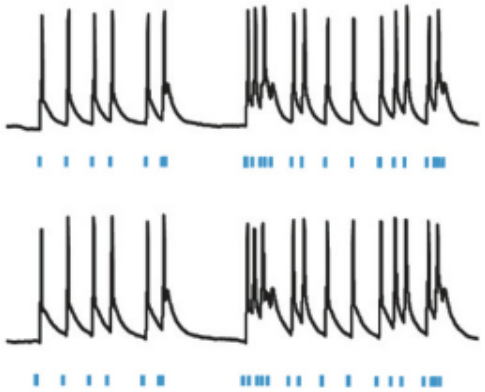


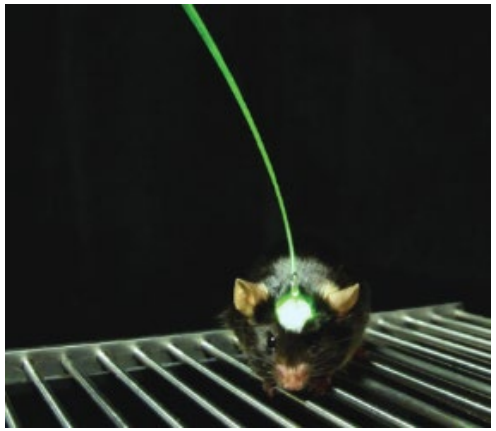


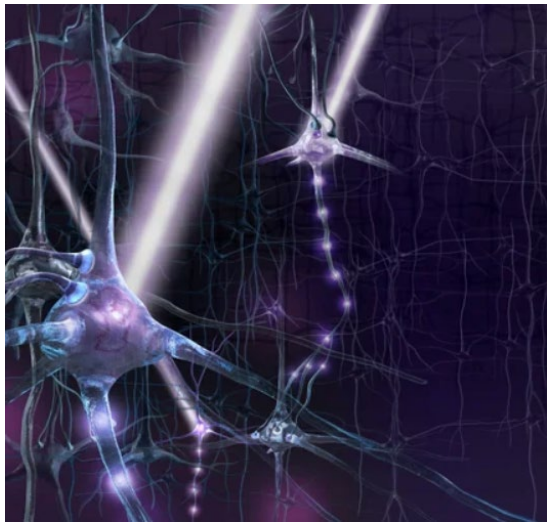


A brief history of Optogenetics in Neuroscience









Discovery of microbial opsins
Bacterialrhodopsin (1971)
Halorhodopsin (1977,1982)
Channelrhodopsin (1984,1991,2002)

Adaptaion for use in NEURONS (2002/2005)

1st in vivo application in mammals (2007)

Extension of applications, circuit dissection, tool refinement

Combination of Optogenetics with other methods

LETTER

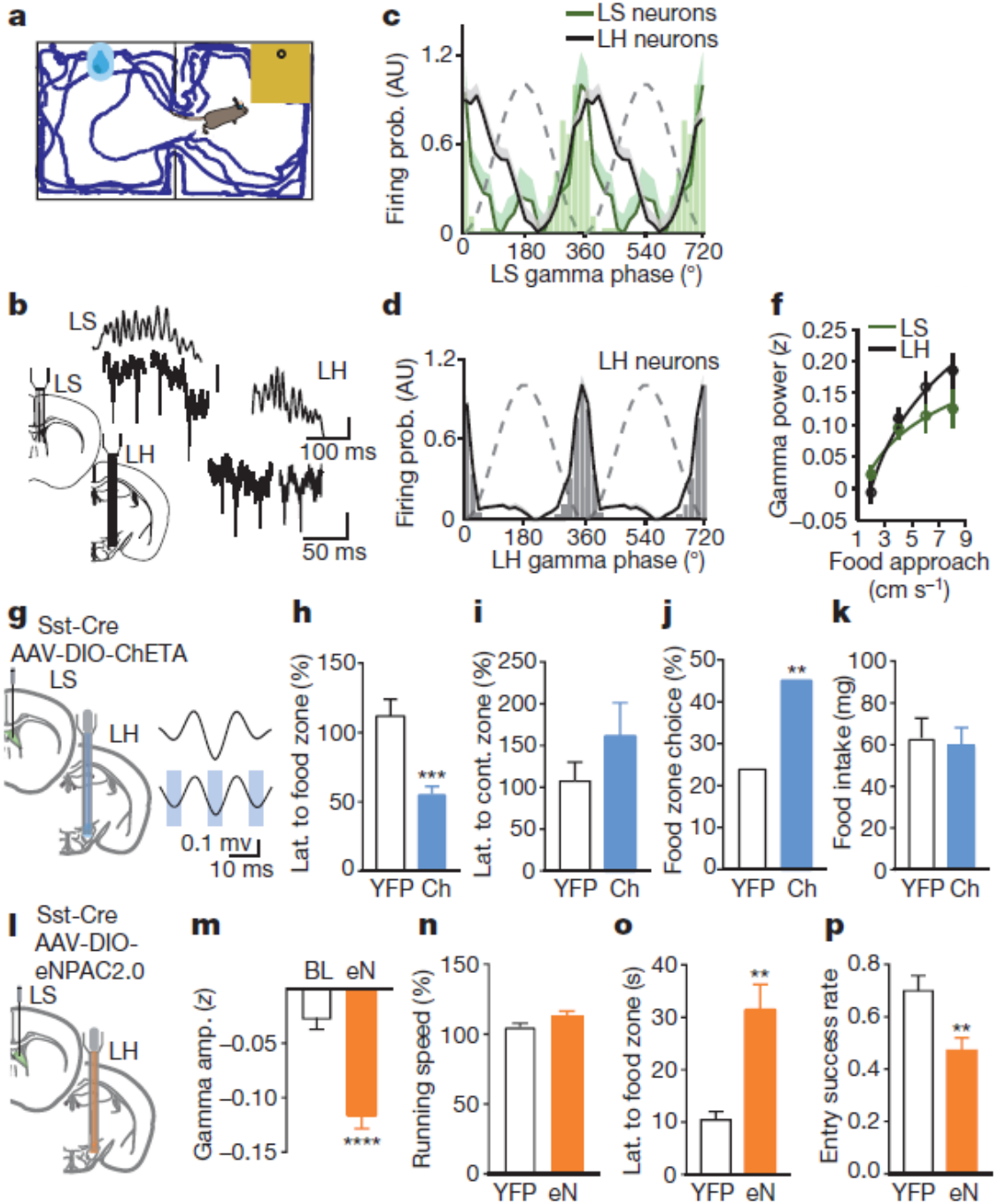
doi:10.1038/nature21066

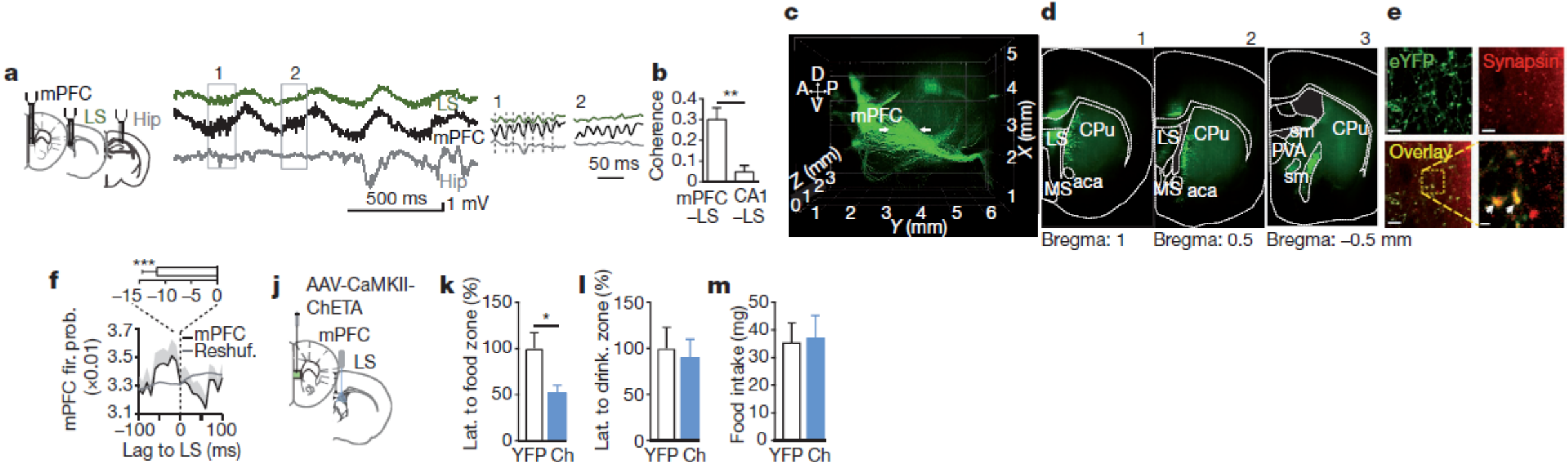
Gamma oscillations organize top-down signalling to hypothalamus and enable food seeking

Marta Carus-Cadavieco[1]*, Maria Gorbati[1]*, Li Ye[2,3], Franziska Bender[1], Suzanne van der Veldt[1], Christin Kosse[4], Christoph Börgers[5], Soo Yeun Lee[2], Charu Ramakrishnan[2], Yubin Hu[1], Natalia Denisova[1], Franziska Ramm[1], Emmanouela Volitaki[1], Denis Burdakov[4], Karl Deisseroth[2,3,6], Alexey Ponomarenko[1]* & Tatiana Korotkova[1]*

Food zone vs drink zone

Gamma band (60-90Hz)





Conclusion: Identification circuit mPFC → LS → LH → food seeking

nature biotechnology

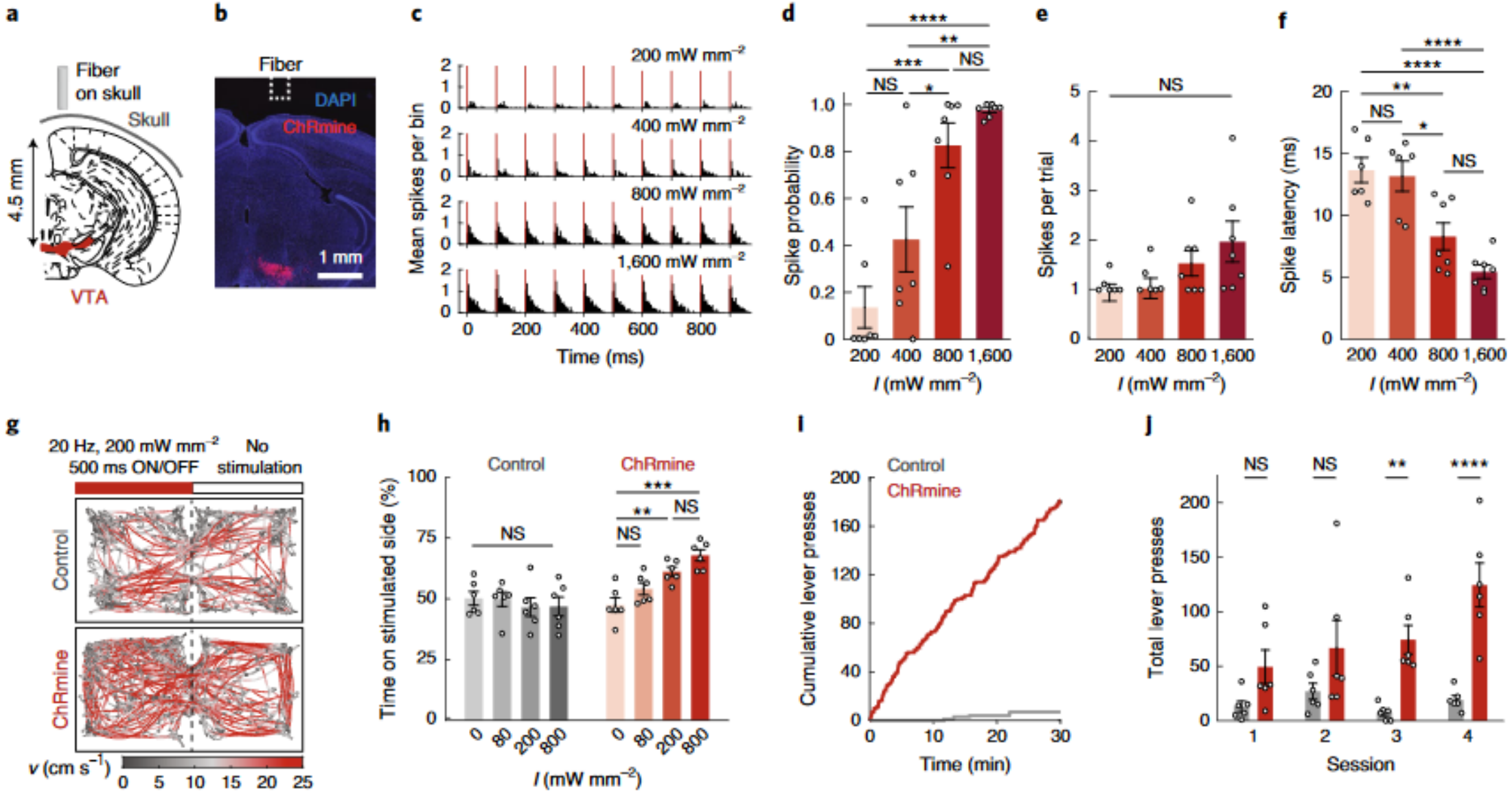
BRIEF COMMUNICATION

https://doi.org/10.1038/s41587-020-0679-9

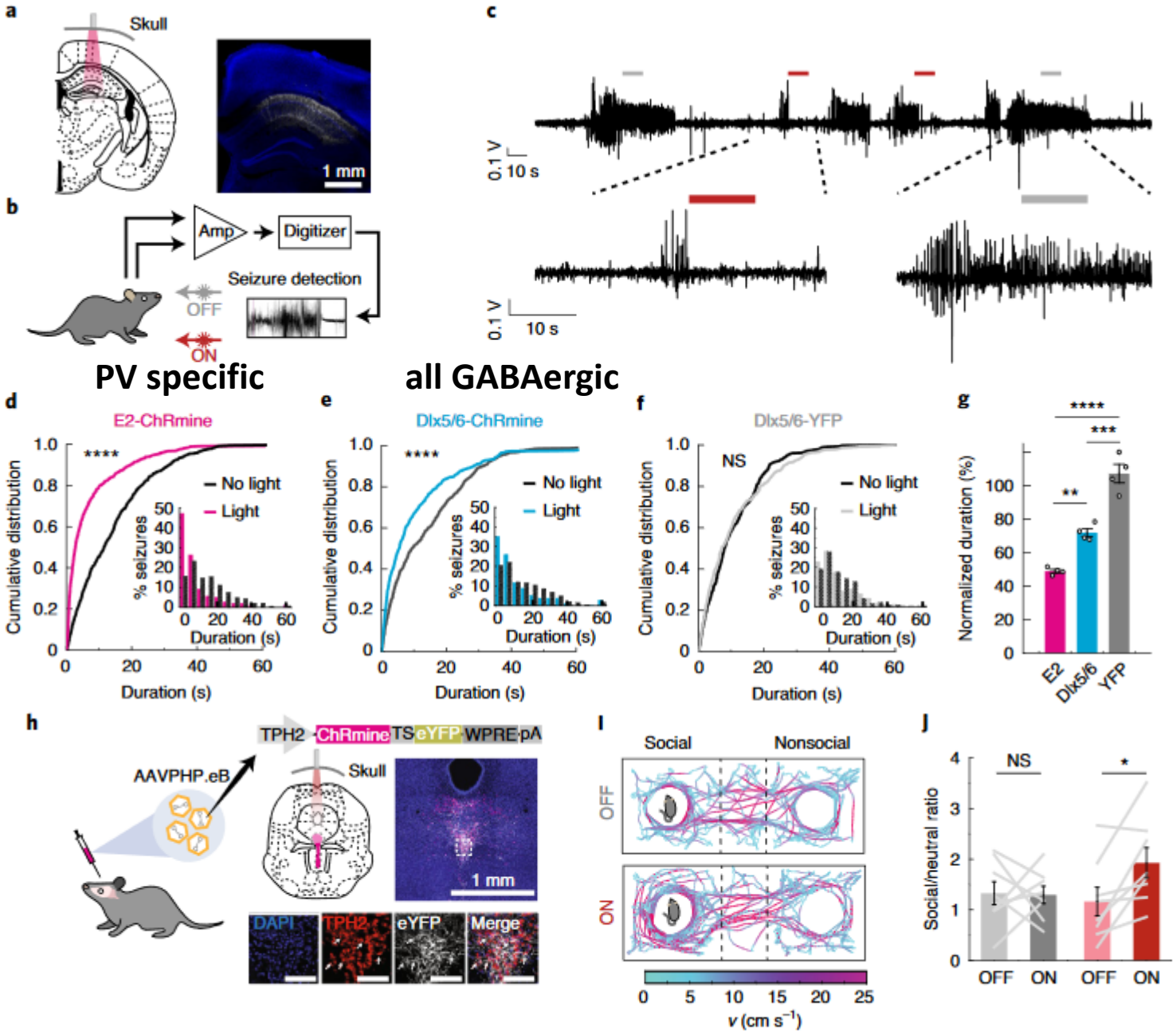
Deep brain optogenetics without intracranial surgery

Ritchie Chen[1,6], Felicity Gore[1,6], Quynh-Anh Nguyen[2], Charu Ramakrishnan[1], Sneha Patel[1], Soo Hyun Kim[1], Misha Raffiee[1], Yoon Seok Kim[1], Brian Hsueh[1], Esther Krook-Magnusson[3], Ivan Soltesz[2] and Karl Deisseroth[1,4,5]

Transcranial optogenetic activation does not require fiber implants



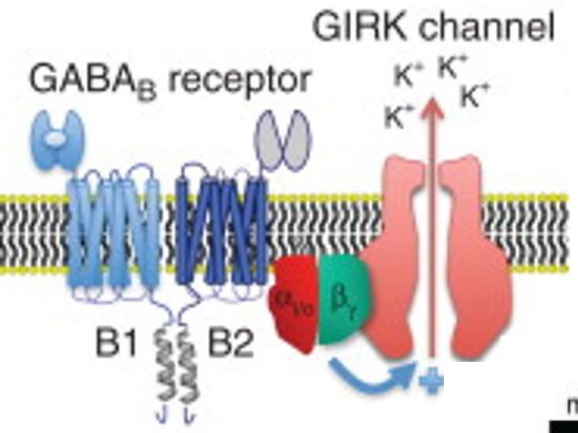
Transcranial optogenetics in translational settings

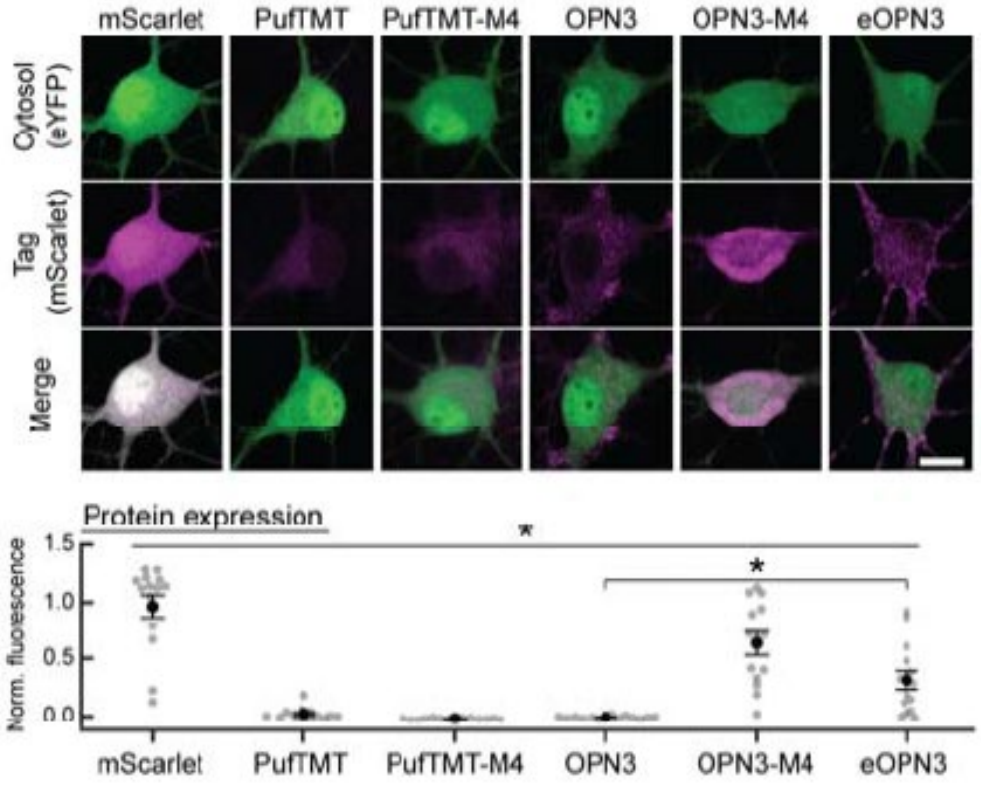


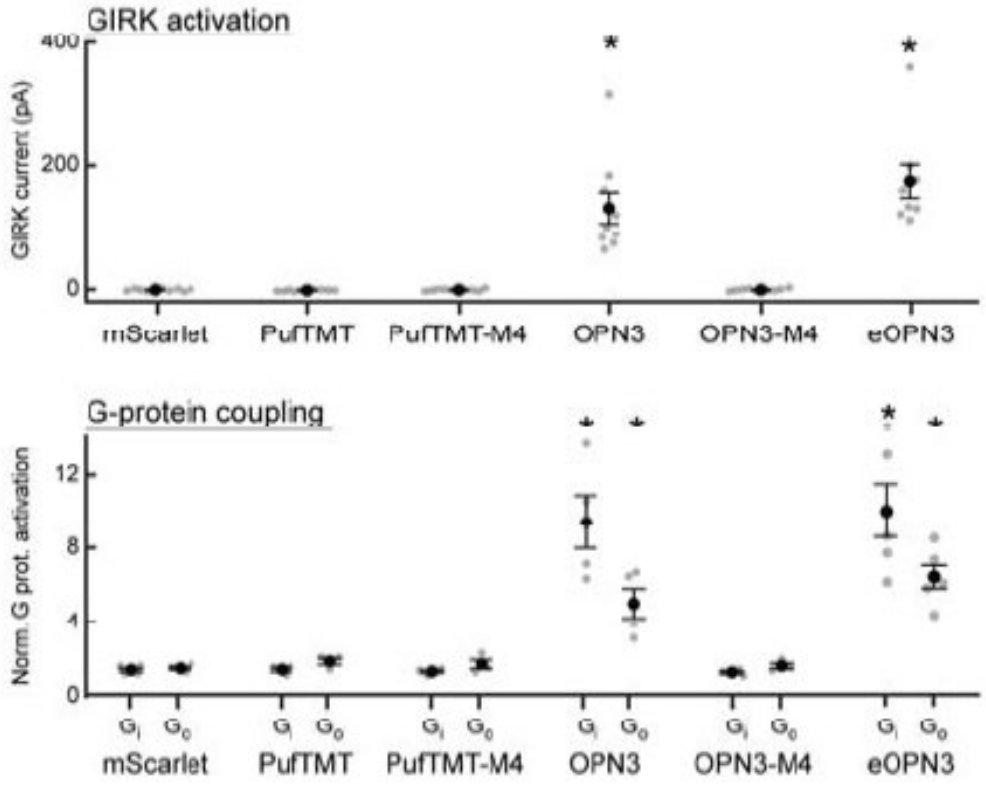
Optogenetic silencing of neurotransmitter release with a naturally occurring invertebrate rhodopsin

Mathias Mahn[1,2]*, Inbar Saraf-Sinik[1]*, Pritish Patil[1]*, Mauro Pulin[3]*, Eyal Bitton[1], Nikolaos Karalis[2], Felicitas Bruentgens[4], Shaked Palgi[1], Asaf Gat[1], Julien Dine[1], Jonas Wietek[1], Ido Davidi[1], Rivka Levy[1], Anna Litvin[1], Fangmin Zhou[3], Kathrin Sauter[3], Peter Soba[3], Dietmar Schmitz[4-9], Andreas Lüthi[2], Benjamin R. Rost[5], J. Simon Wiegert[3] and Ofer Yizhar[1]

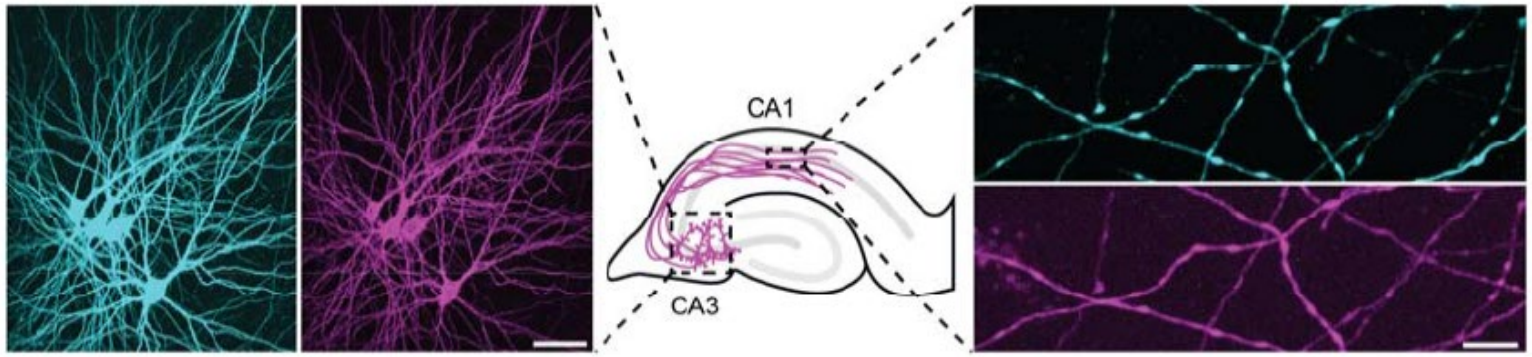
New tools for optogenetic inhibition of axonal projections

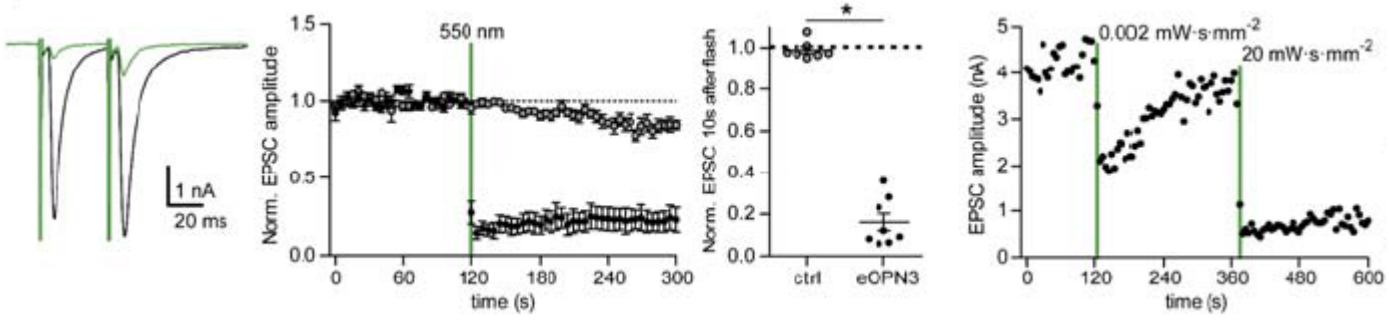




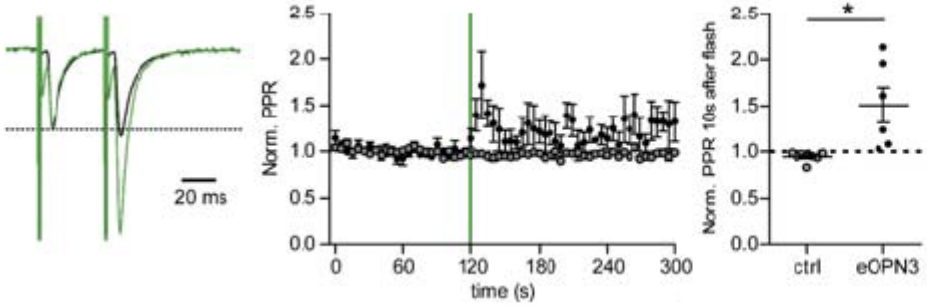


eOPN3 inhibition in cultured electroporated hippocampal cultures

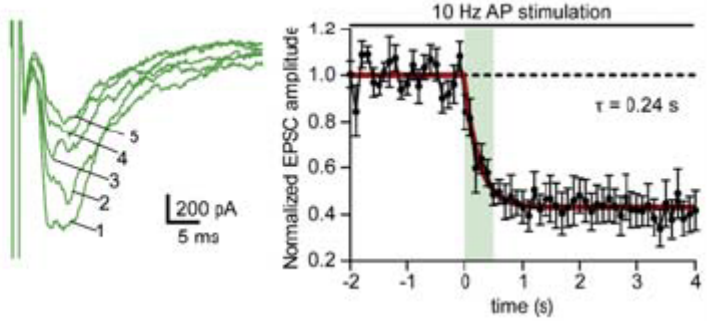




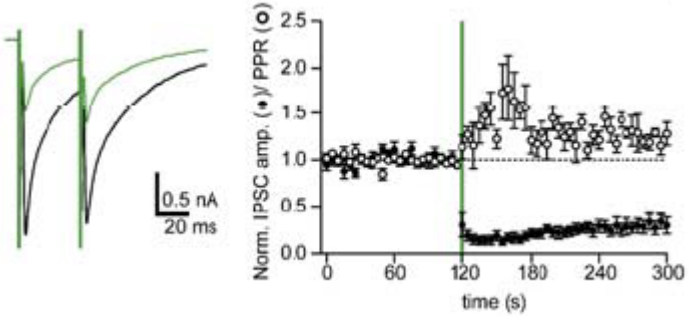
Pair-pulse facilitation → short term synaptic plasticity



240 ms latency

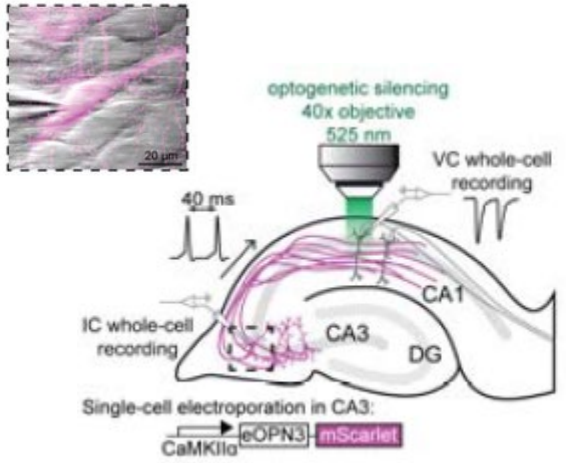


Inhibition of IPSCs



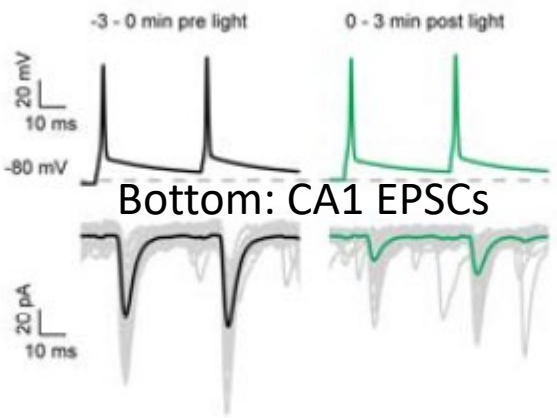
eOPN3 induces long-lasting reversible axonal inhibition

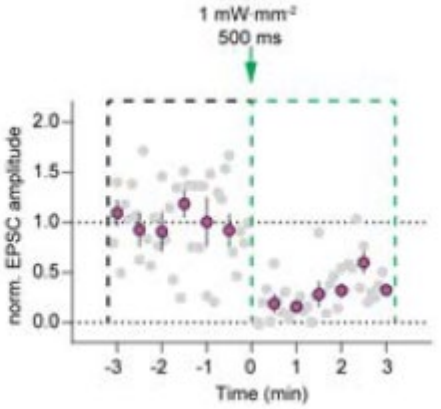
Organotypic slice cultures CA1-CA3 pairs (single cell electroporation)

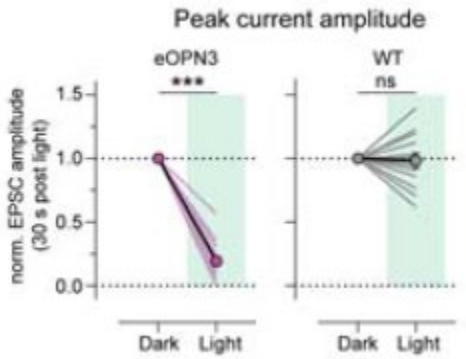


Top: CA3 APs

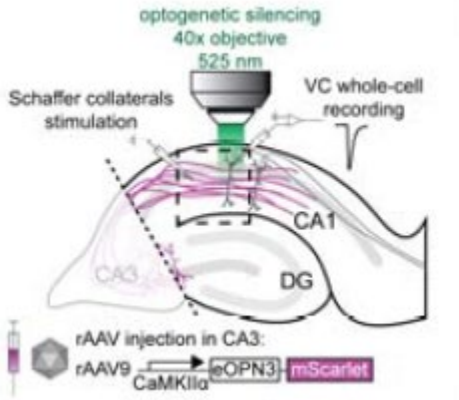
Bottom: CA1 EPSCs

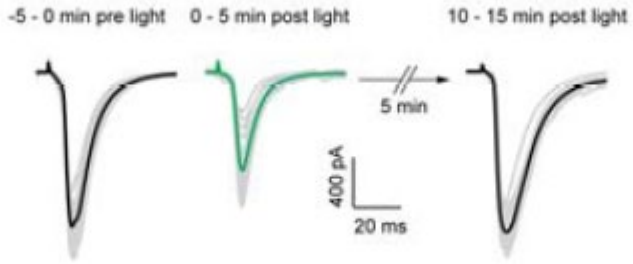


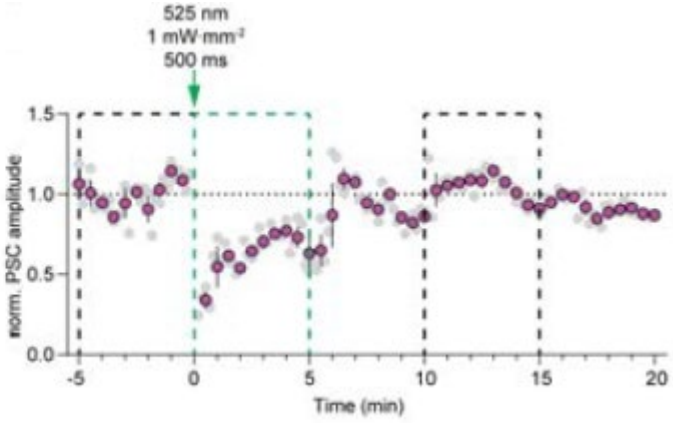


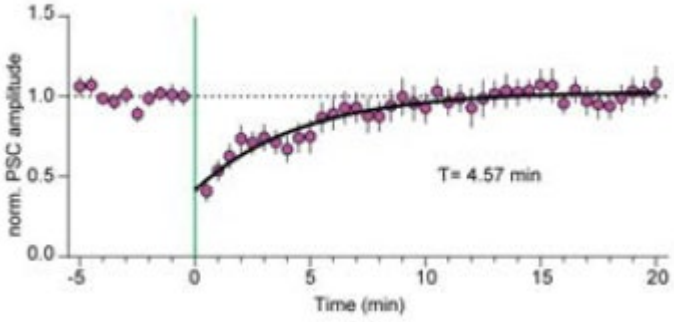


Organotypic slice cultures CA3 axons in CA1 (AAV injection)

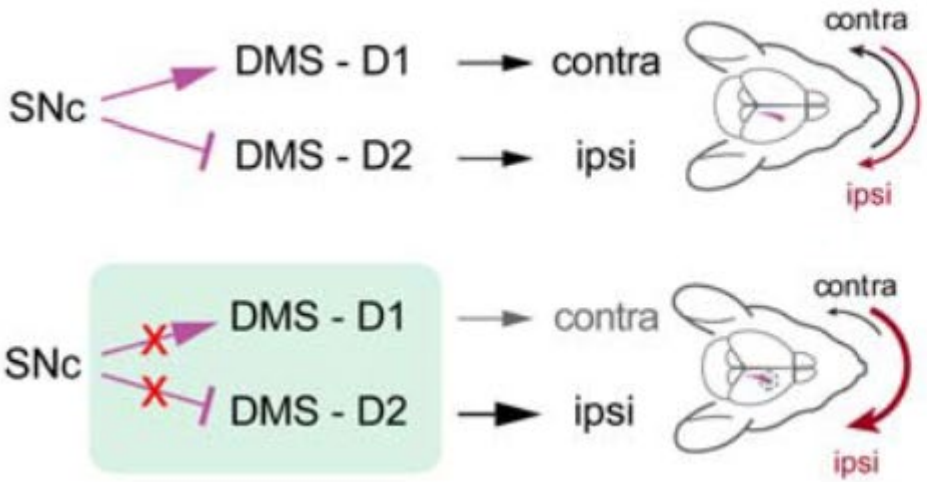


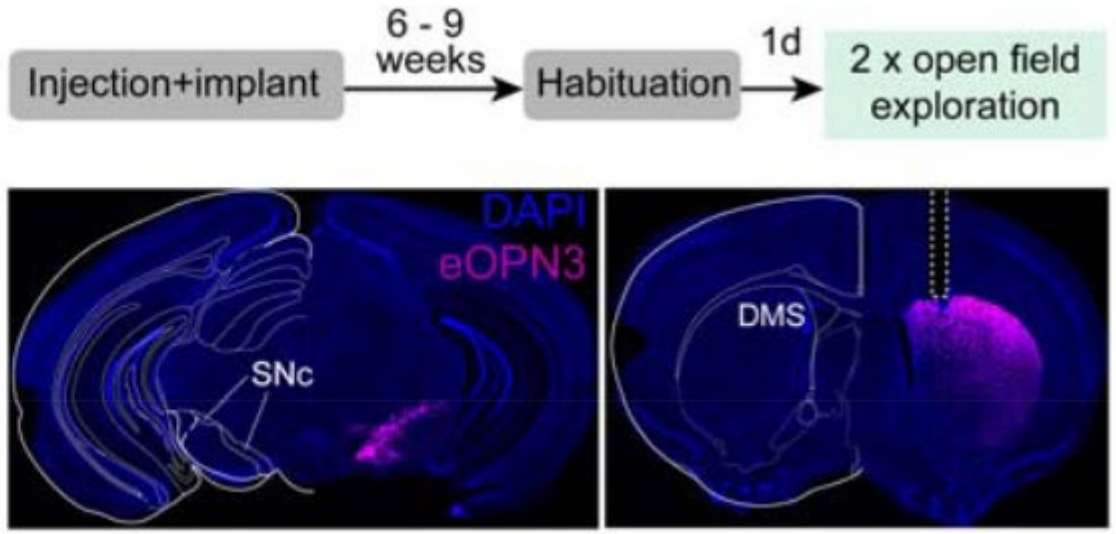


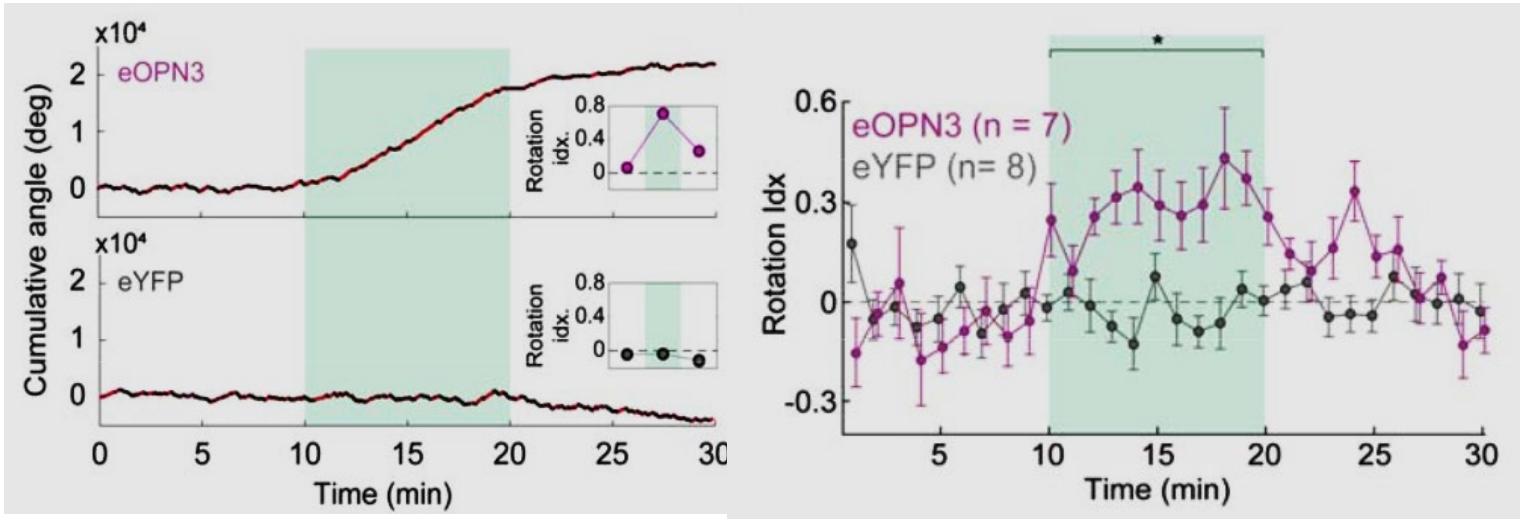




eOPN3 in vivo validation







Same phenotype in 6-OHDA PD mouse model

Outlook

- Potential pitfalls

- Temporal/spatial precision

- Light penetration depth

- Off target effects (signaling cascades, heating, epigenetics)

- In vivo compensation

- Construct delivery for translational use

- Future perspectives

- Tools development (compartments, red shifting)

- Integration with other (optical) methods

- Translational use (cell-type specific)