

Optogenetics and electrophysiology

Lex Kravitz

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I will present data about specific vendors and products, but this is not an endorsement of these products over others on the market.

I have no financial ties to any products, presented here or otherwise.

Outline

Getting Started/Light sources

Opsins

Integration with electrophysiology

Conceptual thoughts about optogenetics

The hardware of optogenetics

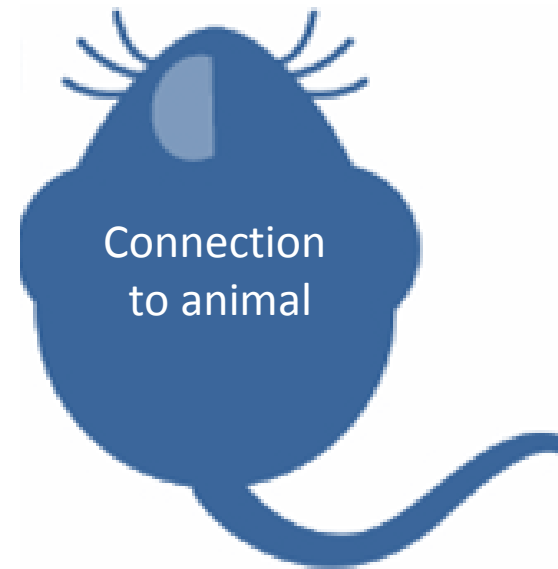
1.



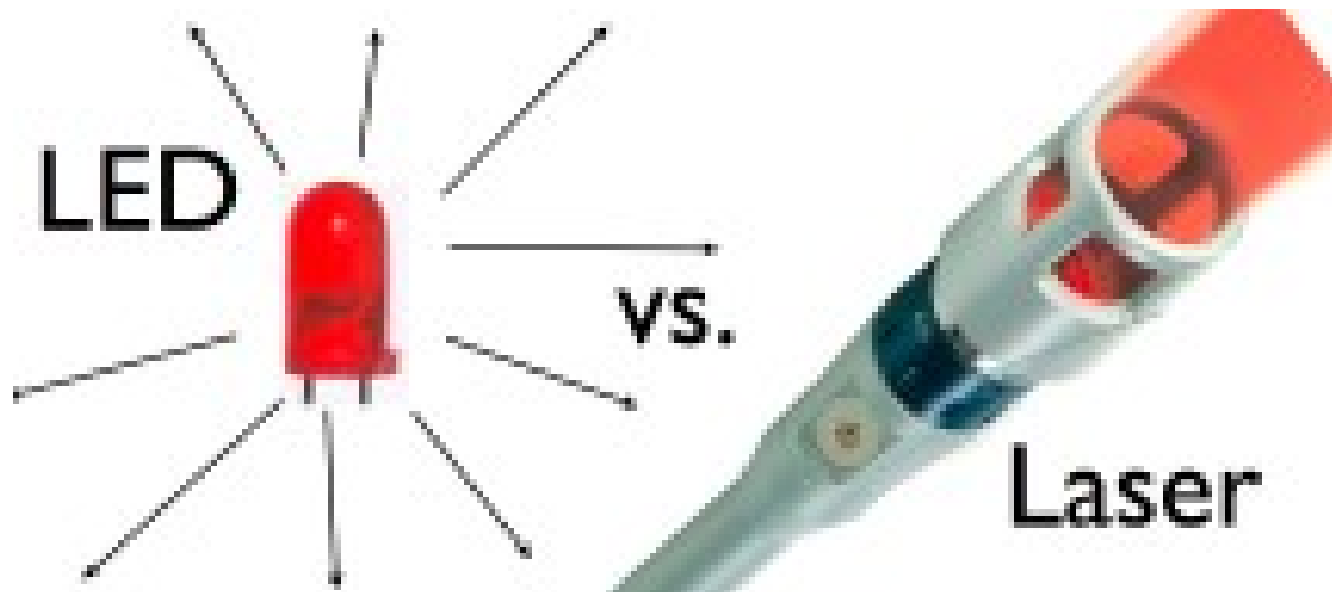
2.



3.



1. Light source

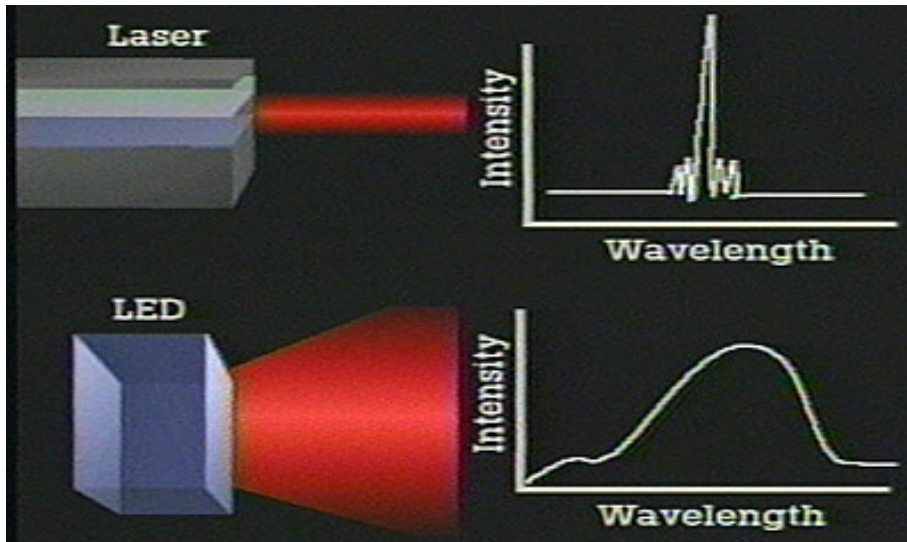


Advantages of Lasers



- Can more efficiently couple light into a fiber
- Can be used with small core (62.5micron) fiber

Advantages of Lasers



- Can achieve a more specific output wavelength

Advantages of LEDs

- Cheaper (~\$350)
- Multiple color options



Royal 450nm



Blue 465nm



Green 525nm



Yellow 590nm



Orange 615nm



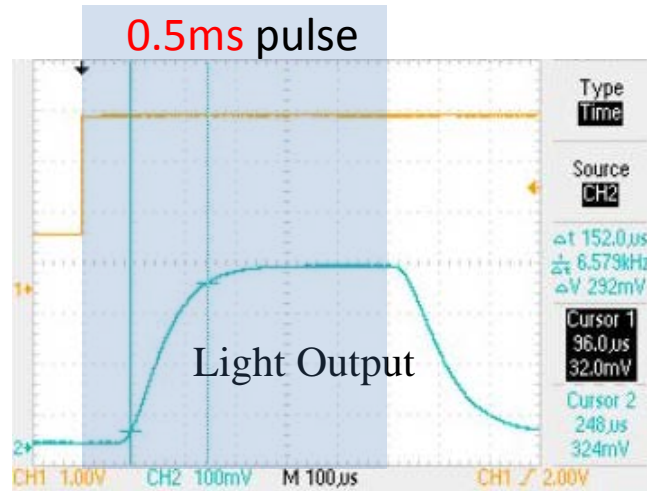
Red 625nm



Crimson 645nm

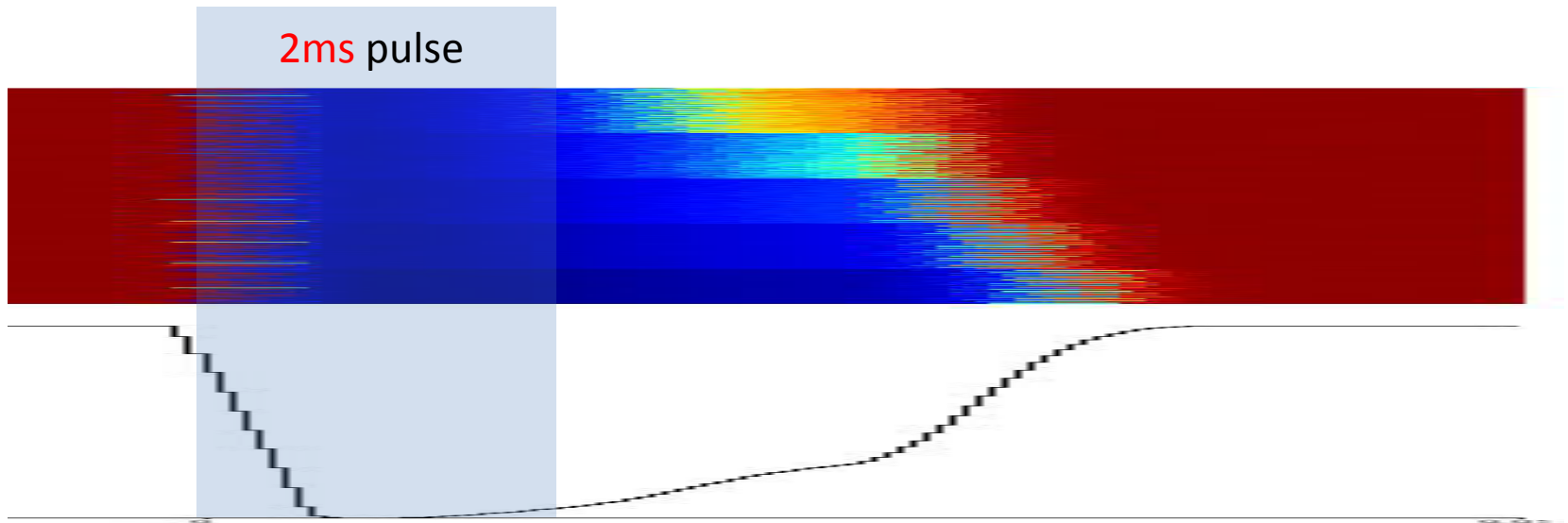
Advantages of LEDs

LED



- Better temporal precision when switching on and off

laser



Mechanical shutters



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CONNECTORIZED MECHANICAL SHUTTER ADAPTER

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LED Assemblies ▶

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**Great news for users of laser shutter systems:
Add-on connectorized mechanical shutter adapter for SR475**

The modulation of light signal is very important for optogenetics experiments. The light sources, like LEDs or laser diodes are well-suited for direct electrical modulation, while some laser types require external modulation via mechanical shutters or acousto-optic modulators.

Recently we have connectorized 3 mm aperture SR475 shutter head from Stanford Research Systems Inc with an add-on accessory . The assembly provides relatively inexpensive alternative to acousto-optic modulators. We can supply the adapter only or connectorized SR475 shutter head with or w/out SR470 Laser Shutter Controller.

ORDERING CODE: CMSA-SR475_FC-FC

Optical Input Receptacle Code
FC is stock item, SMA is custom product

Optical Output Receptacle Code
FC is stock item, SMA and M3 available as custom products.



[CONTACT US](#)

© DORIC LENSES INC

357 rue Franquet - Québec, (Québec) - G1P 4N7, CANADA

Tel. : (418) 877-5600 - Fax. : (418) 877-1008

Advantages of LEDs

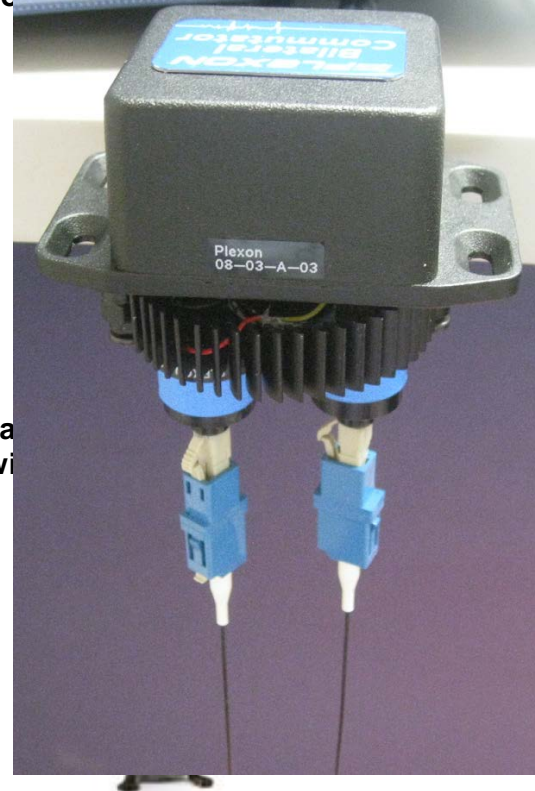
Much simpler to deploy

Fiber optic rotary joint



LED power/control signals and optional neural recording lines

Comp
rotate wi

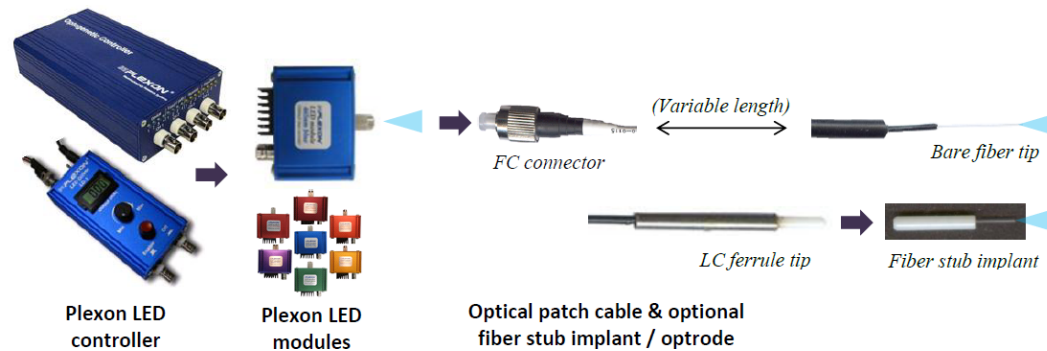


LEDs vs lasers

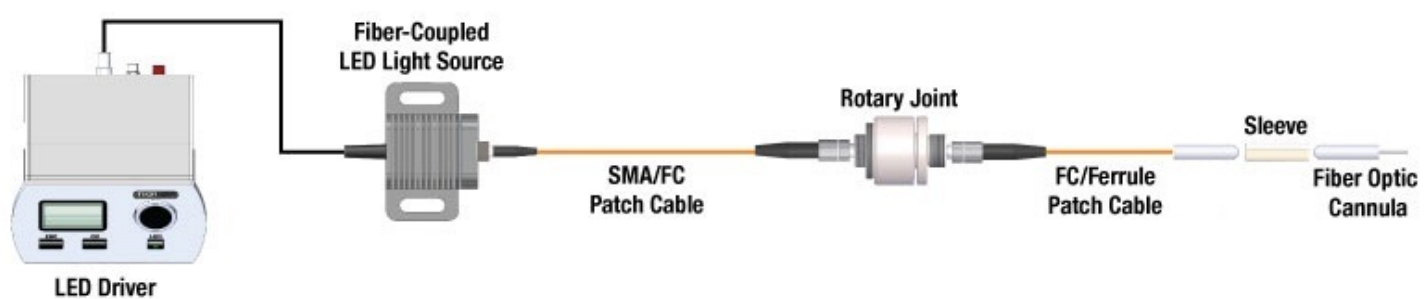
Lasers	LEDs
Can more efficiently couple light into a fiber	Cheaper
Can be used with small core (62.5micron) fiber	Multiple color options
Can achieve a more specific output wavelength	Better temporal precision
	Simpler to deploy
~\$4000 laser, mechanical shutter, rotary joint	~\$2000 LED driver, LED on commutator

Starter kits (~2000-\$4000)

Plexon:



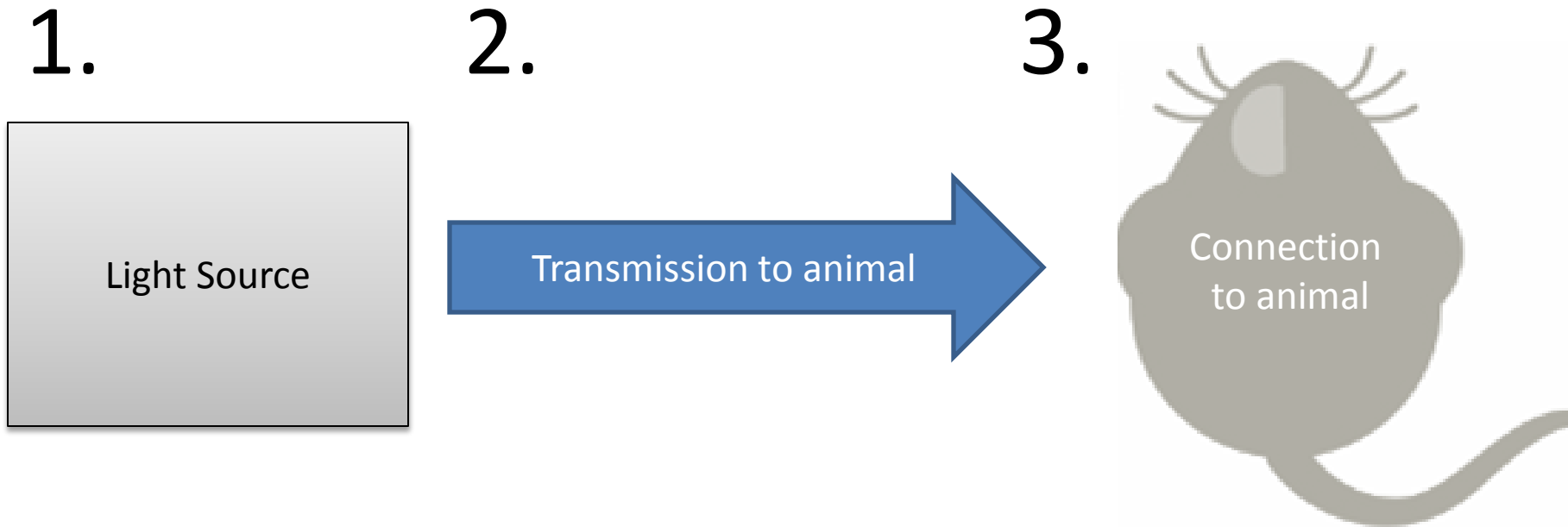
ThorLabs:



Doric Lenses:

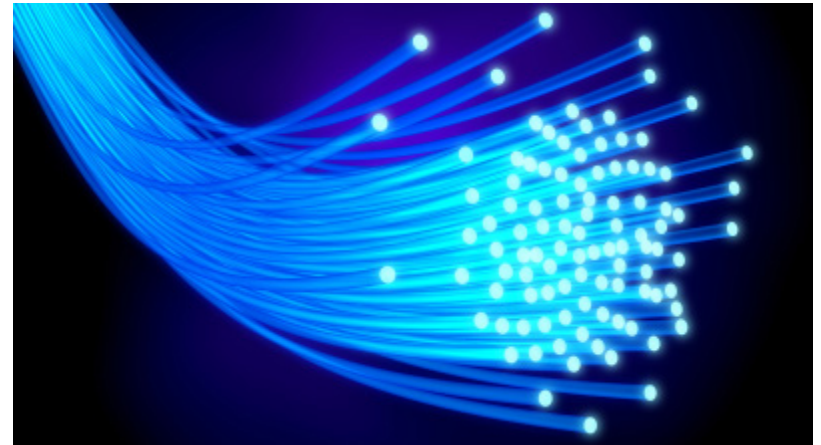


Getting started with optogenetics



2. Transmission to the animal

- LEDs require larger (<200 micron) core fiber
 - \$\$\$
- Lasers require optical commutator
 - \$\$\$
- Other considerations such as NA, core material, cladding material, etc may affect specific applications



In general, the specific fiber is probably not as important as the total light output of the fiber - if you get enough light your fiber choice is fine

2. Transmission to the animal

THORLABS

FN96A

**Guide to Connectorization and
Polishing Optical Fibers**

- Cable Assembly
- Manual Fiber Polishing
- Manual Fiber Cleaving



2. Transmission to the animal

- Power meters - ~\$500-2500

Optical Power Meter Kits

- ▶ Kits Include Meter, Sensor, and Post Assembly
- ▶ Digital or Analog Meter
- ▶ Wavelengths from 200 nm to 25 μm
- ▶ Powers from 500 pW to 10 W



PM130D

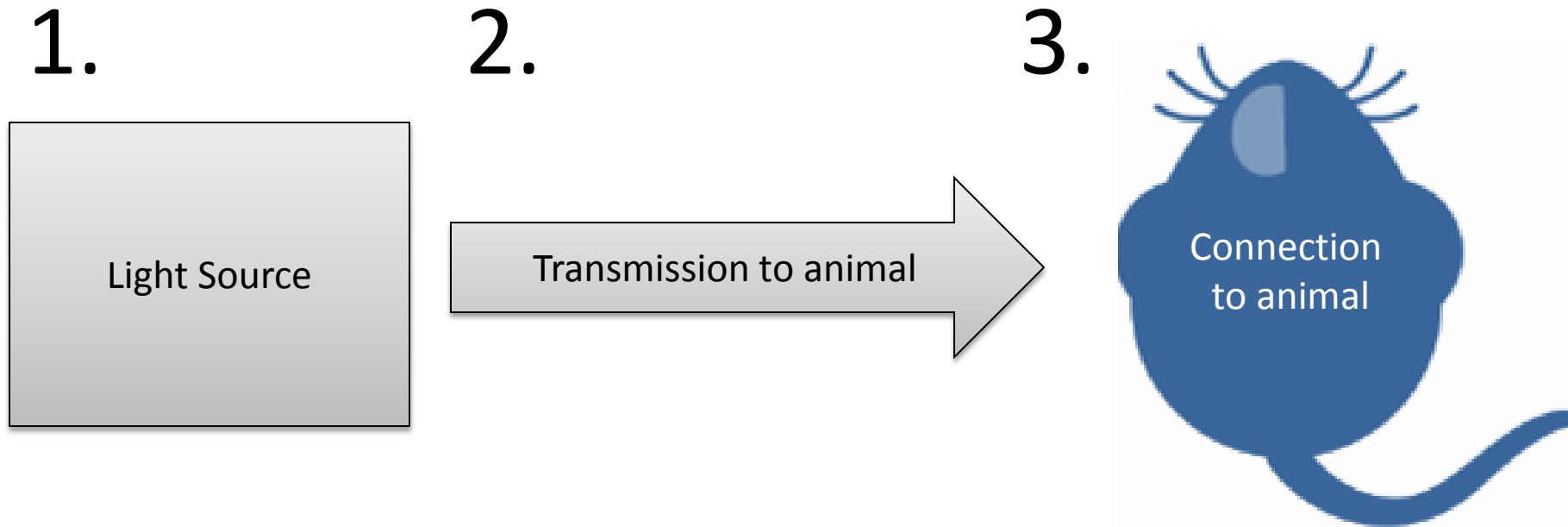


PM206



PM120VA

Getting started with optogenetics



3. Connection to animal

- 3 ways:
 - Cannulas
 - Ferrule implants
 - Head mounted LEDs (wireless)

Cannulas

- Plastics1.com

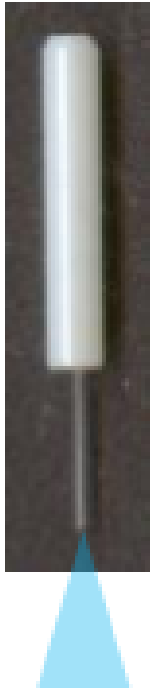


Ferrule connectors



Ferrule connectors

Fiber stub implant



Ferrule connectors

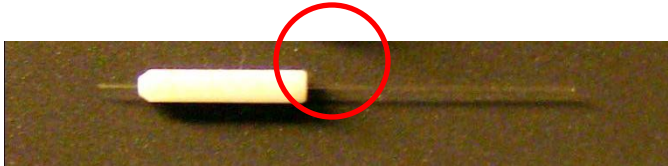
- These can be purchased for ~\$25 each (\$50/bilateral)
 - Doric Lenses
 - ThorLabs
 - Plexon, Inc
- Reusable?



Ferrule connectors

- These can be made for ~\$5 each.

Glue fiber into ferrule



Polish ferrule



What's on the horizon?



Wireless LEDs



Teleopto, Eicom

Wireless LEDs

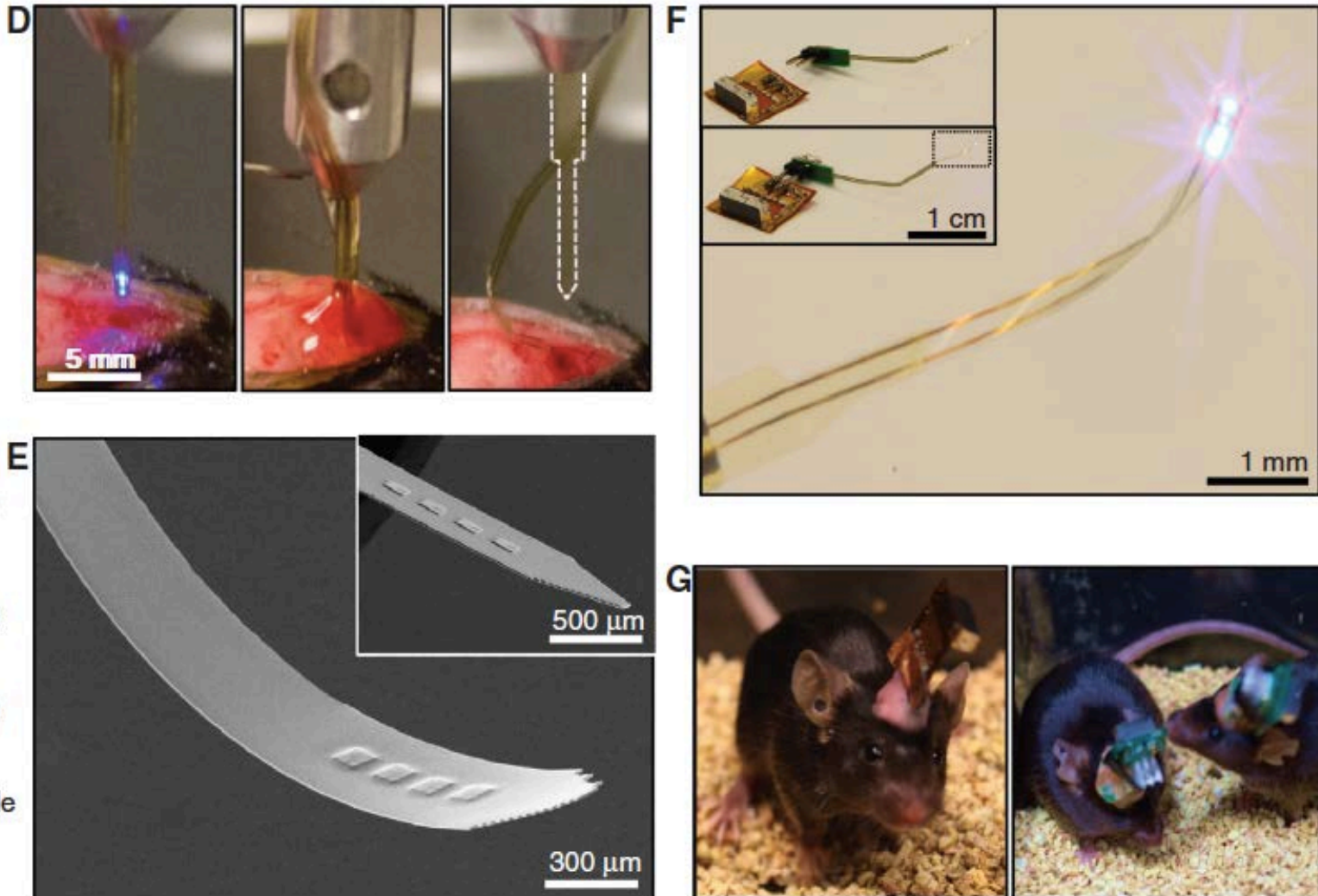


Wireless microLEDs

Injectable, Cellular-Scale Optoelectronics with Applications for Wireless Optogenetics

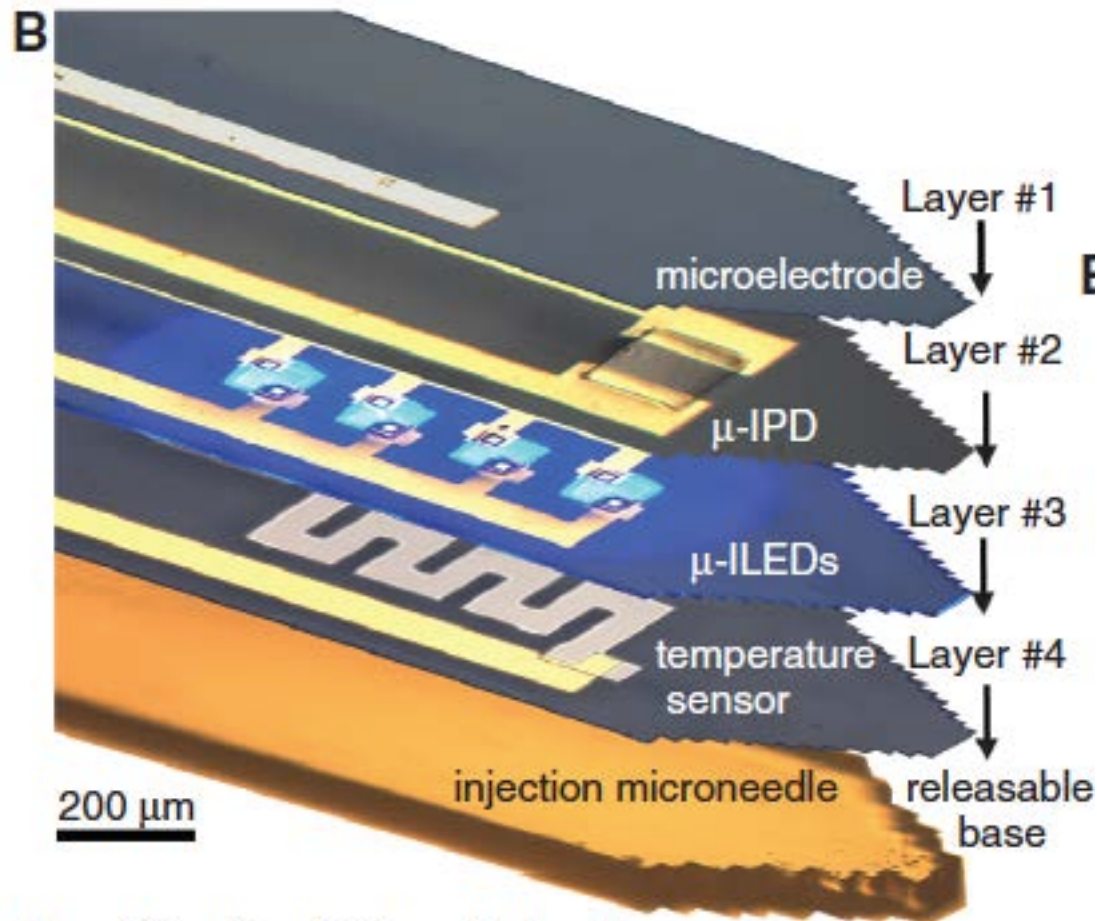
Tae-il Kim,^{1,2*} Jordan G. McCall,^{3,4,5,6*} Yei Hwan Jung,^{1†} Xian Huang,¹ Edward R. Siuda,^{3,4,5,6}
Yuhang Li,⁷ Jizhou Song,⁸ Young Min Song,¹ Hsuan An Pao,¹ Rak-Hwan Kim,¹
Chaofeng Lu,⁹ Sung Dan Lee,¹⁰ Il-Sun Song,¹¹ Gunchul Shin,¹ Ream Al-Hasani,^{3,4,5}
Stanley Kim,¹ Meng Peun Tan,¹⁰ Yonggang Huang,⁷ Fiorenzo G. Omenetto,^{12,13}
John A. Rogers,^{1,10,11,14*} ‡ Michael R. Bruchas^{3,4,5,6*} ‡

Wireless microLEDs



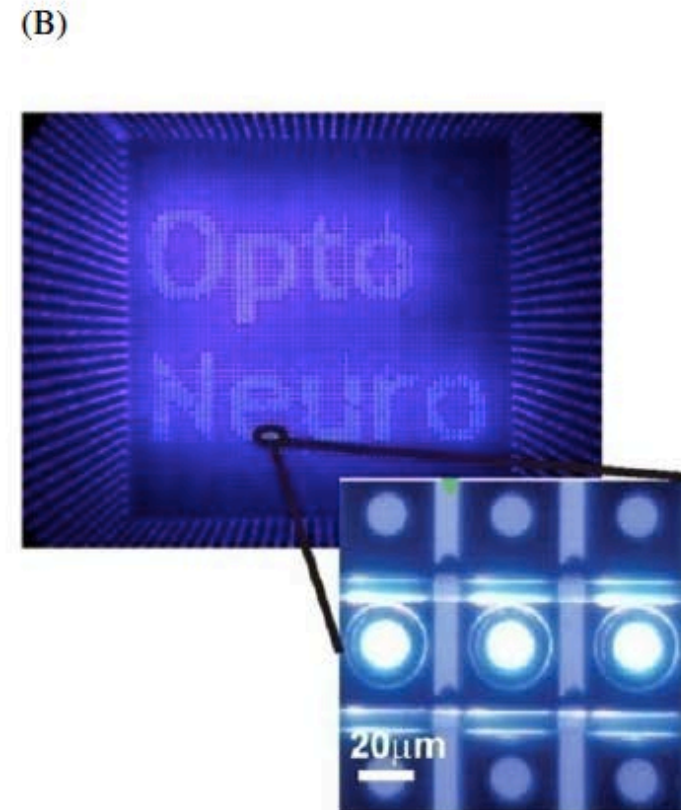
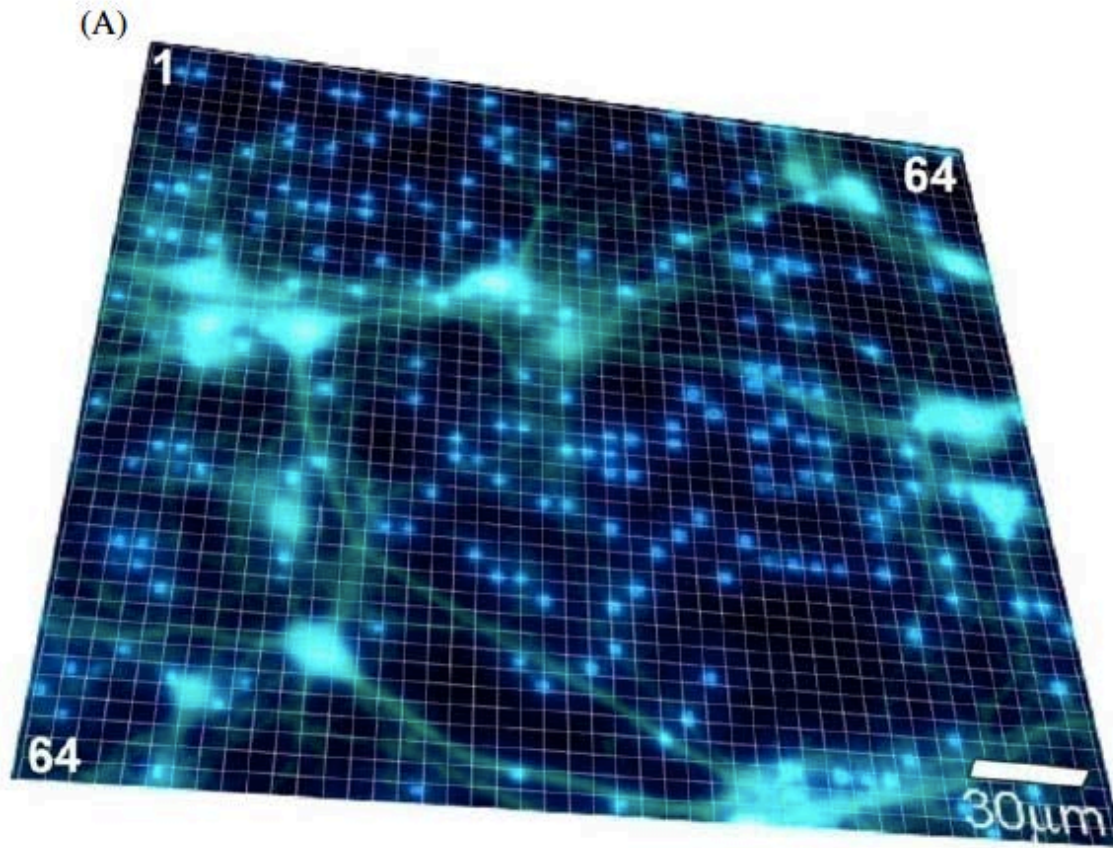
Kim, et al, Science 2013

Wireless microLEDs

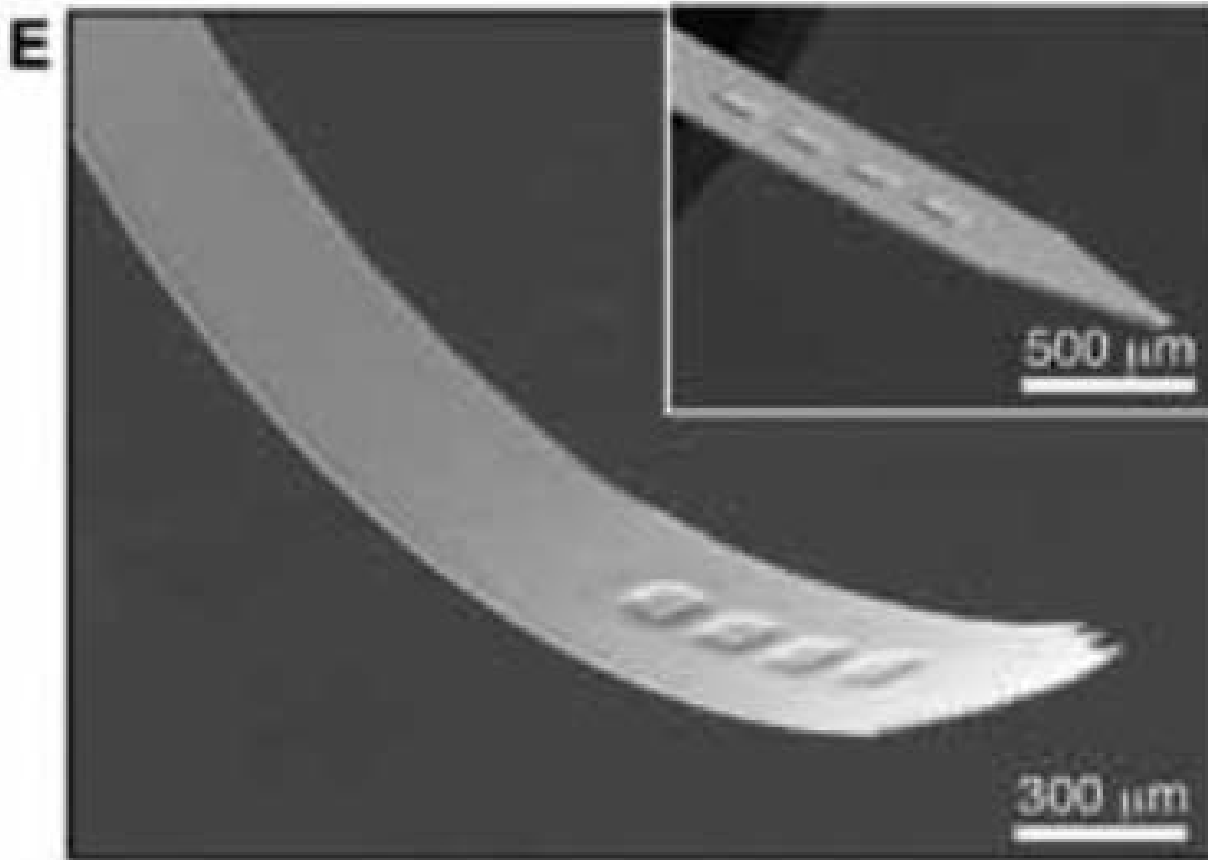


Kim, et al, Science 2013

Multi-site applications

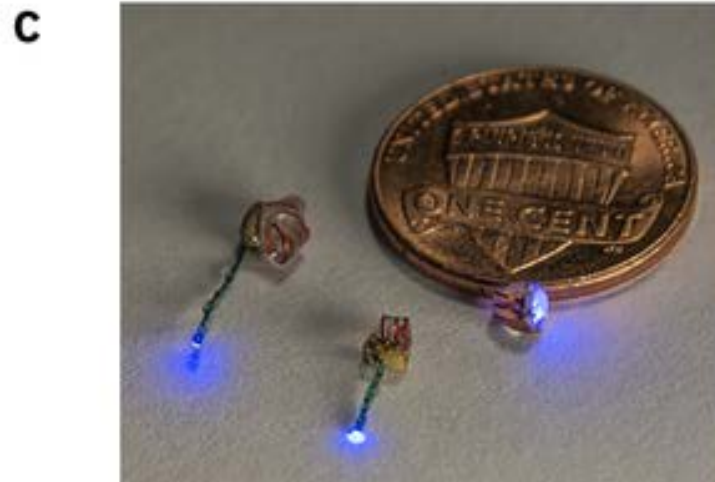
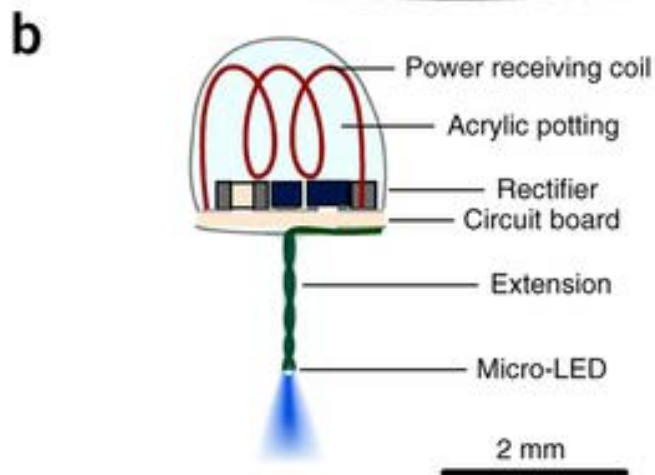


Multi-site applications

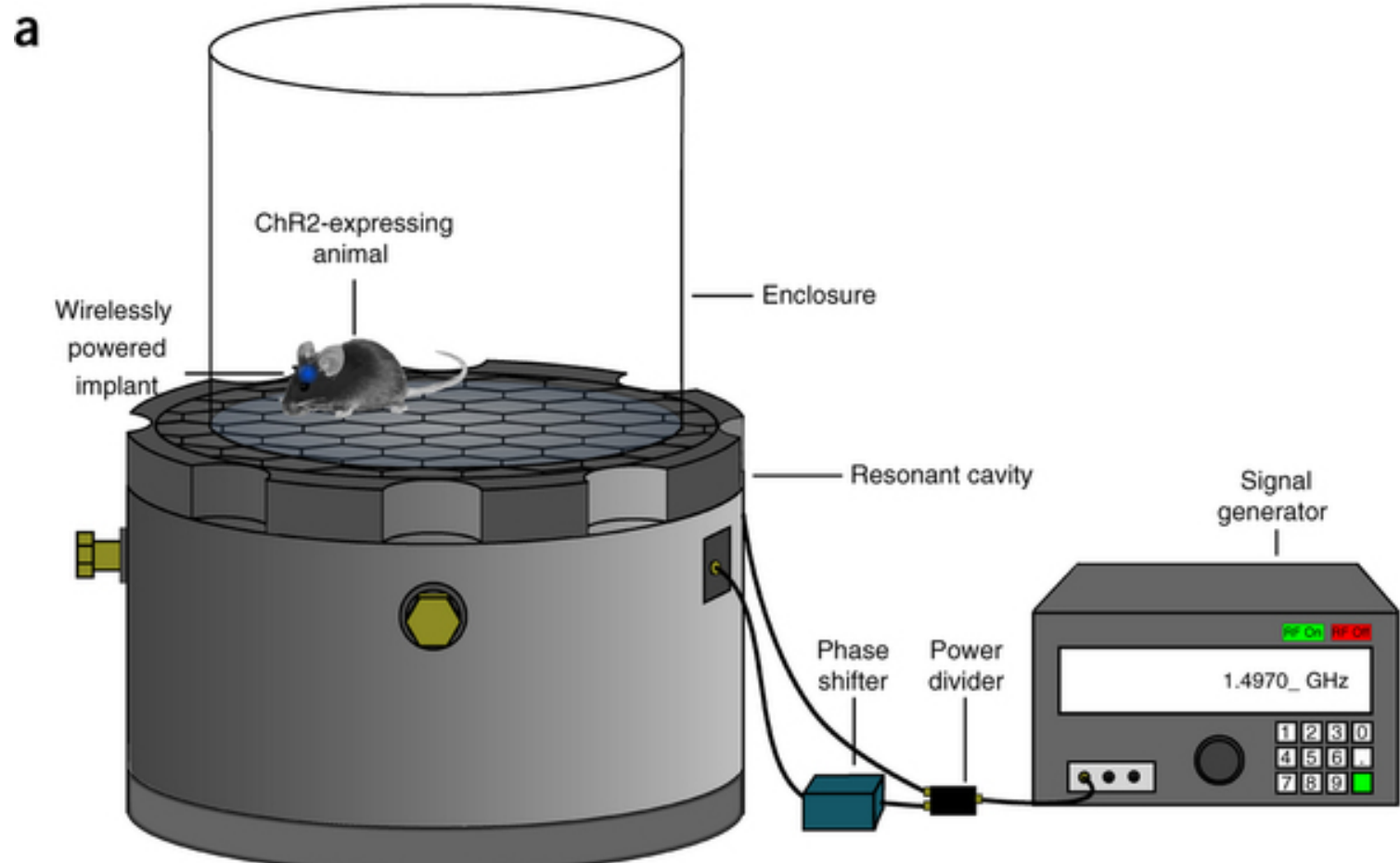


Kim, et al, Science 2013

Wireless microLEDs

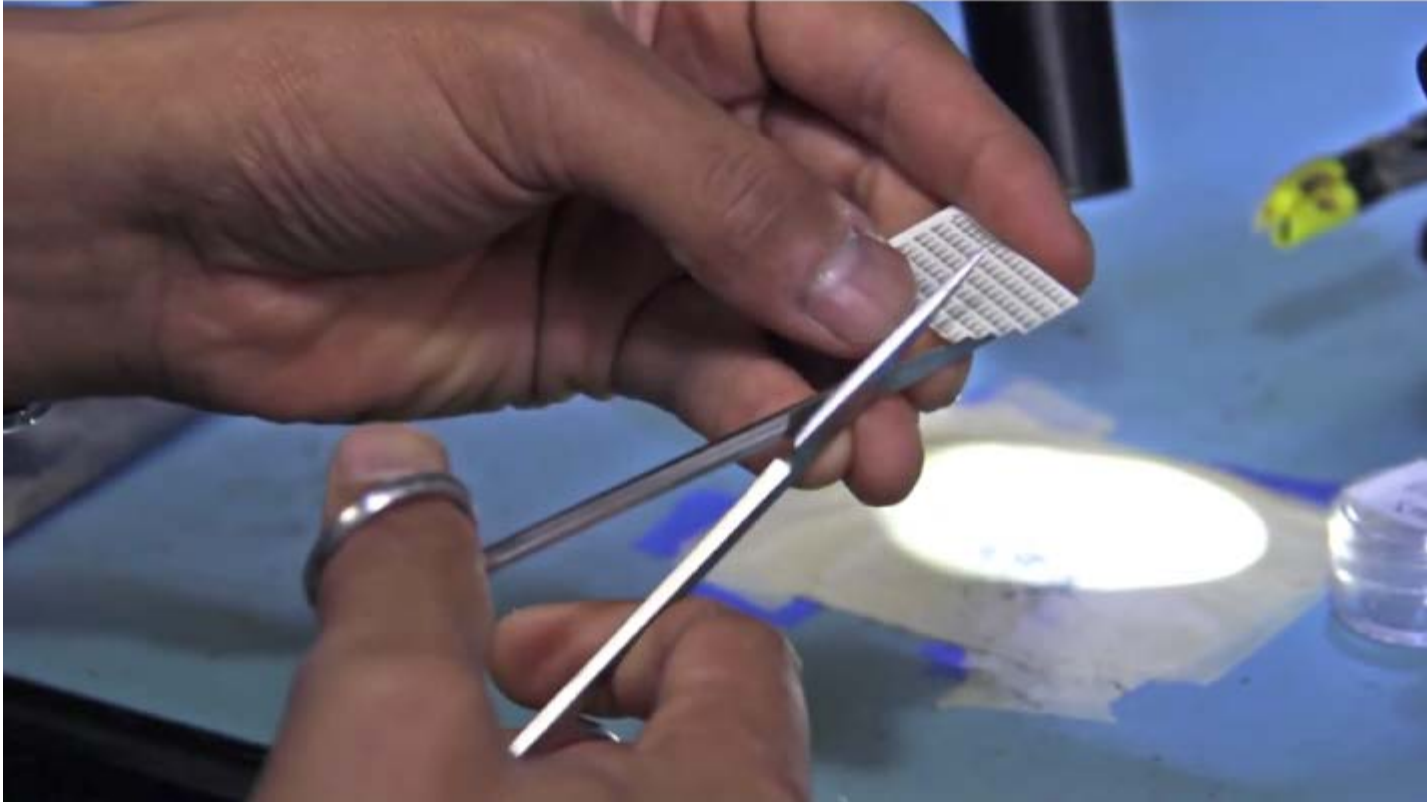


Wireless microLEDs



Montgomery, et al., *Nature Methods* (2015) doi:10.1038/nmeth.3536

Wireless microLEDs



Montgomery, et al., Nature Methods (2015) doi:10.1038/nmeth.3536

Resources

- <http://thorlabs.com>
(power meters, everything optical)
- <http://plexoninc.com> (LED light sources)
- <http://www.doriclenses.com/produits/195.html>
(LED light sources, fiber rotary joints, have developed many optogenetics devices)
- <http://www.precisionfiberproducts.com/>
(cheap source for ferrules, tools)
- <http://www.openoptogenetics.org/>

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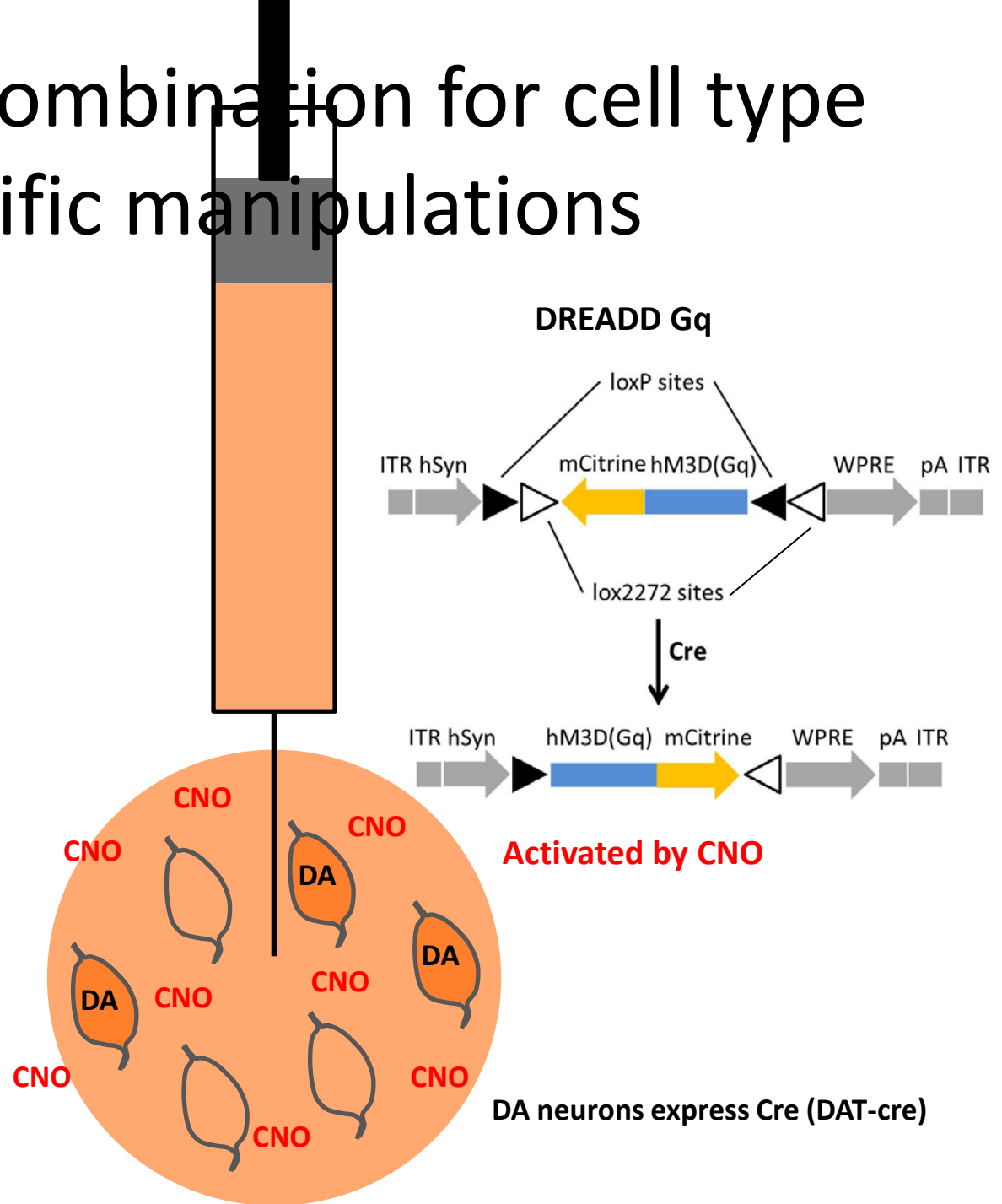
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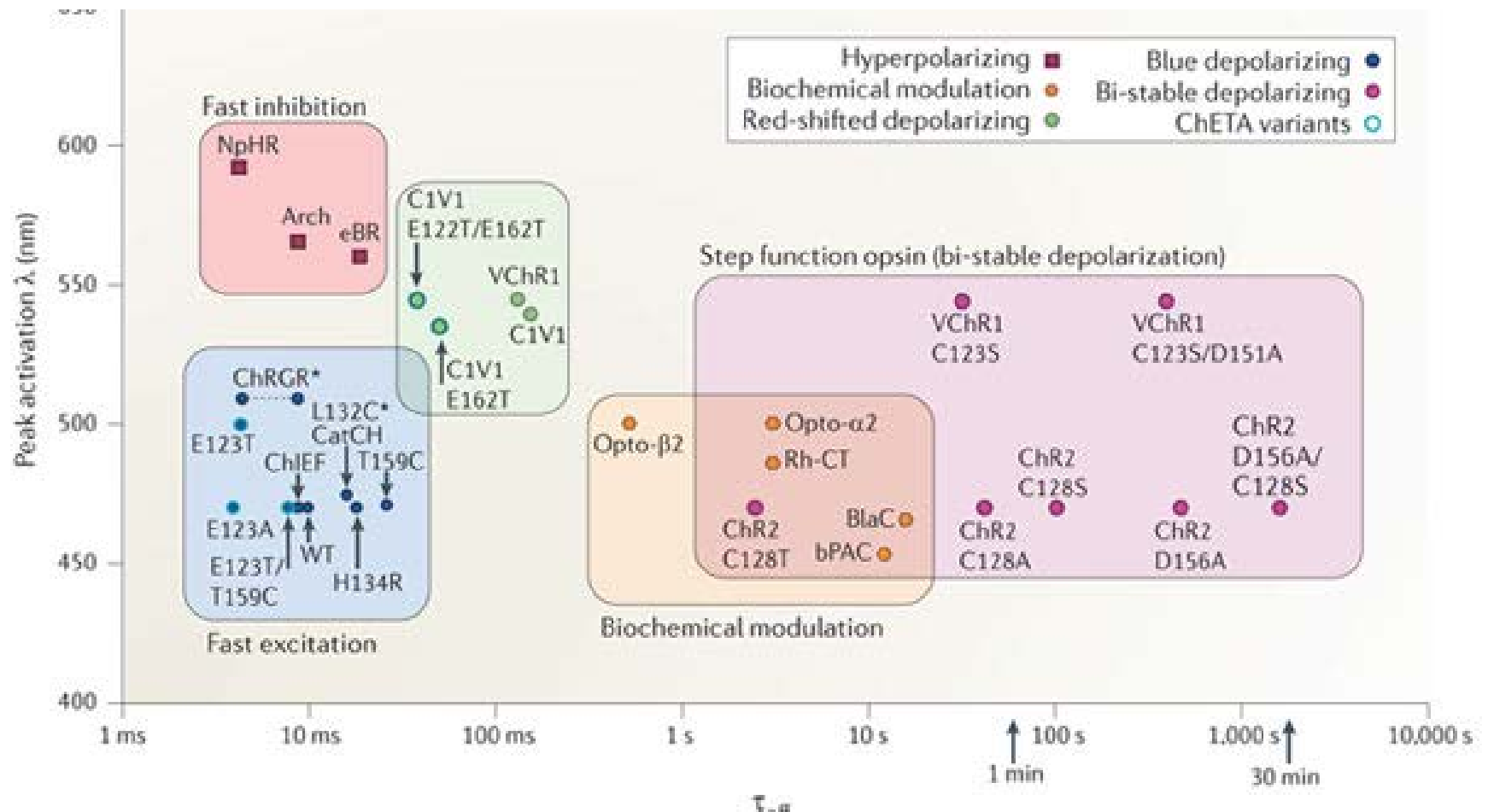
Integration with electrophysiology

Conceptual thoughts about optogenetics

Cre-lox recombination for cell type specific manipulations

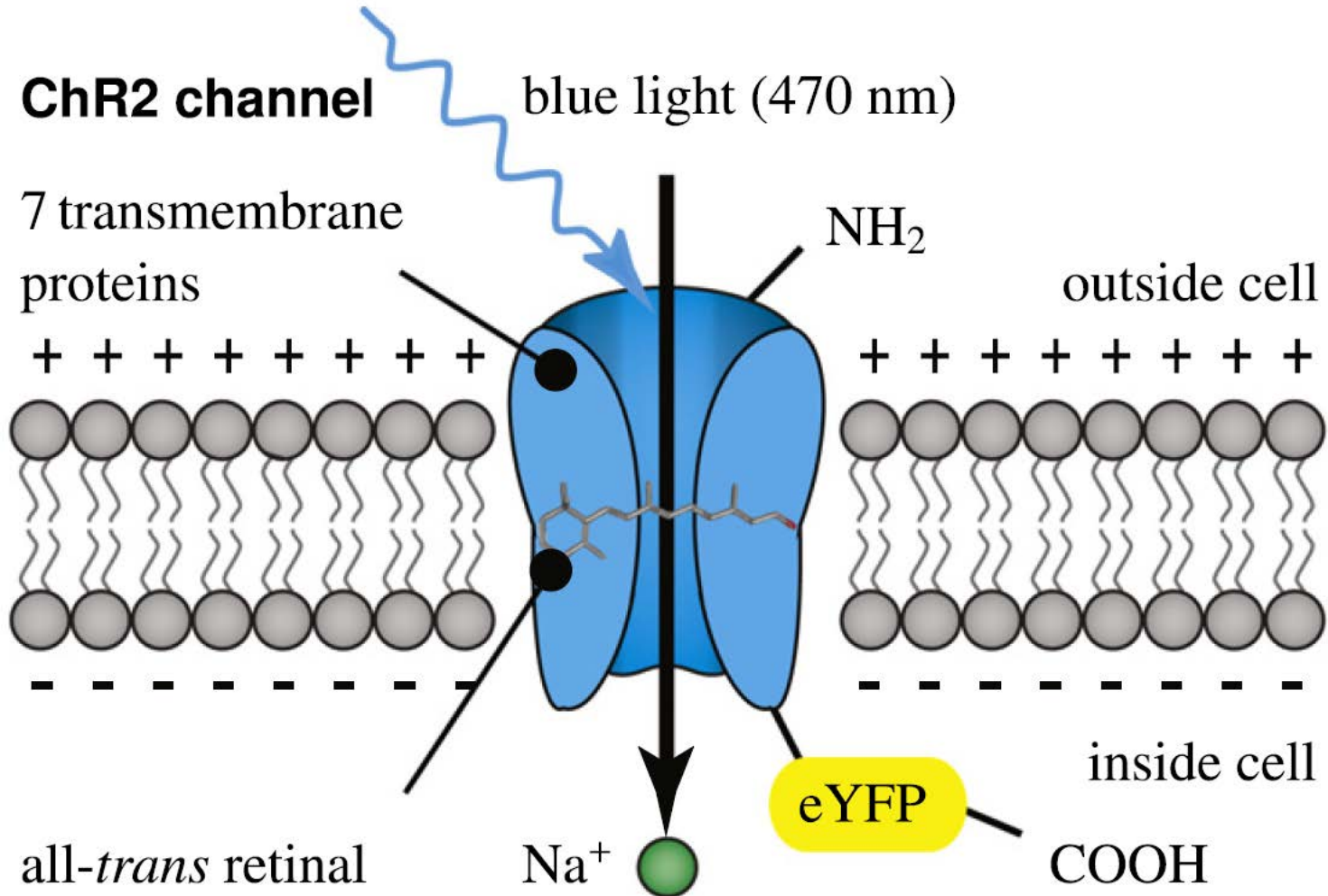


A brief survey of optogenetic tools

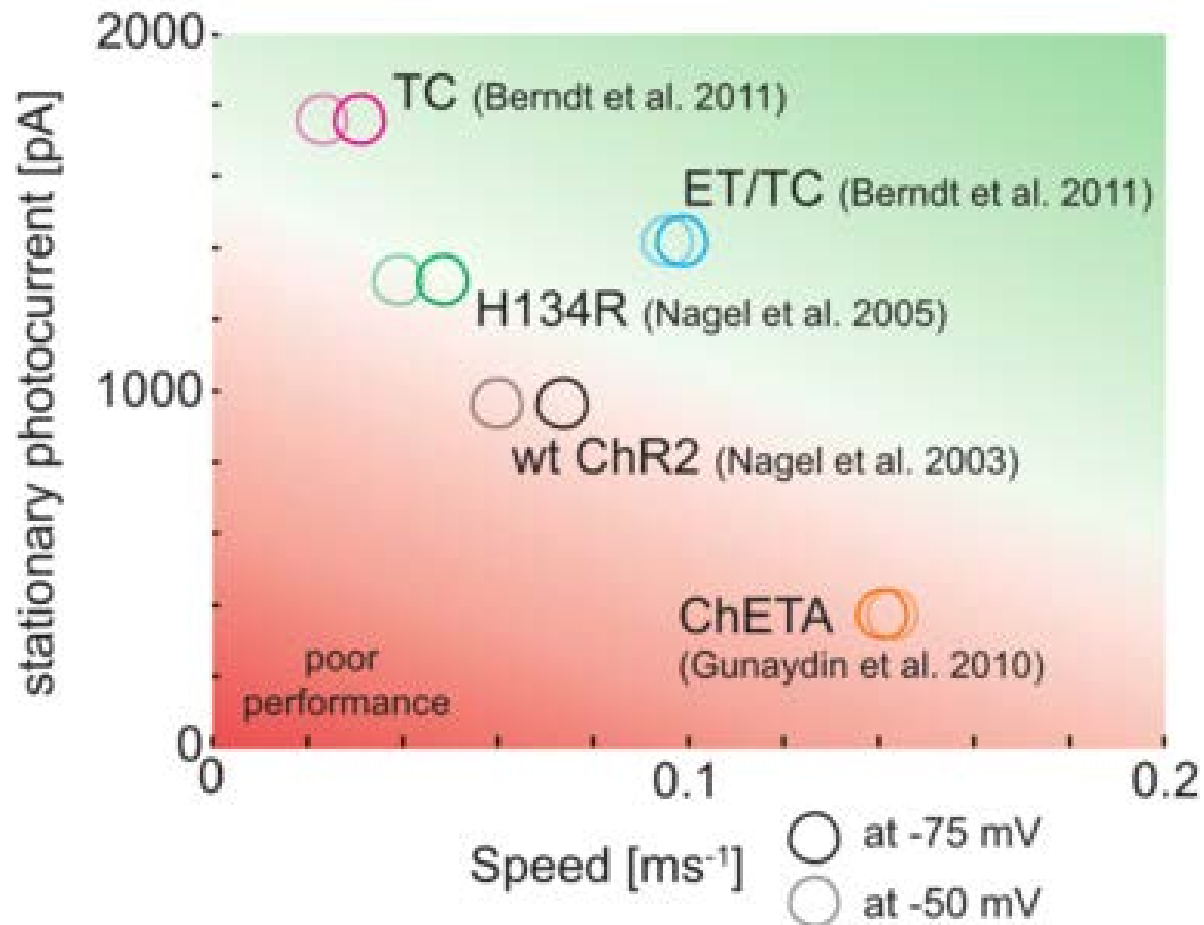


Tye and Deisseroth, *Nature Reviews Neuroscience* **13**, 251-266

Channelrhodopsin-2



Channelrhodopsin-2 variants



Red-shifted excitatory opsins

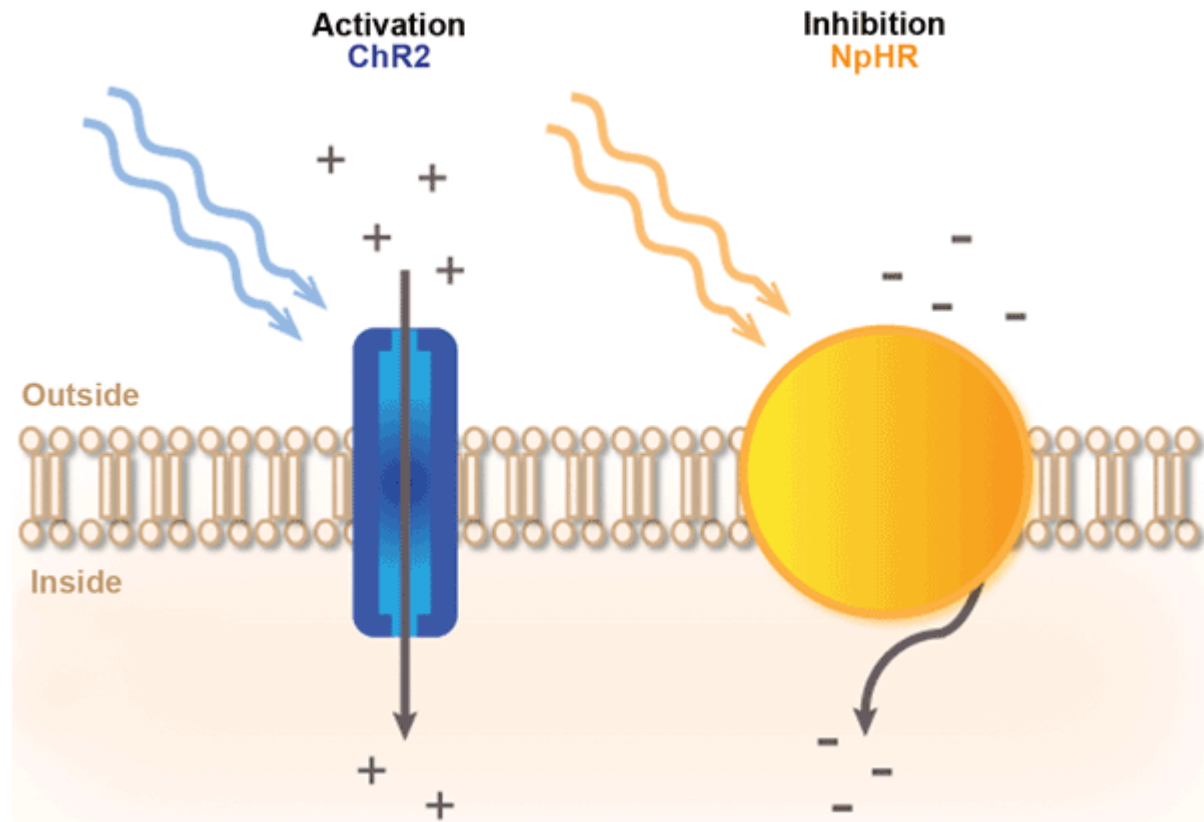
NATURE METHODS | ARTICLE



Independent optical excitation of distinct neural populations

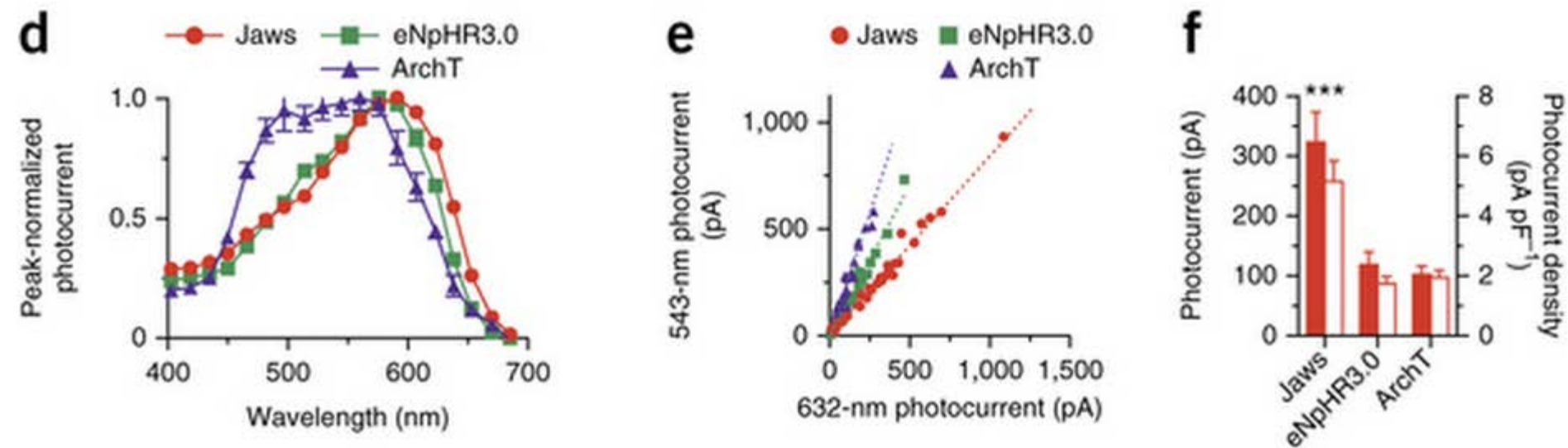
Nathan C Klapoetke, Yasunobu Murata, Sung Soo Kim, Stefan R Pulver, Amanda Birdsey-Benson, Yong Ku Cho, Tania K Morimoto, Amy S Chuong, Eric J Carpenter, Zhijian Tian, Jun Wang, Yinlong Xie, Zhixiang Yan, Yong Zhang, Brian Y Chow, Barbara Surek, Michael Melkonian, Vivek Jayaraman, Martha Constantine-Paton, Gane Ka-Shu Wong & Edward S Boyden

Inhibitory opsins



Inhibitory opsins

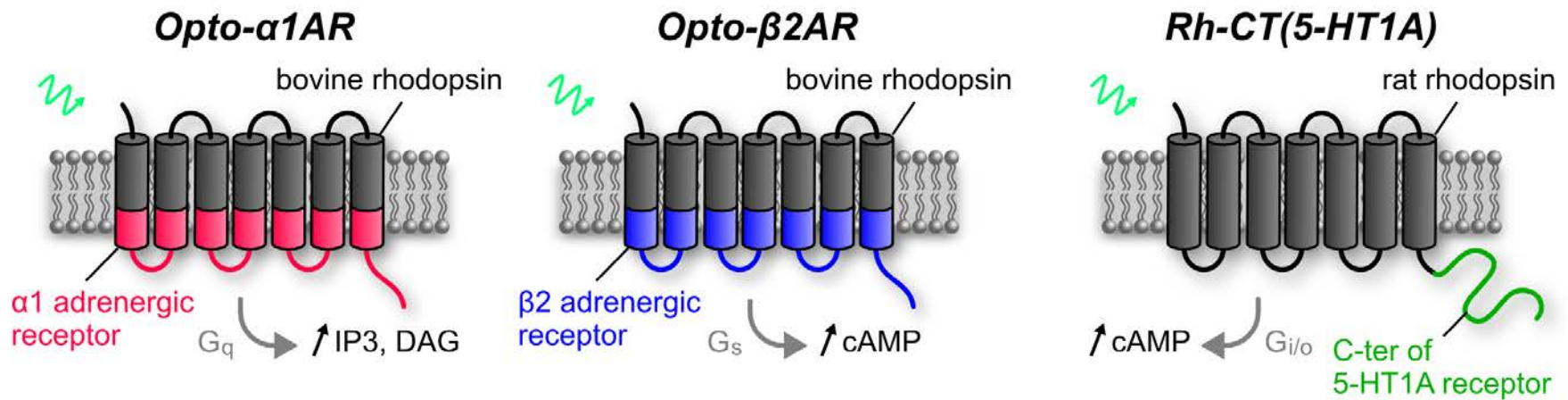
NATURE NEUROSCIENCE | TECHNICAL REPORT



Ramamani, [Rachel C Bandaru](#), Brian D Allen, Craig R Forest, Brian T Chow, Xue Han, Yingxi Lin, Kay M Tye, Botond Roska, Jessica A Cardin & Edward S Boyden

Opto-XRs

- Light activated GPCRs



Activation of motor cortex drives locomotion



Activation of hypothalamic circuits alters feeding



Activation of striatal circuits controls locomotion



Outline

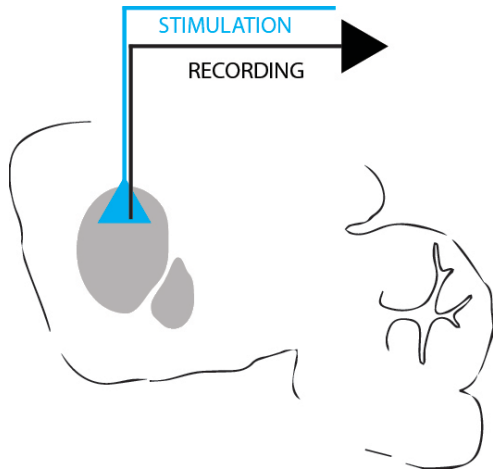
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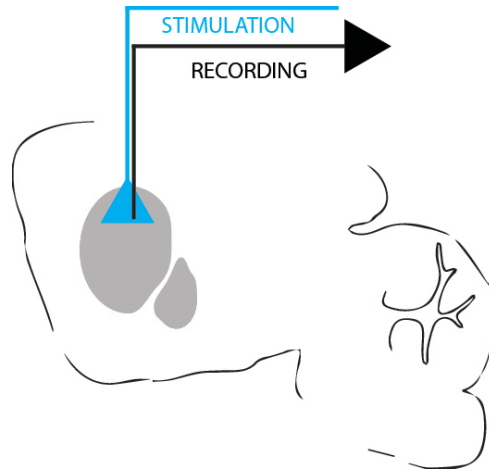
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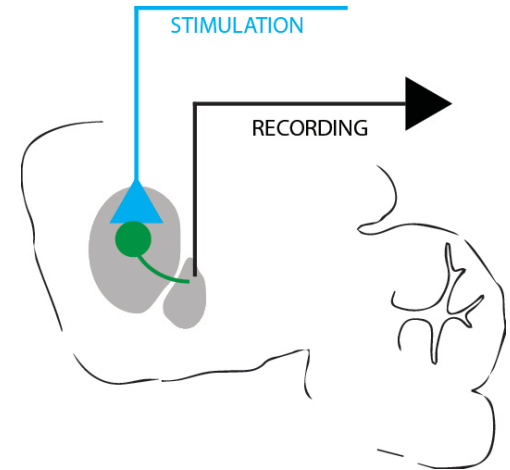
Three experimental designs



“Tagging”
Specific
Neurons

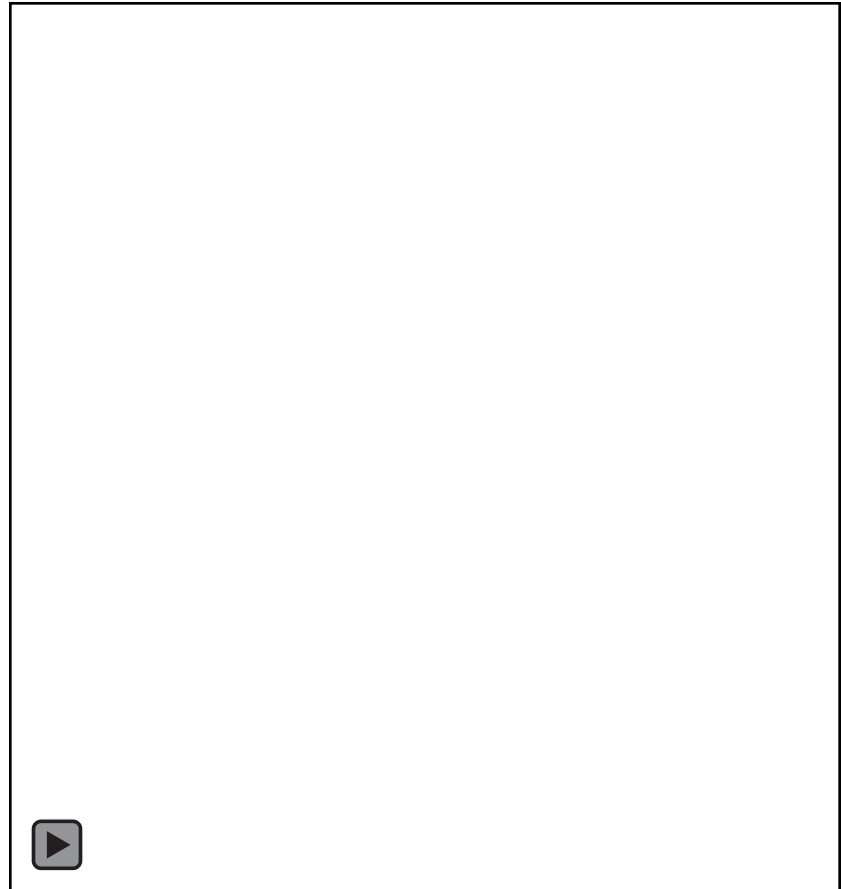
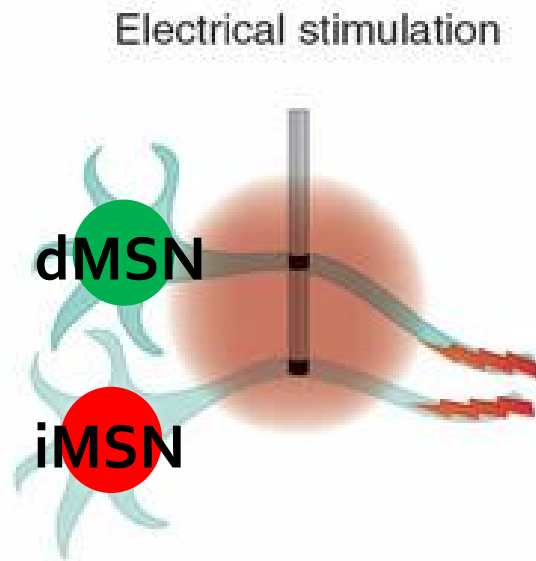


Validating
Stimulation

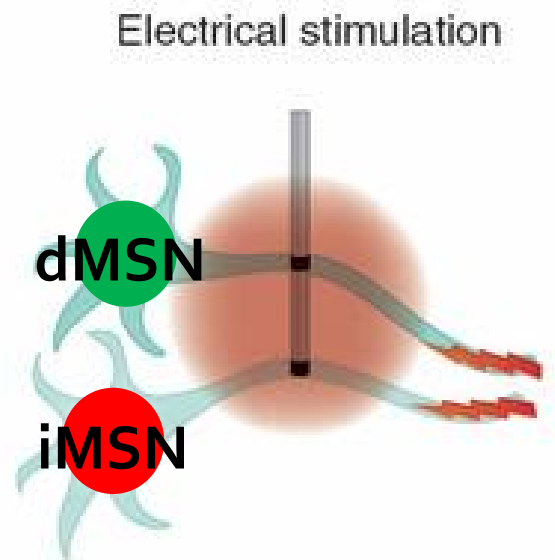


Testing
Circuit
Effects of
Stimulation

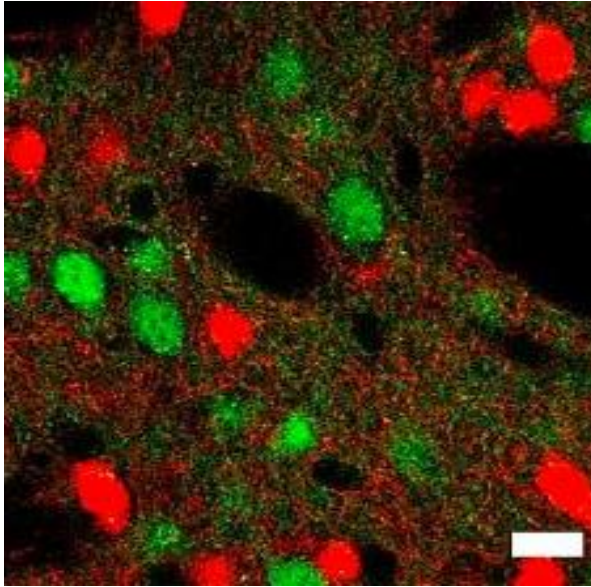
Direct (dMSN) and indirect (iMSN) pathway neurons are intermingled in the striatum



Optogenetics allows for cell-type specific control of neural populations



Historically, it has been difficult to independently study these cell populations

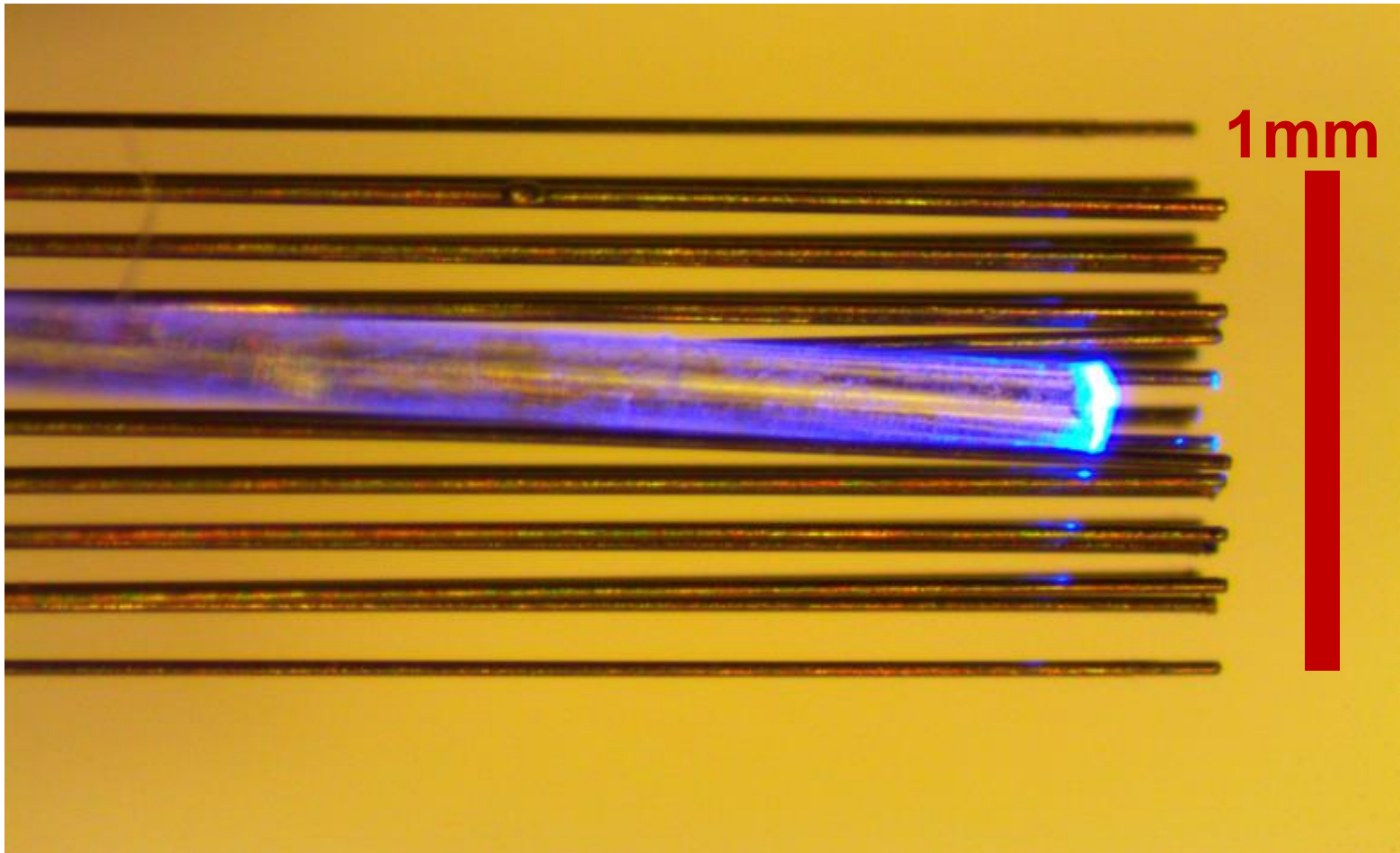


D₁-RFP

D₂-GFP



Combining *in vivo* electrophysiology with optogenetics

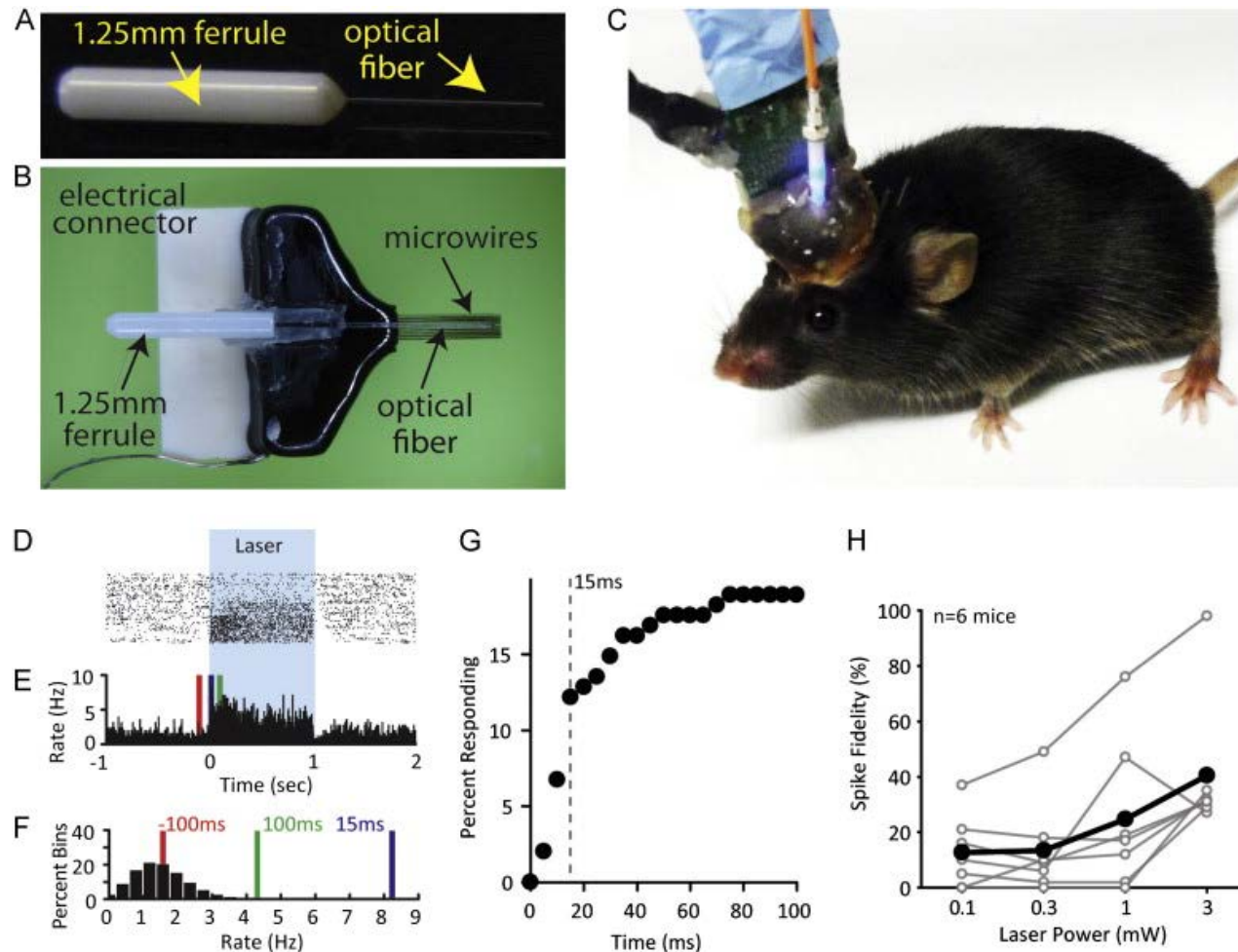




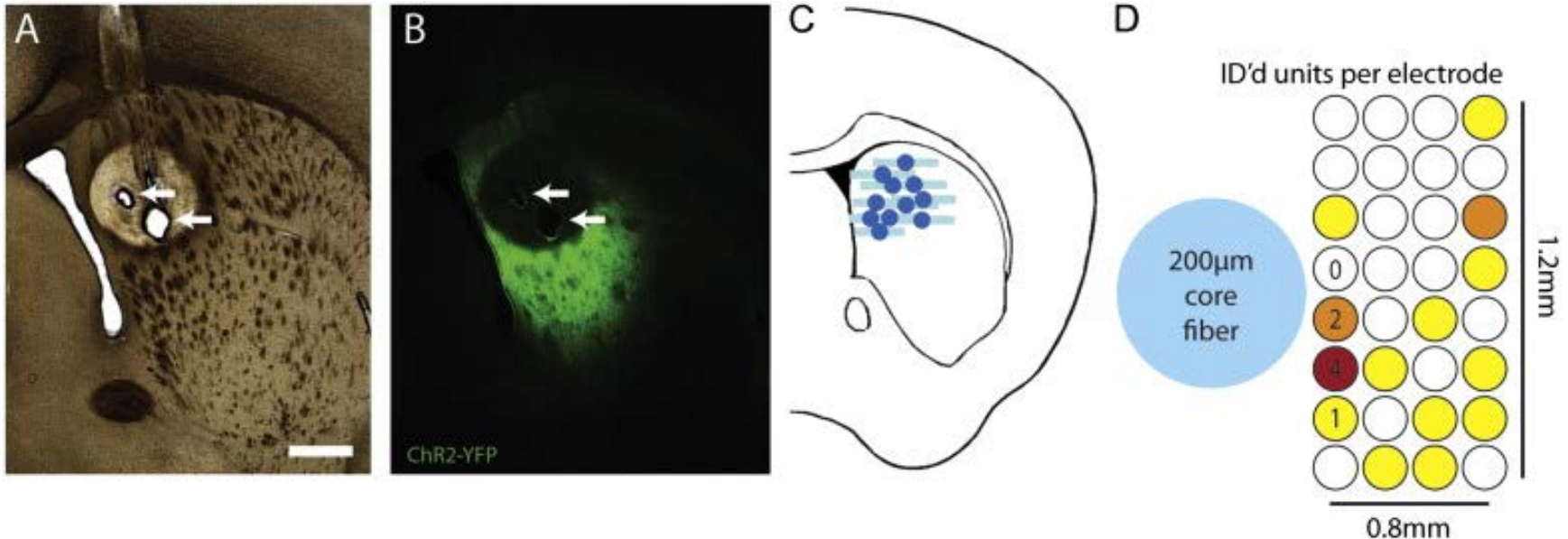
Combining *in vivo* electrophysiology with optogenetics



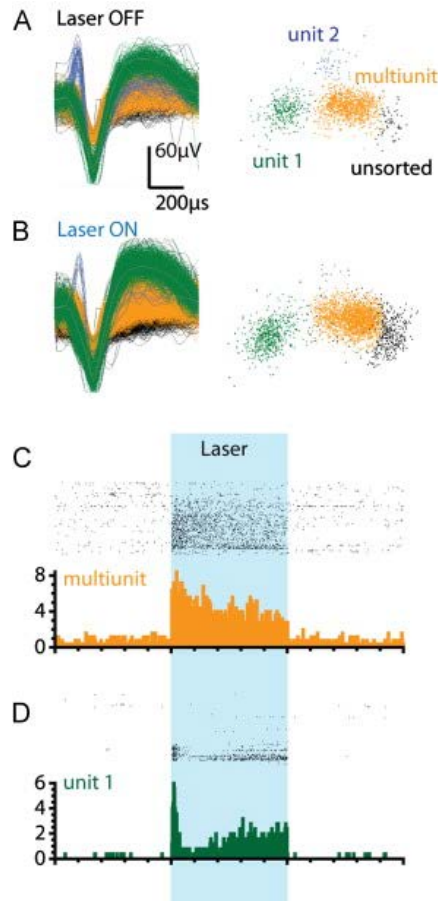
It is possible to identify light-activated neurons



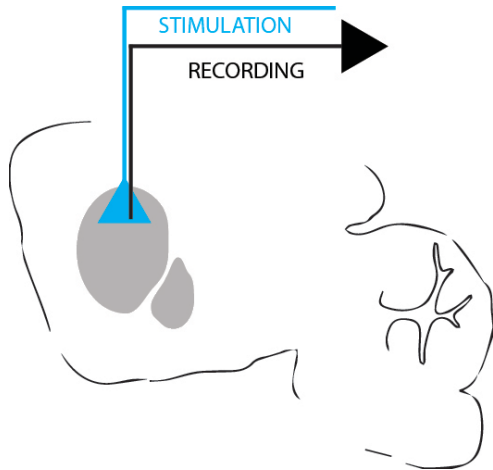
We detected activated neurons >1mm from the fiber tip



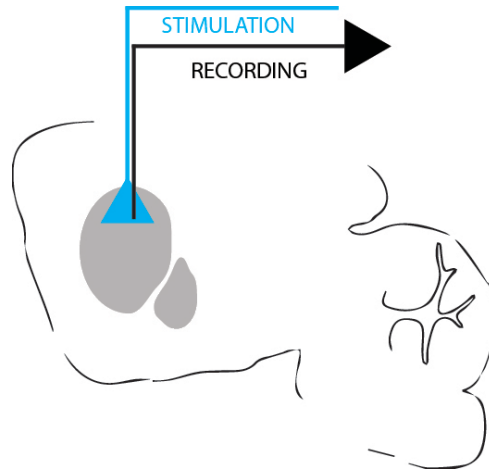
However several concerns came up...



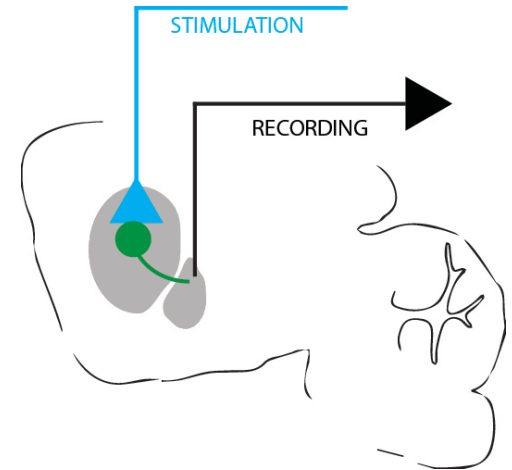
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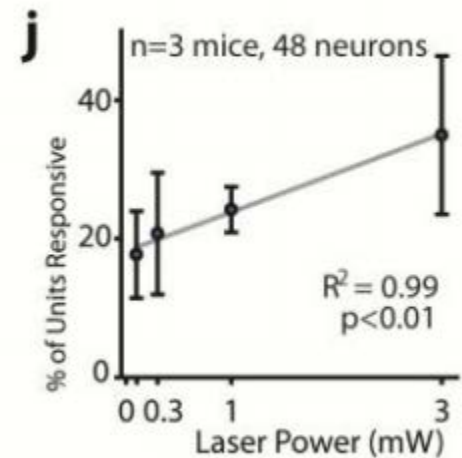
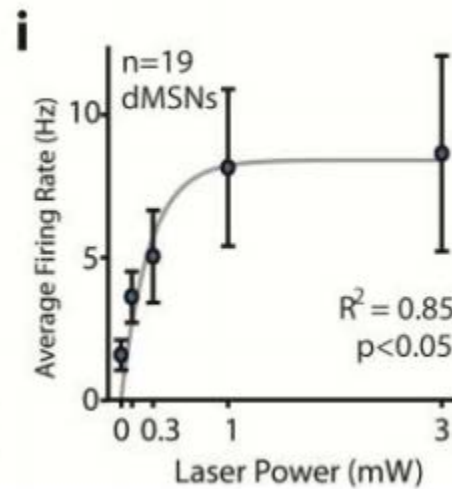
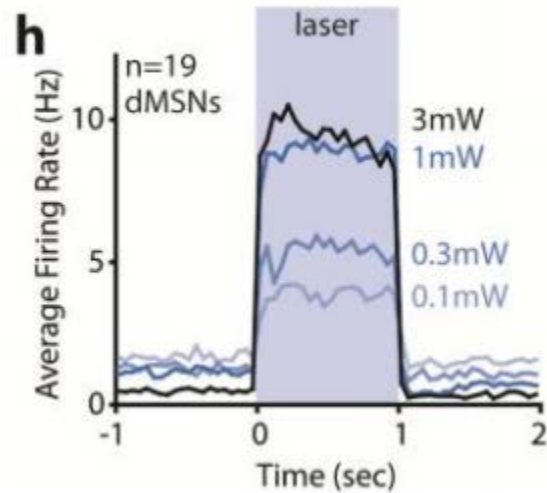


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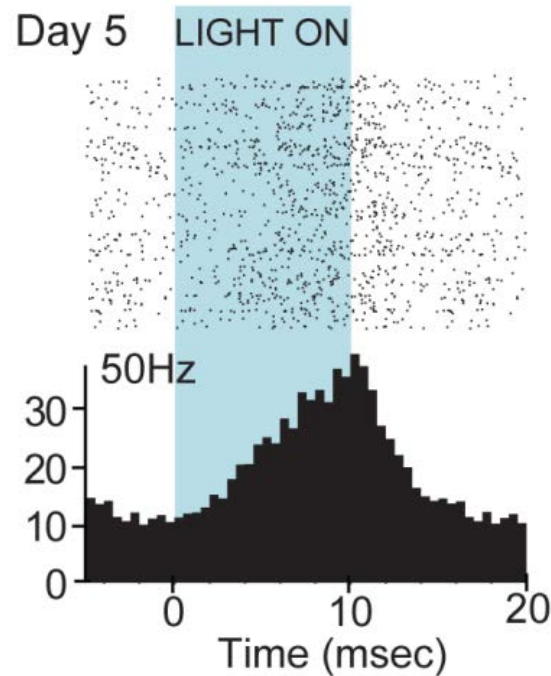


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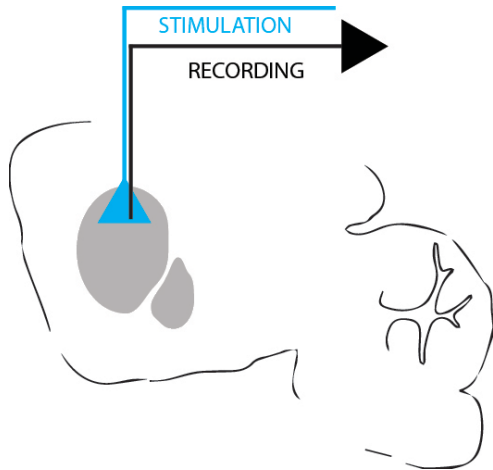
In vivo recording to validate effects of stimulation



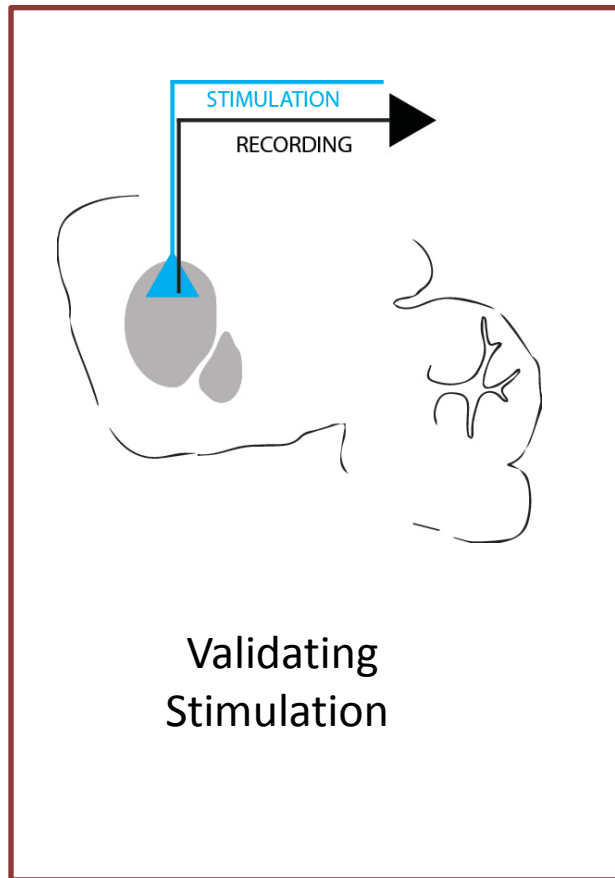
Using in vivo recording to validate optogenetic protein expression



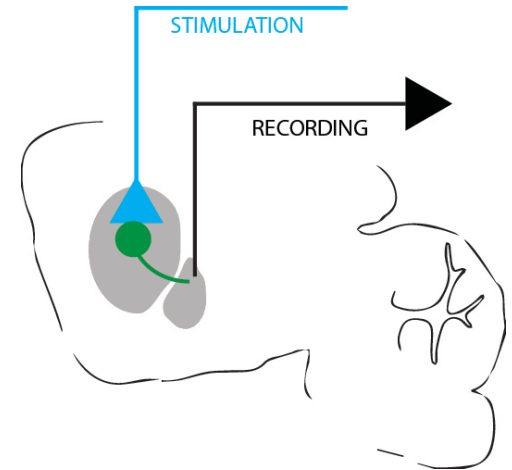
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Summary

- Tagging neurons can be a difficult game...
- Validating the function of opsins is much higher throughput.
- Testing effects of optogenetic stimulation of downstream structures is also a good use of integrated optogenetics and recording.

Outline

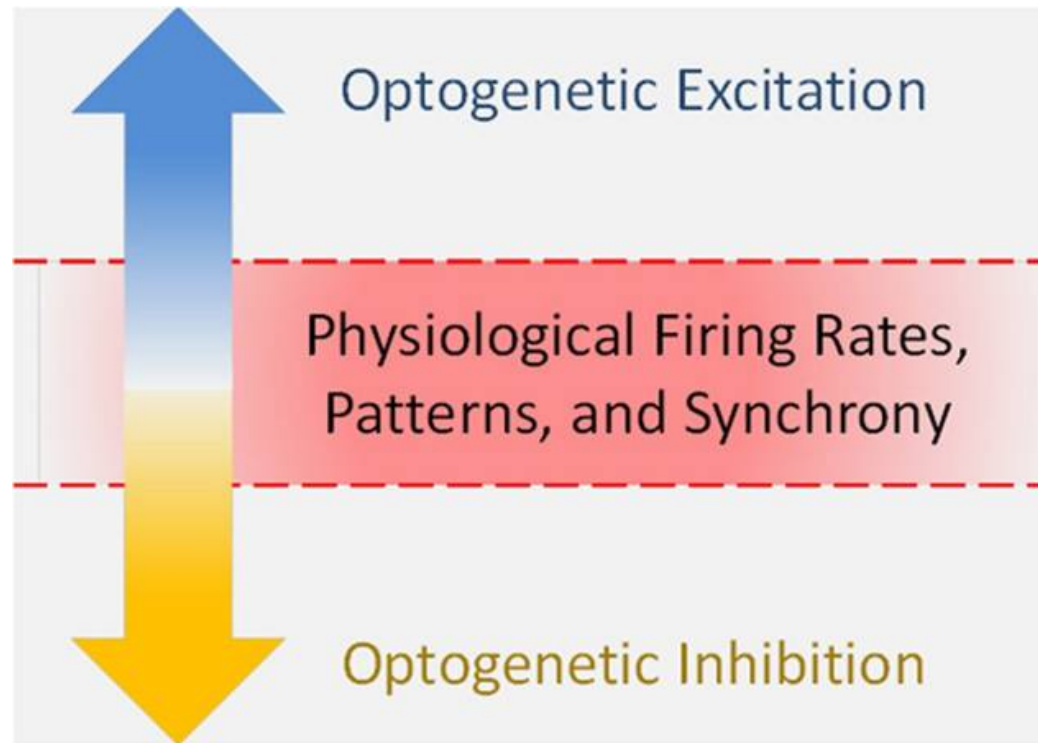
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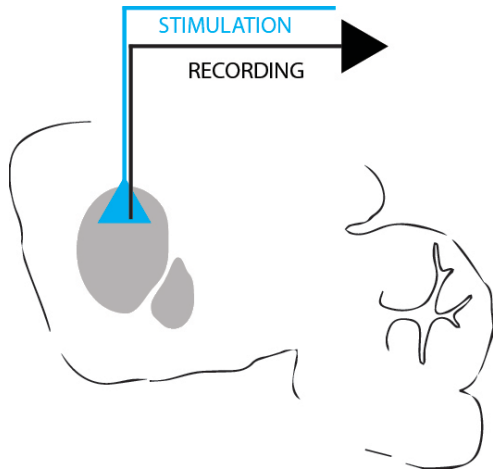
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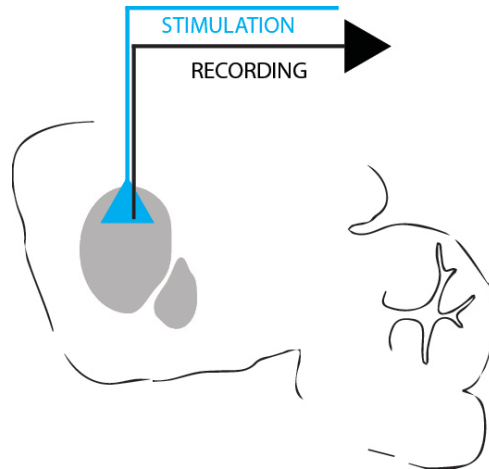
Optogenetics can drive extra-physiological changes in firing



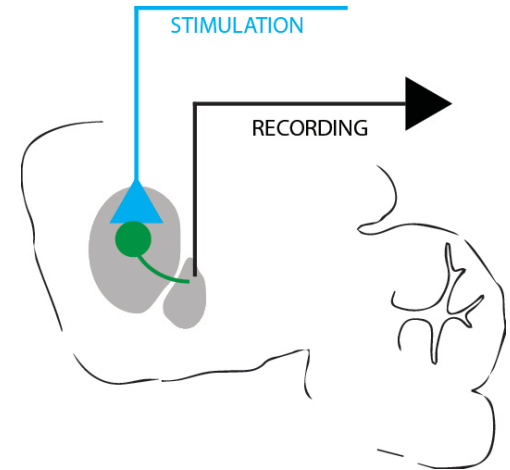
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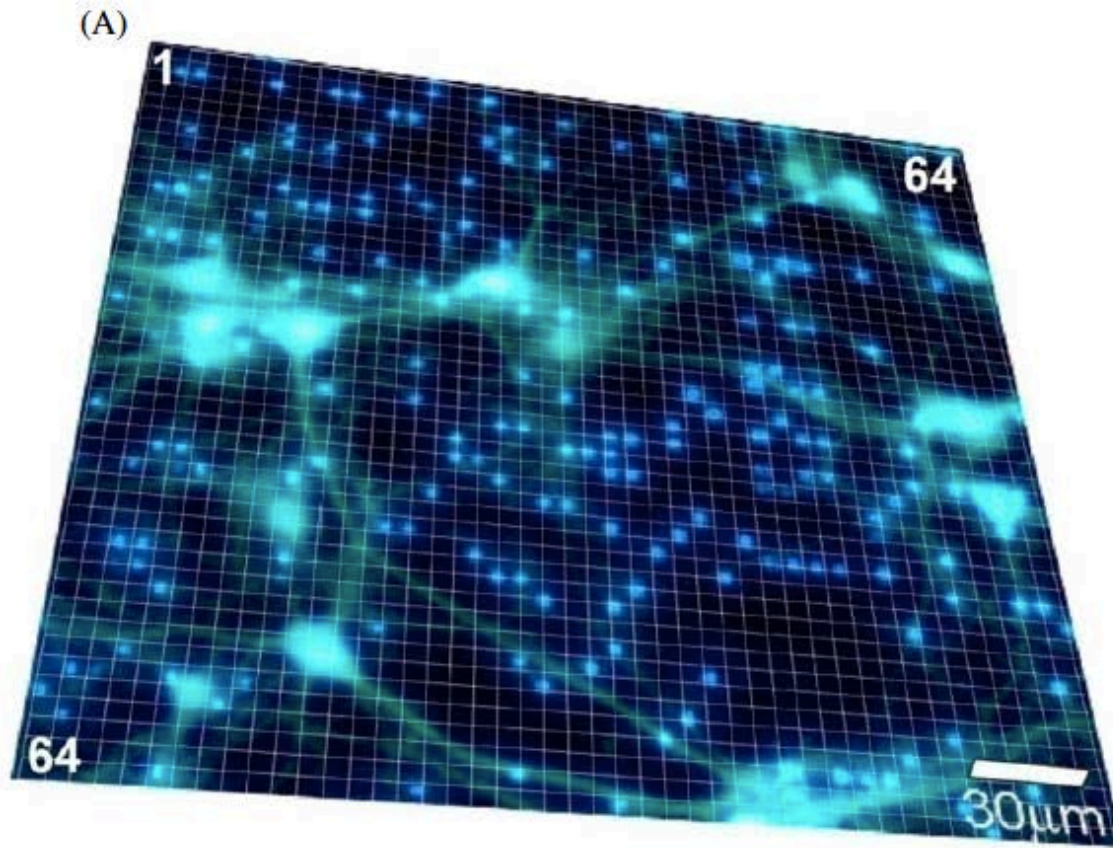


Validating
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Multi-site applications



Questions?

Lex.kravitz@nih.gov

