Manipulating neurons with light

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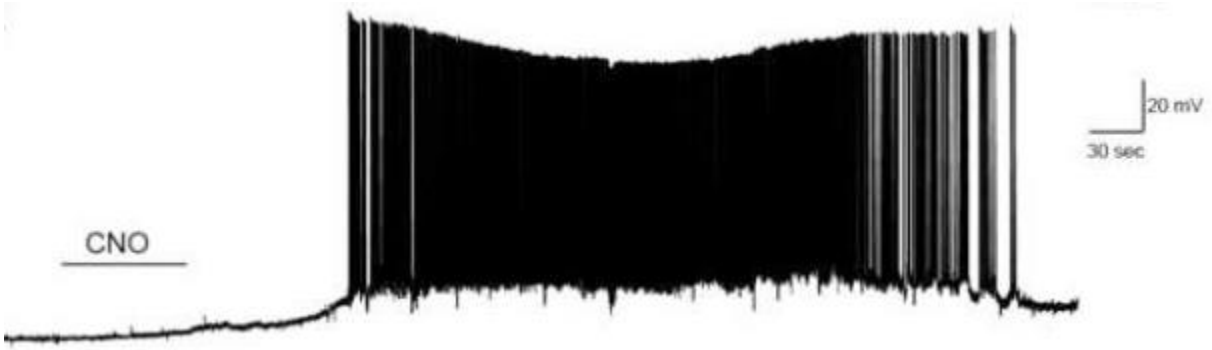
Why bother with light, isn't pharmacology good enough?

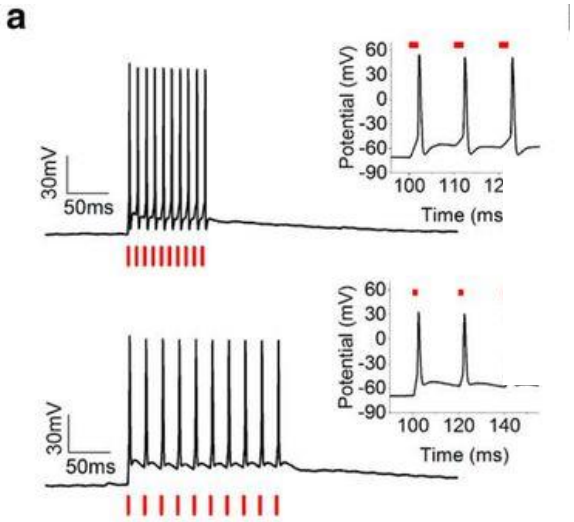
Light gives us temporal precision!

- Optogenetics
- Uncaging

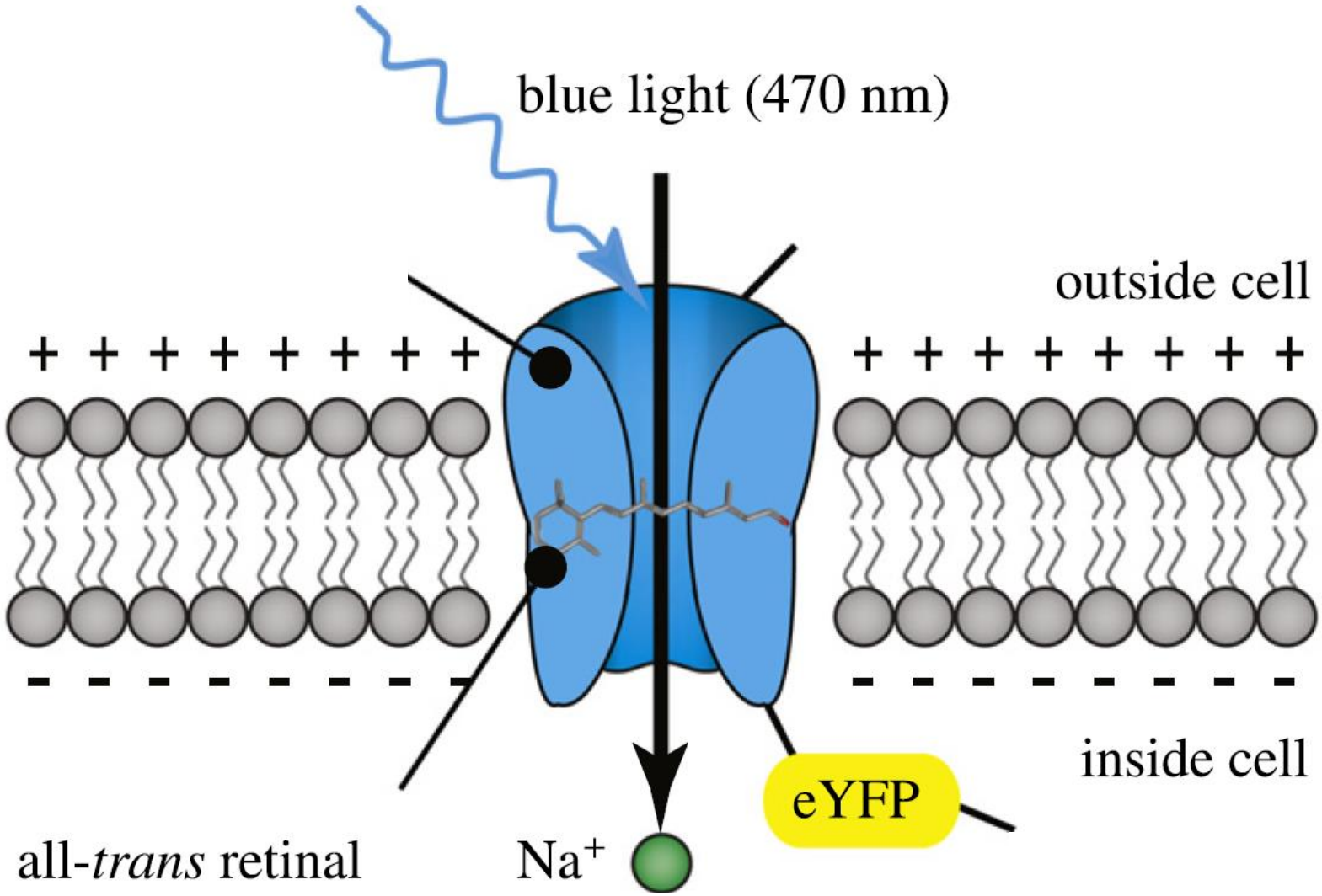
DREADDs



optogenetics



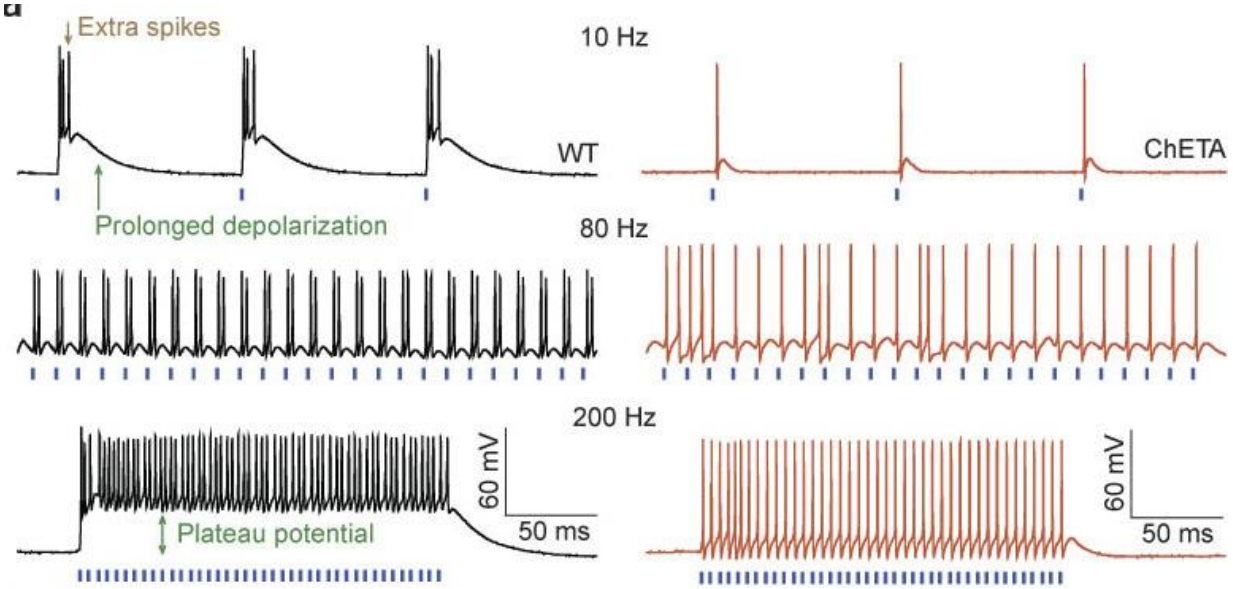
Channelrhodopsin basics



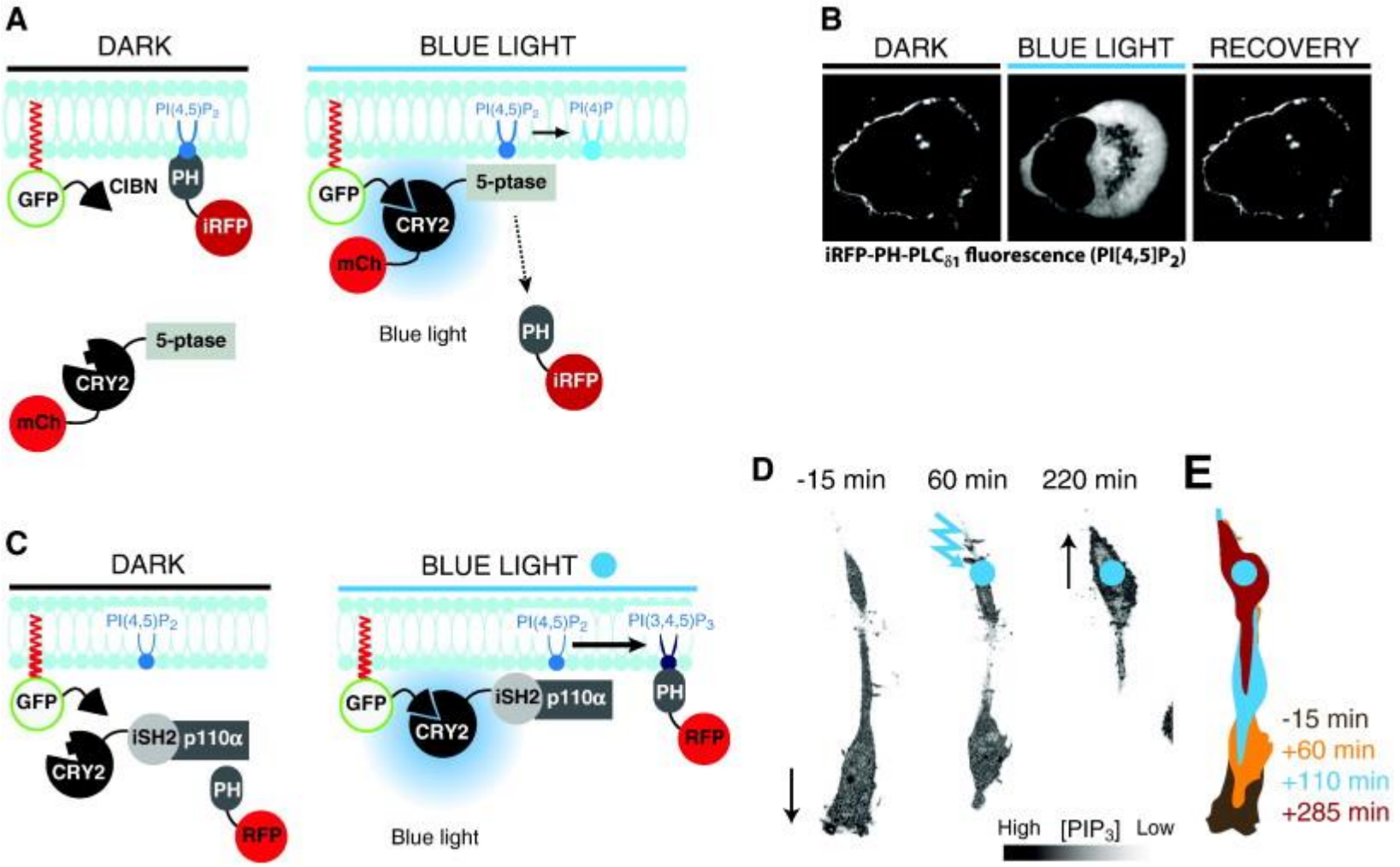
Advanced opsins

Increased axonal targeting
Increased soma targeting
Increased speed (Cheeta) = better temporal precision
Red shifted opsins (C1V1, Crimson) -> dual color optogenetics
Step function opsins
Optically driven GPCRs

Still incomplete list:
https://web.stanford.edu/group/dlab/optogenetics/sequence_info.html



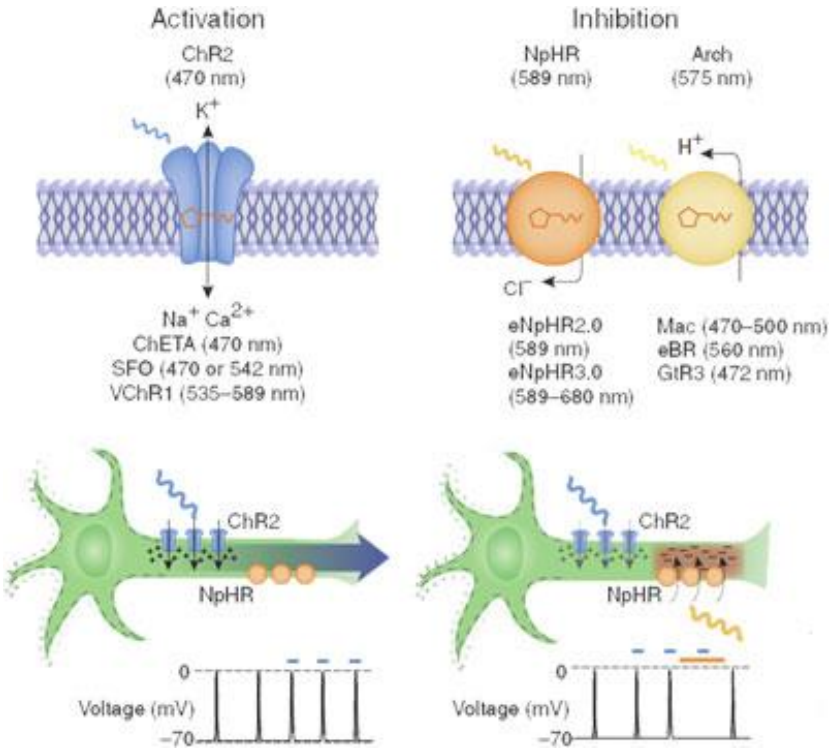
Not only for neuroscience: optically driven kinases, phosphatases etc.

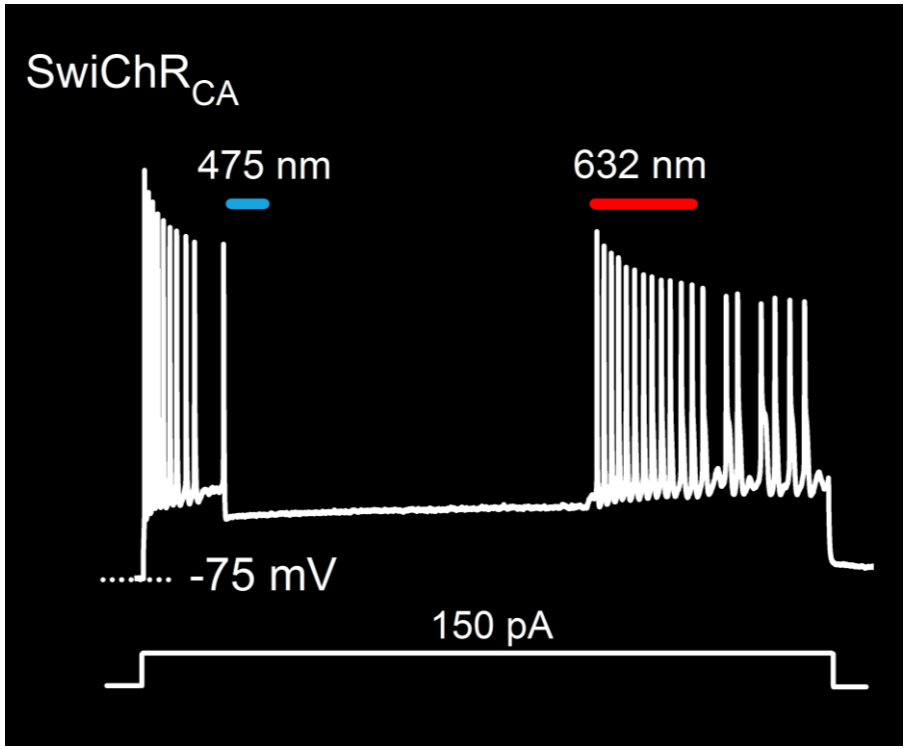


Detection and manipulation of phosphoinositides

Idevall-Hagren, 2015

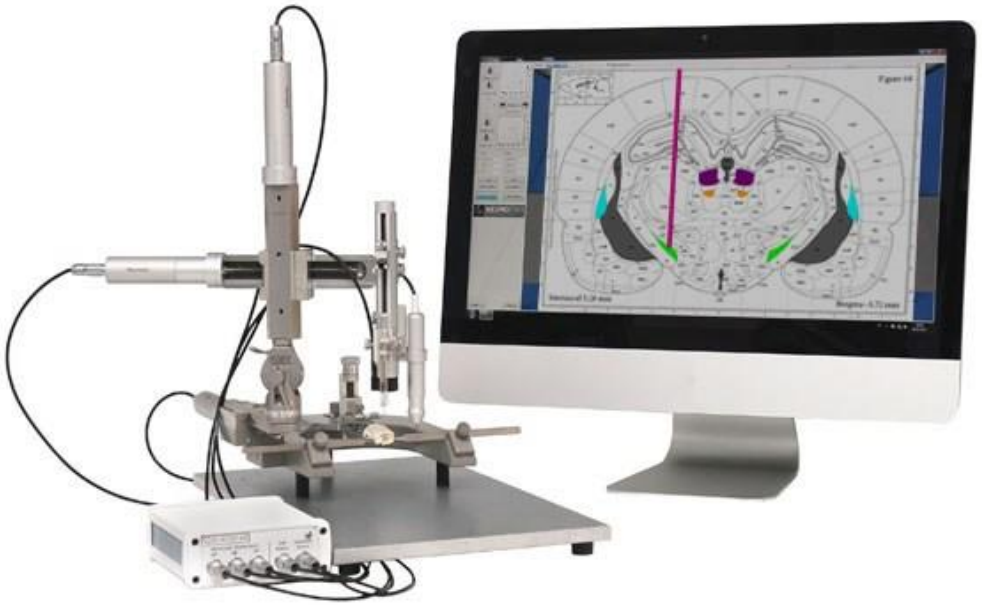
Optogenetic inhibitions

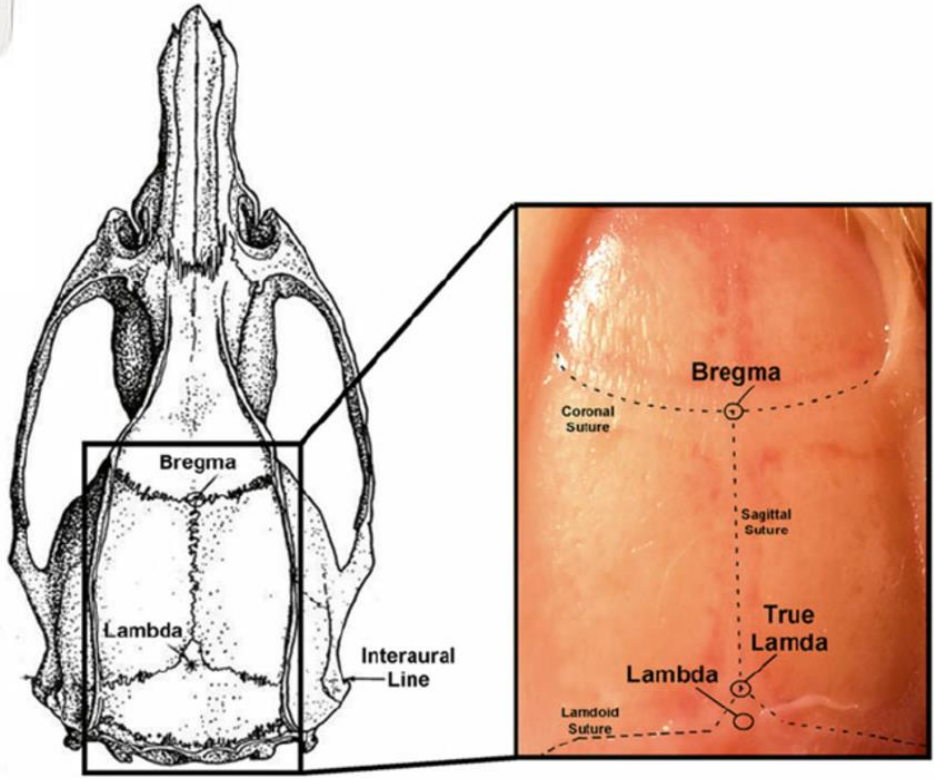




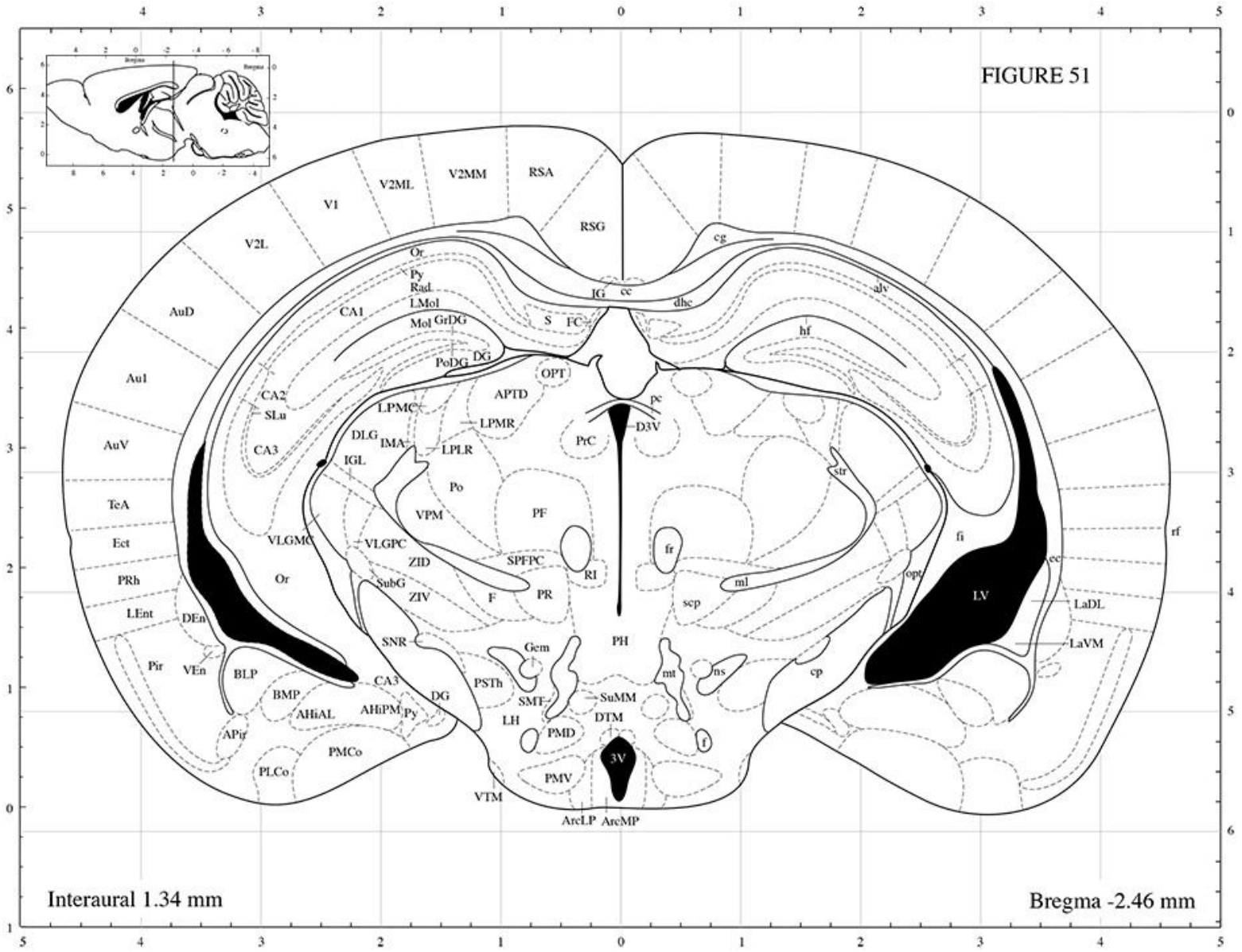
Step-**W**aveform **I**nhibitory **C**hannel**R**hodopsin (SwiChR)

How to target expression: stereotaxic virus injections





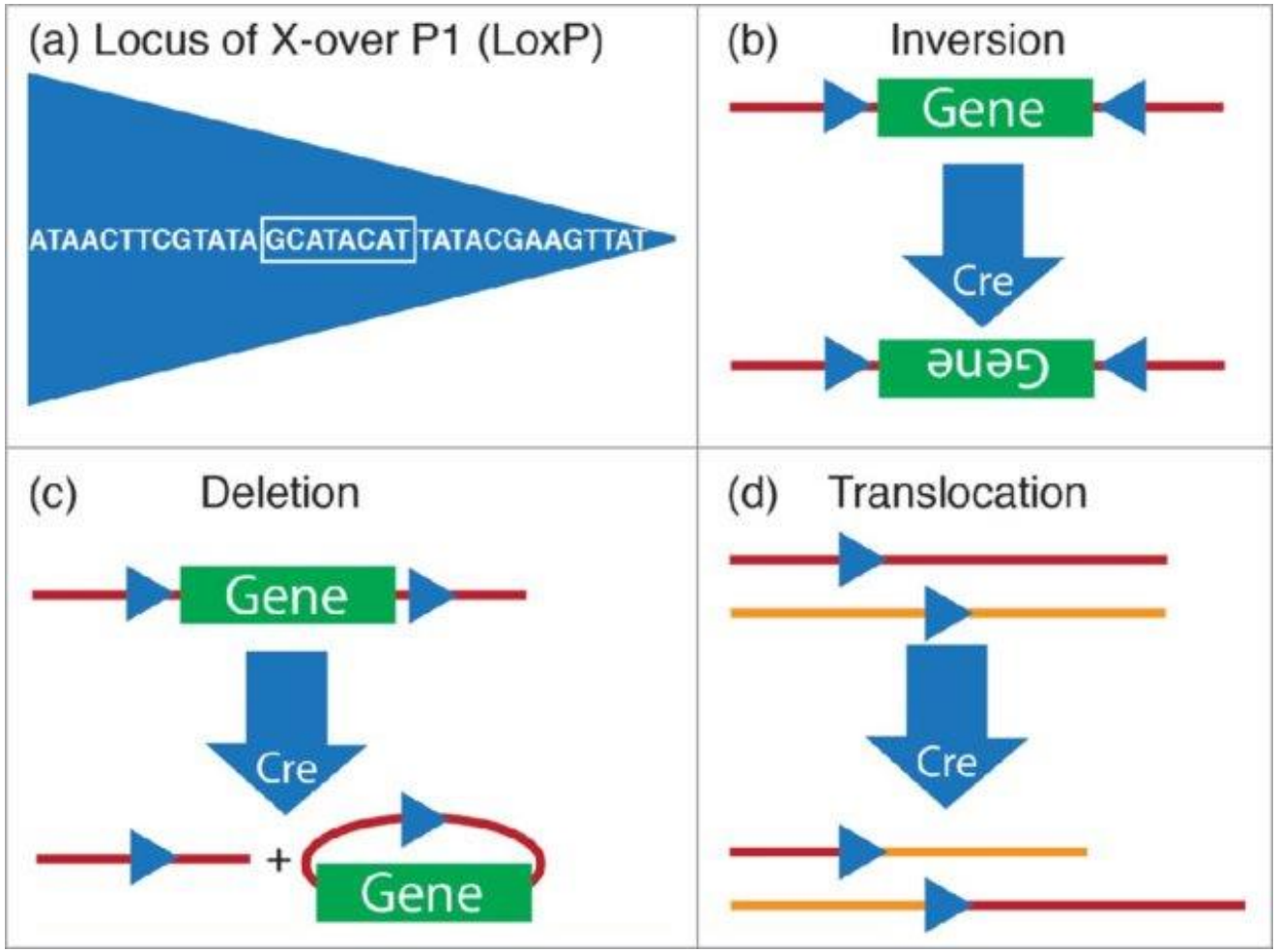
Where to inject?



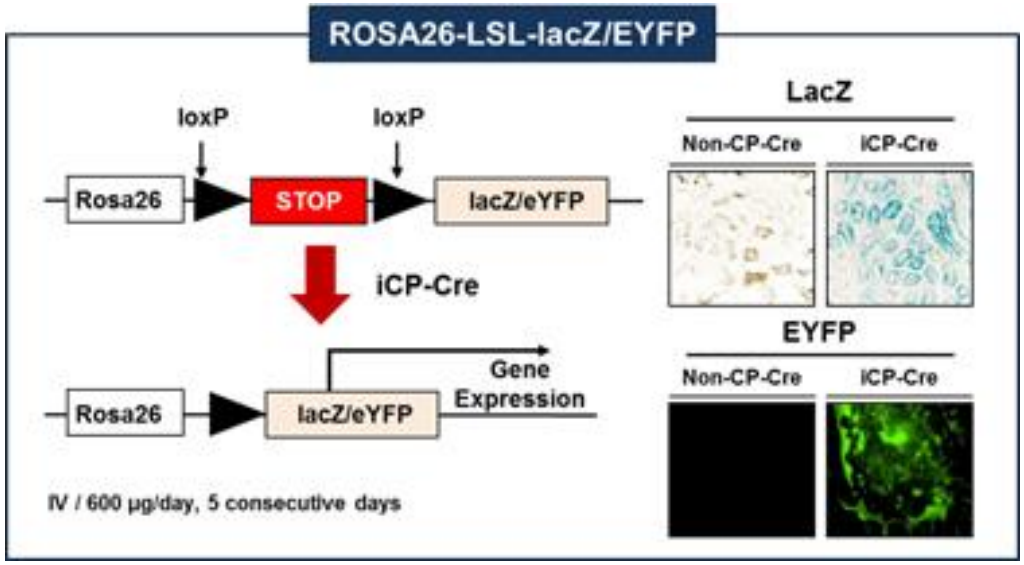
Cell type specific expression: The Cre – loxP system

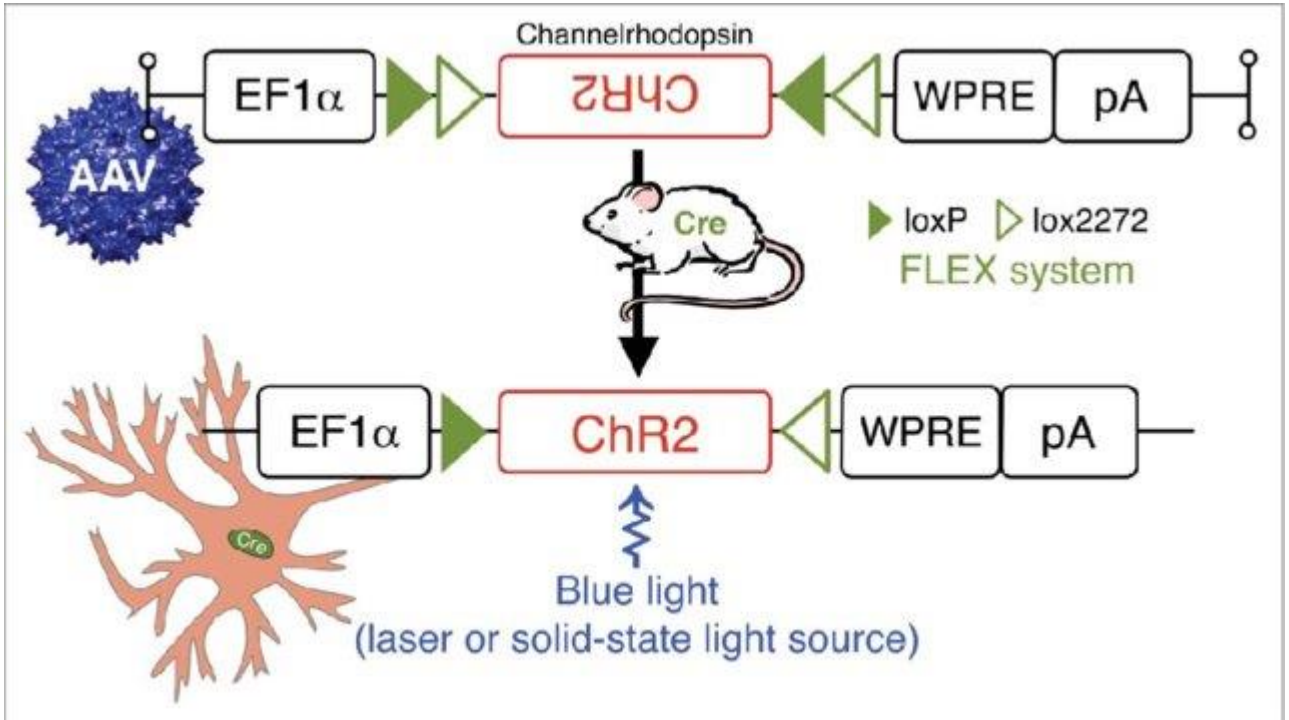
Cre (**C**auses **re**combination)

LoxP (***l***ocus ***o***f ***X***(cross)-over in ***P***1)

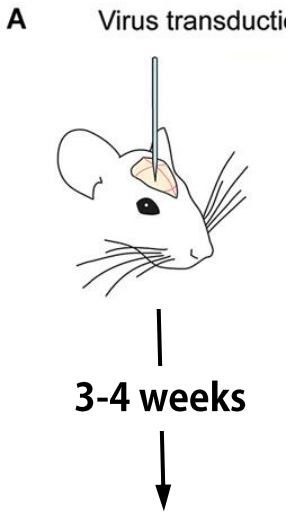


How to control gene expression with Cre-loxP?

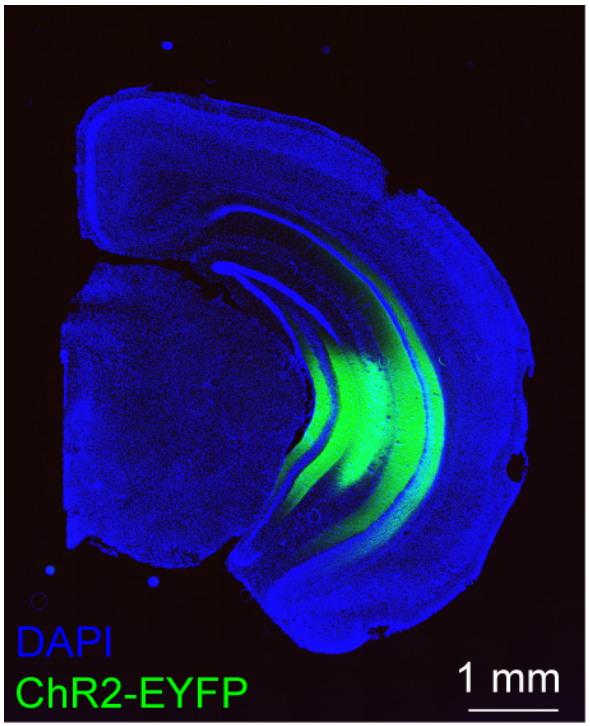


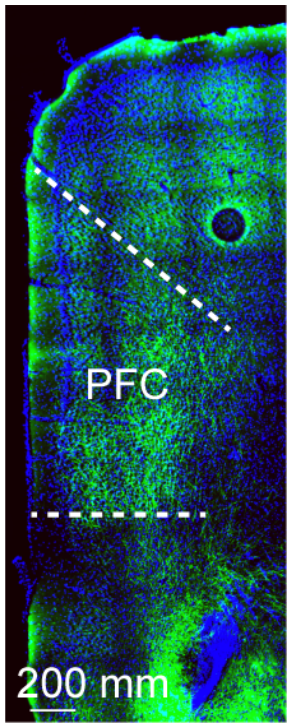


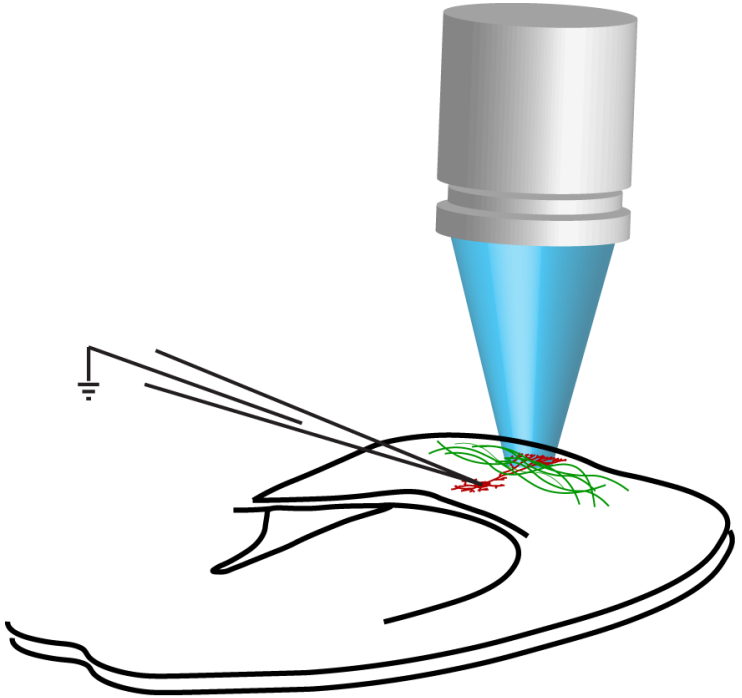
Ex vivo optogenetics



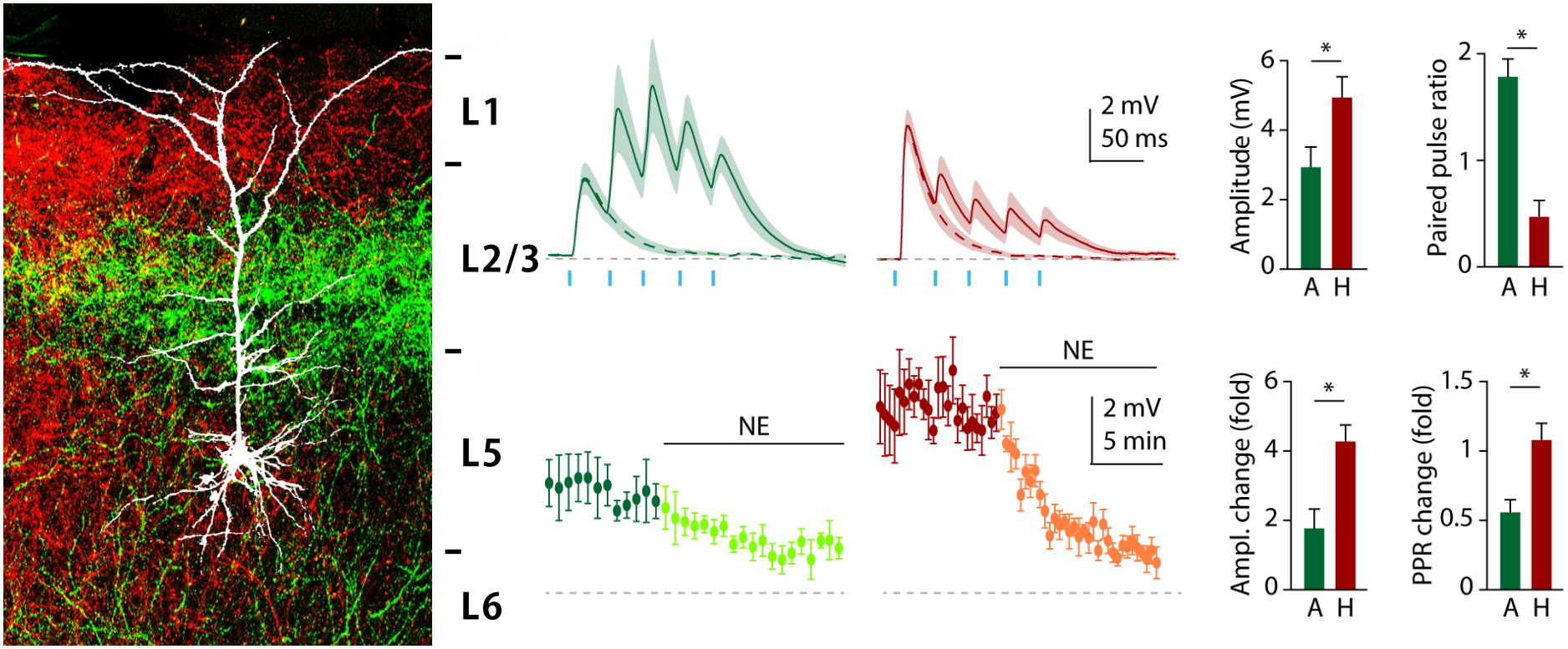
You can cut off the cell body, still get responses
-> test inputs from far away brain regions







Comparing inputs form different regions



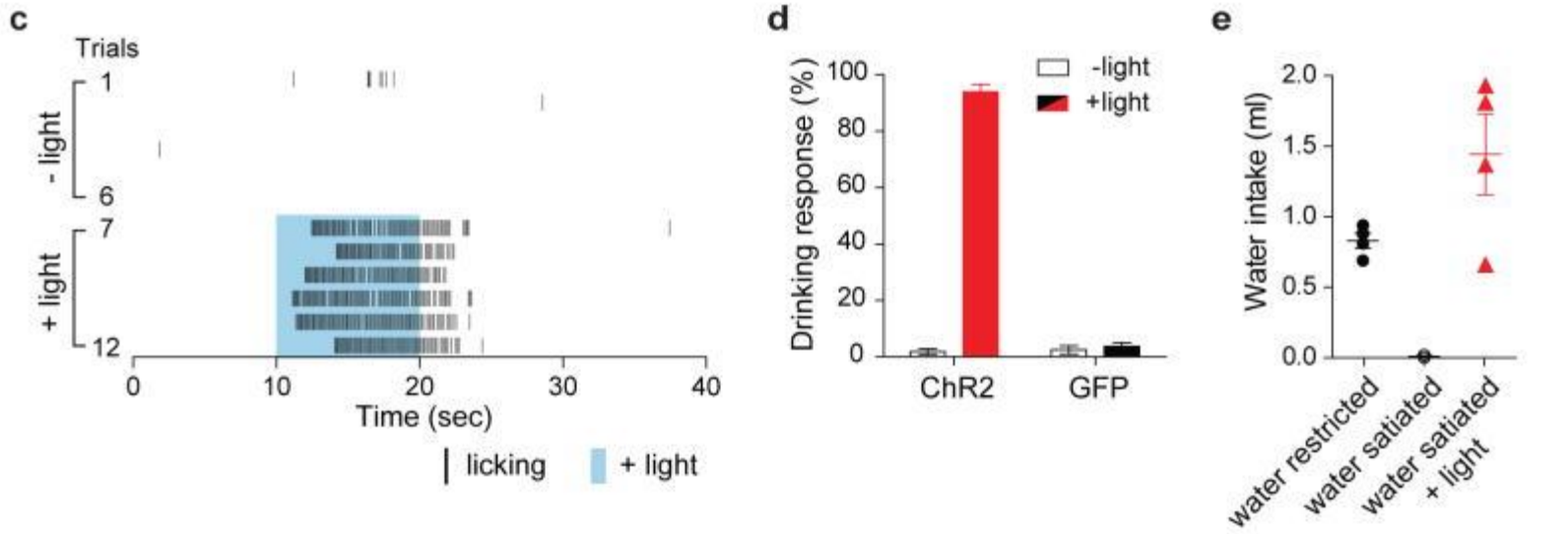
Lur G. unpublished

In vivo optogenetics - manipulating behavior

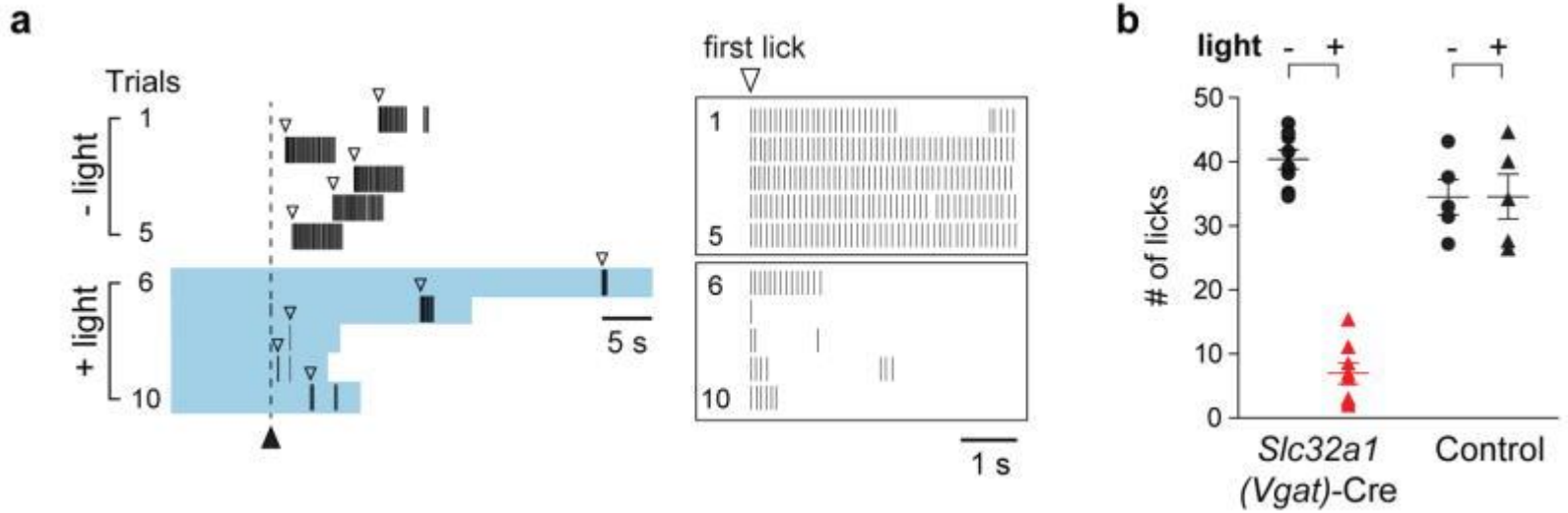
Yuki Oka, Mingyu Ye & Charles S Zucker, Nature 2015

SFO neurons control thirst

CaMK2



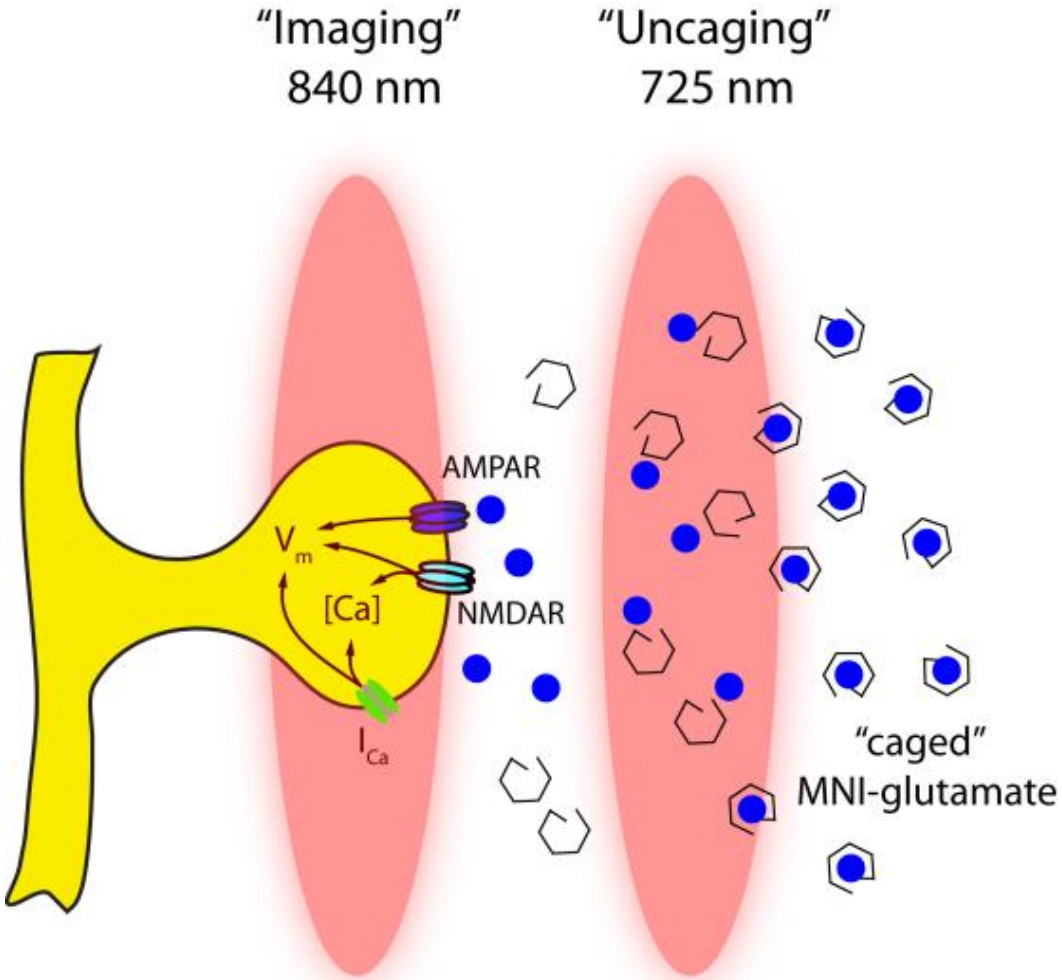
Vgat



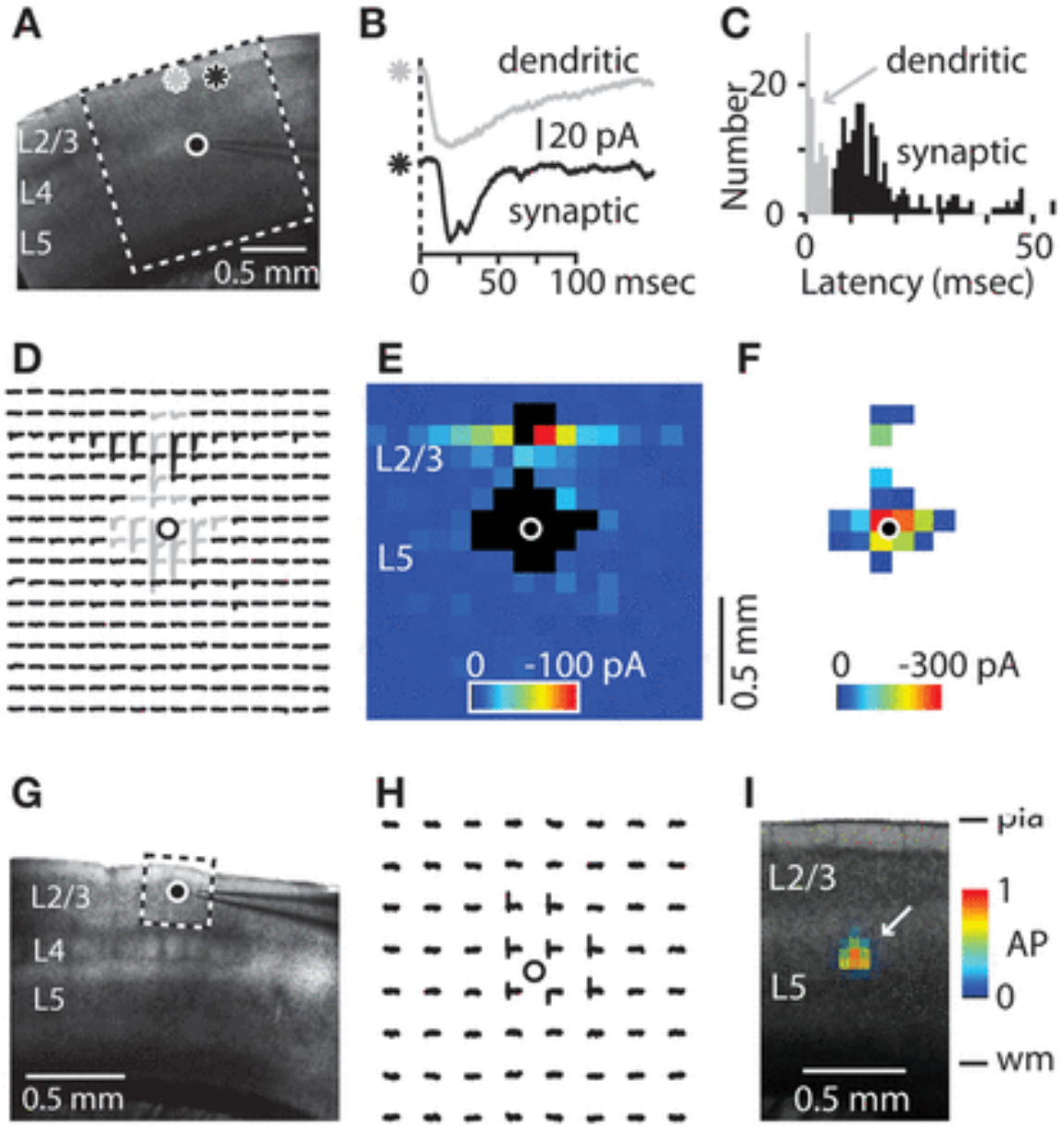
Uncaging – basic principles

Goal: spatiotemporally precise neurotransmitter release
Mostly in vitro (but there are exceptions)

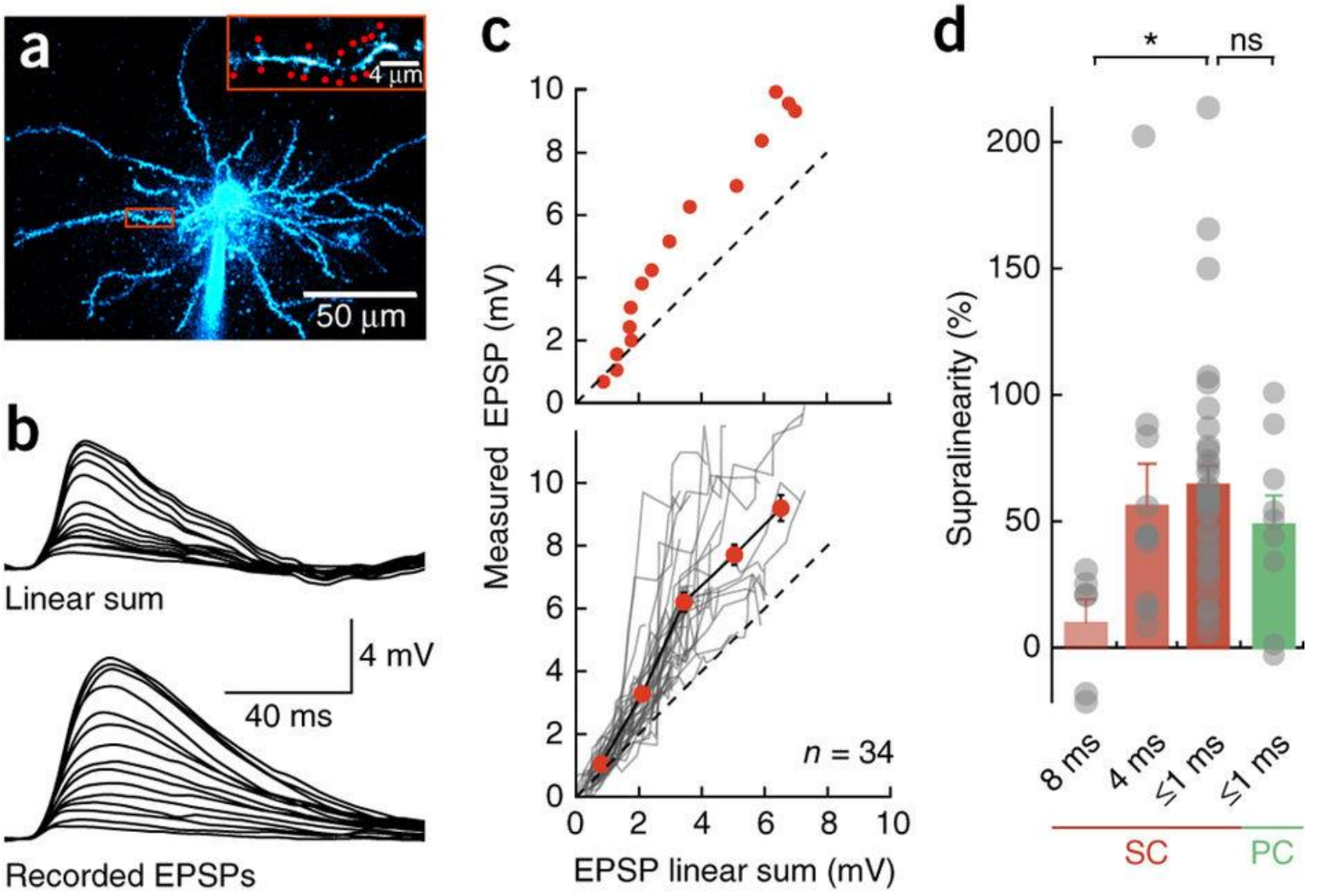
Caged compounds:
Glutamate
GABA
IP3
Ca2+
Neuromodulators
Nucleotides like ATP
mRNA & DNA
proteins



Local circuit mapping using one-photon glutamate uncaging

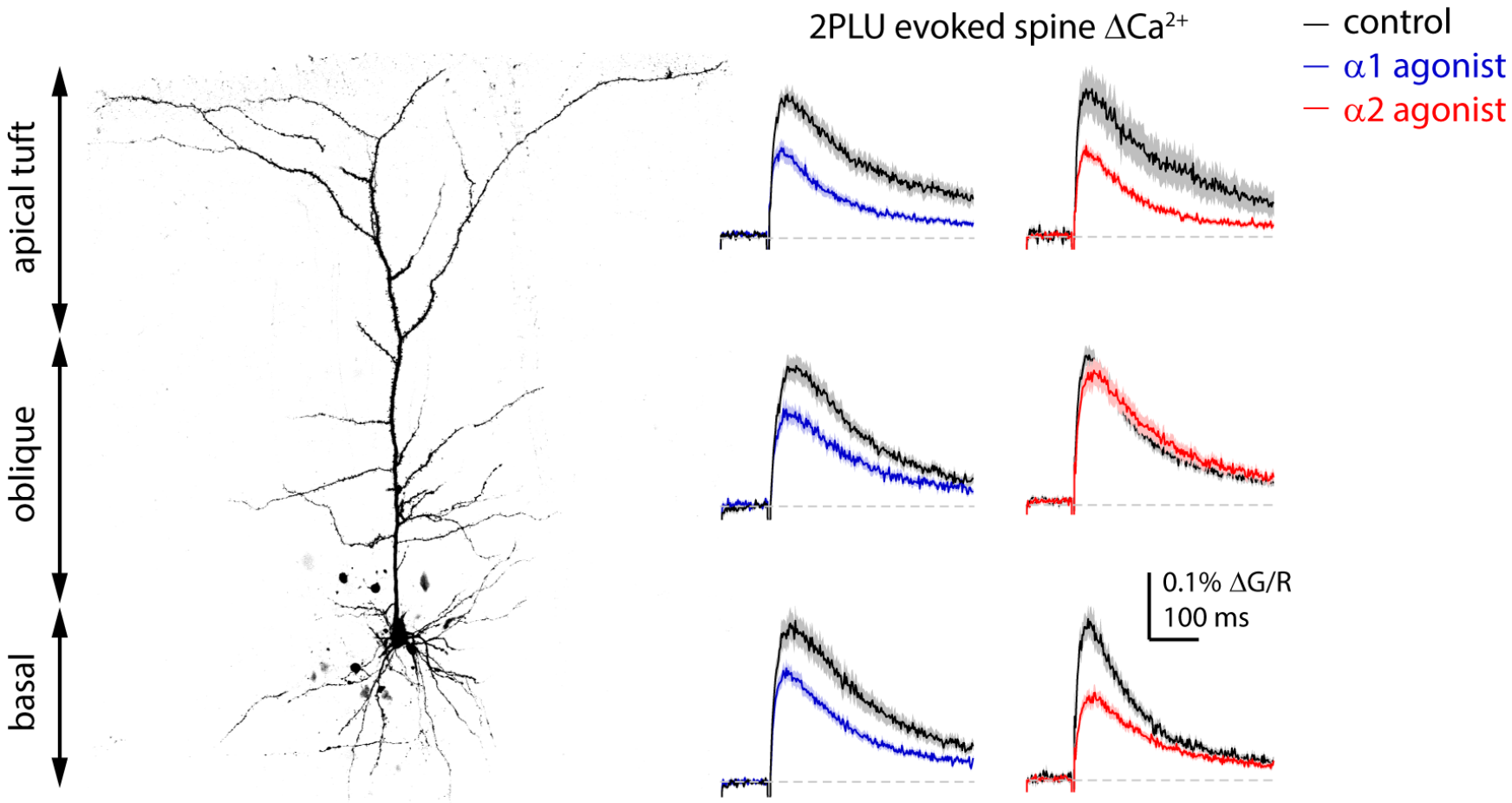


Supra-linear dendritic integration – two-photon glutamate uncaging



Look for work by Jeff Magee and Michael Hausser

Spatial mapping of cellular receptor composition



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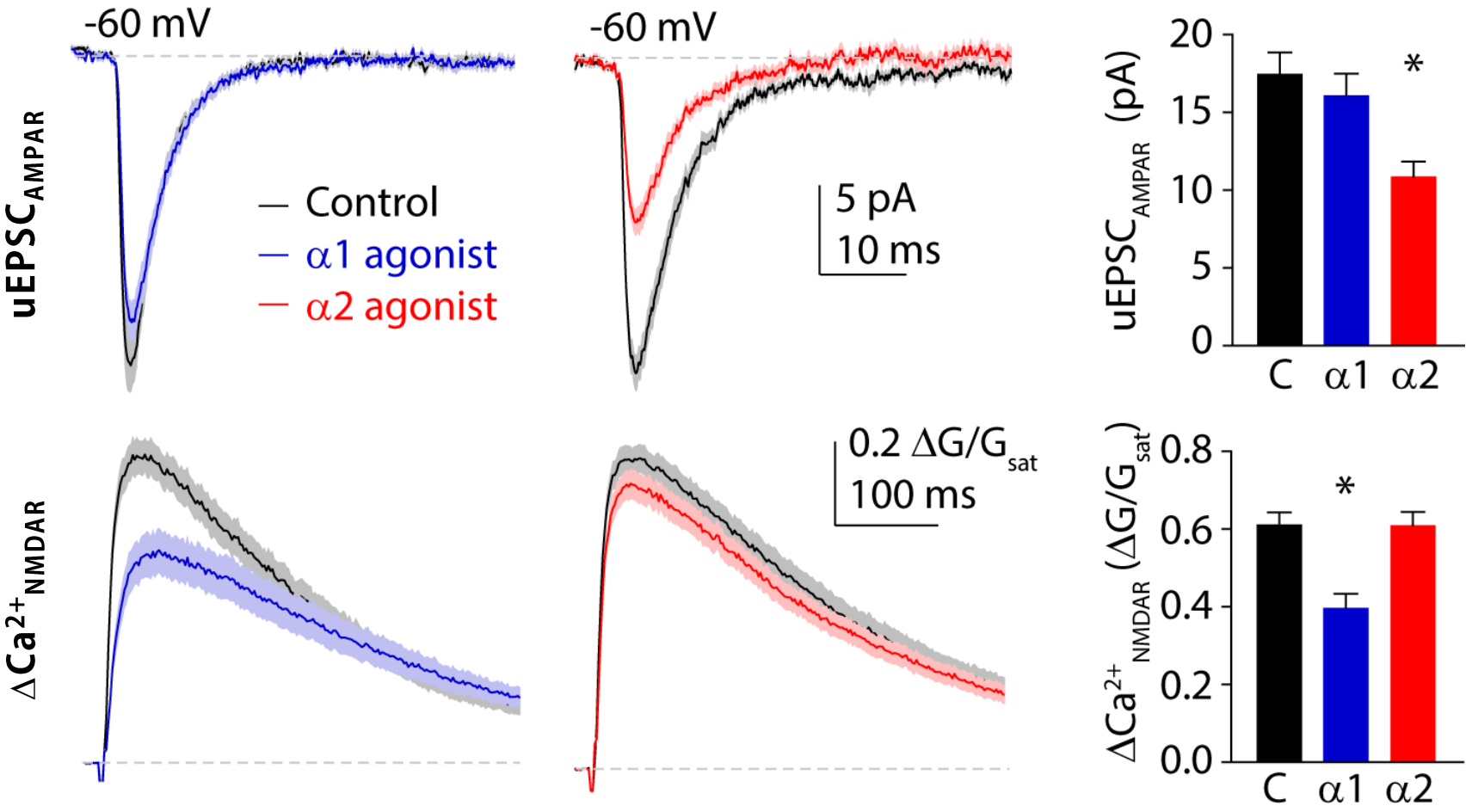
Specific control of postsynaptic glutamate receptors



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