

Manipulating neurons with light

Spotlight on opsins

Emerson Harkin

Supervised by Jean-Claude Béïque

Introduction

Canonical model of neuroscience

Behaviour



Networks



Cells

Addiction



**Limbic
system**

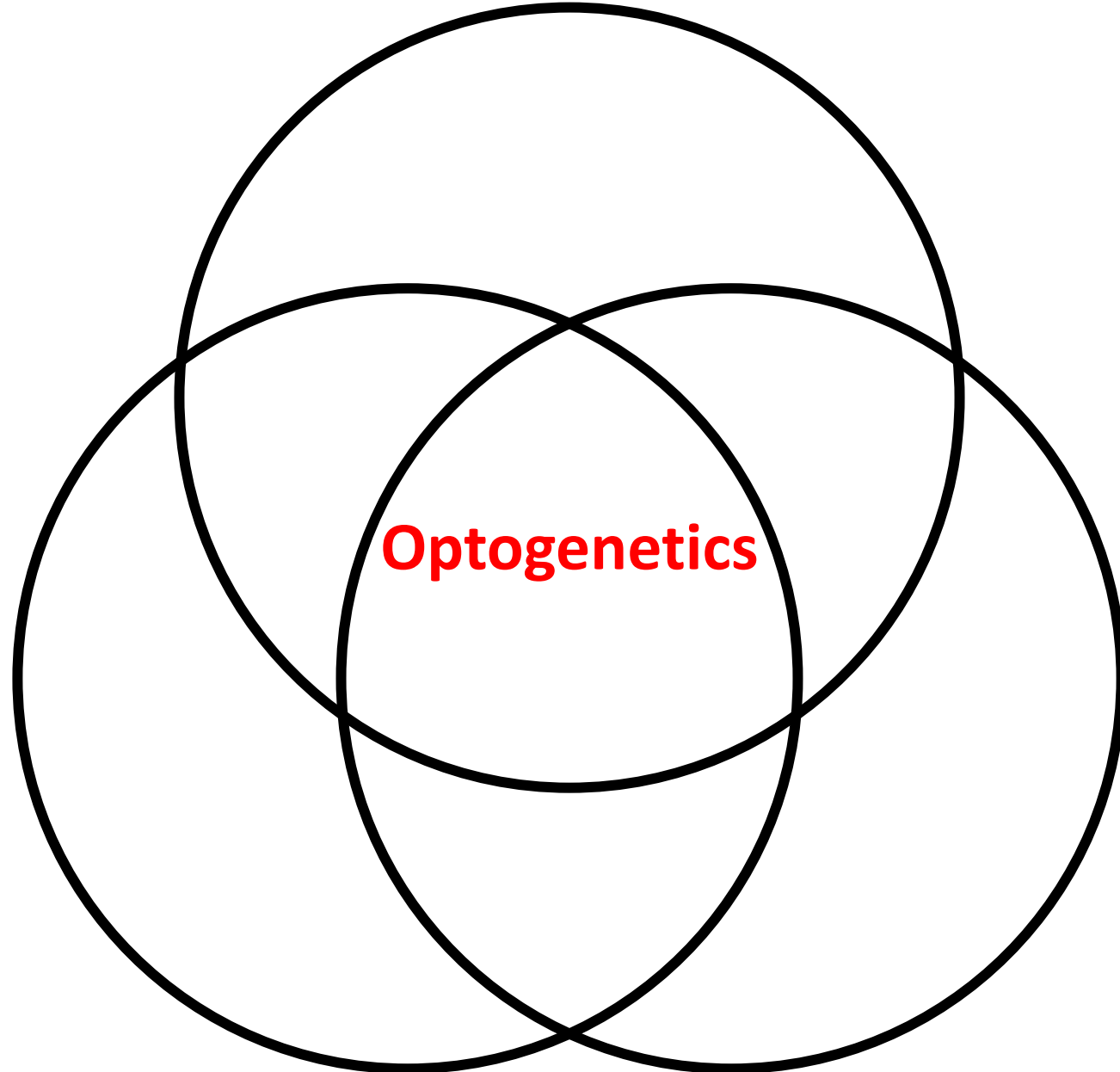


**Dopamine
neurons**

Cell-type specificity

**Regional
specificity**

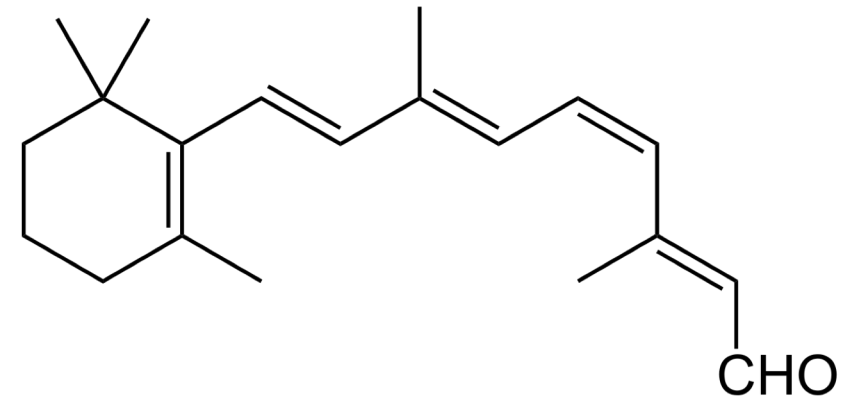
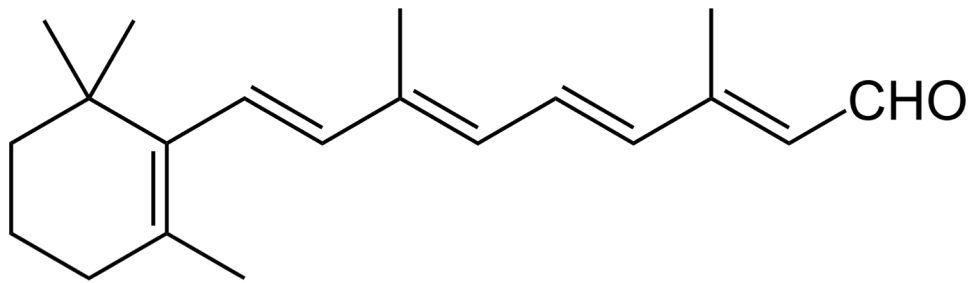
**Temporal
precision**



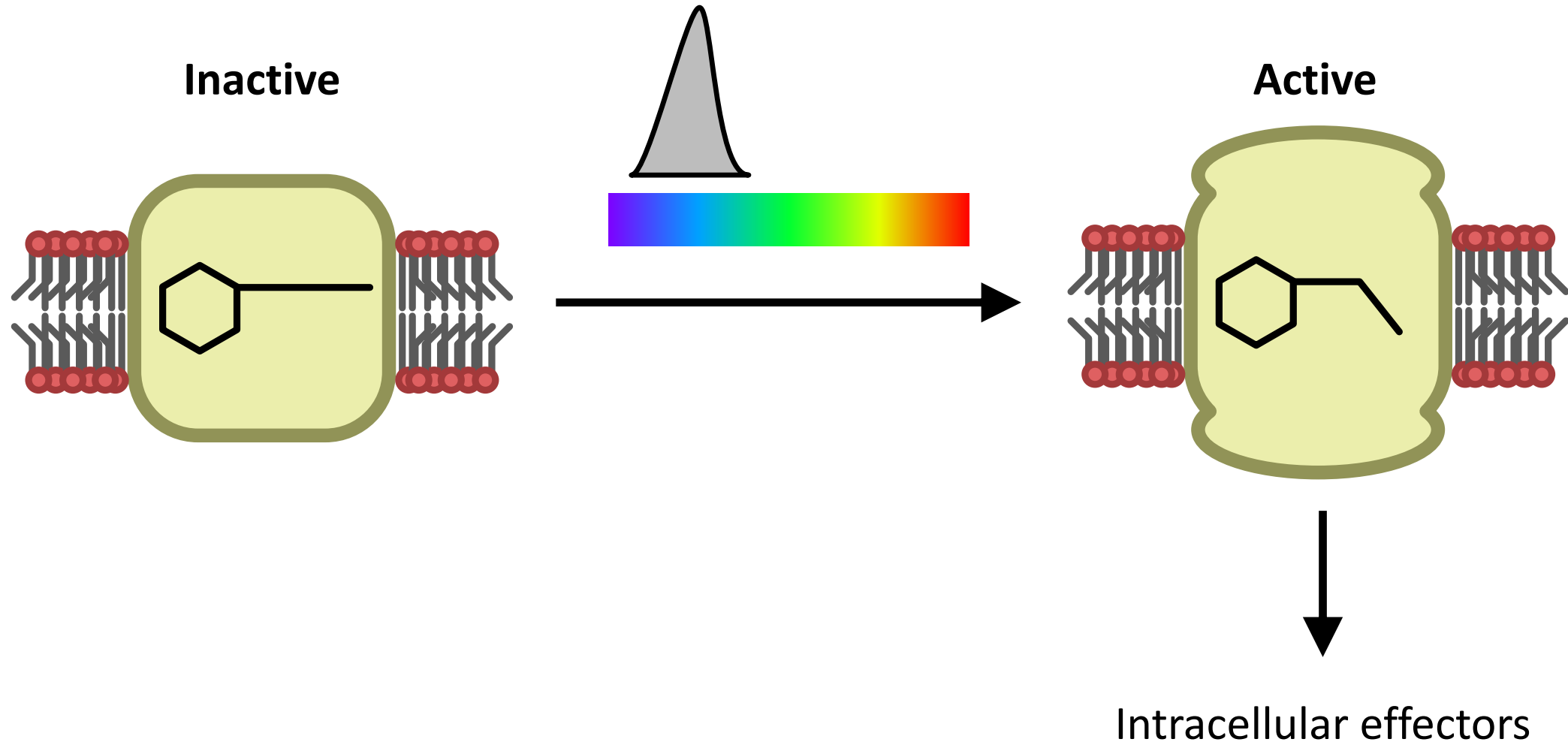
Optogenetics

Fundamentals of optogenetics

Retinal mediates light sensitivity

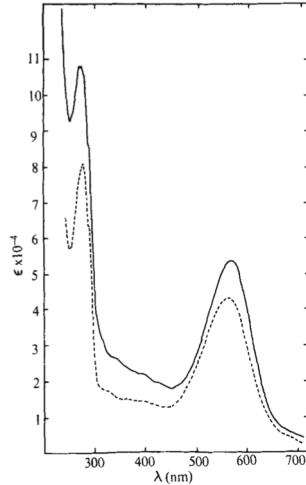


Opsins are photoreceptors

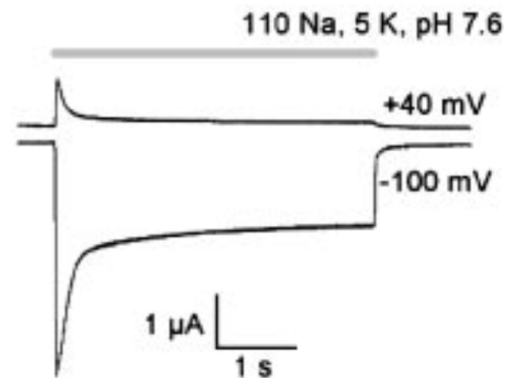


Development of optogenetics

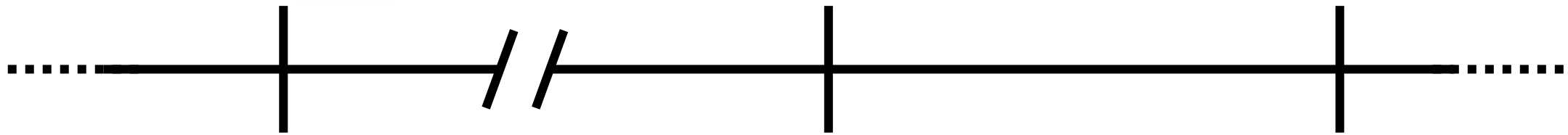
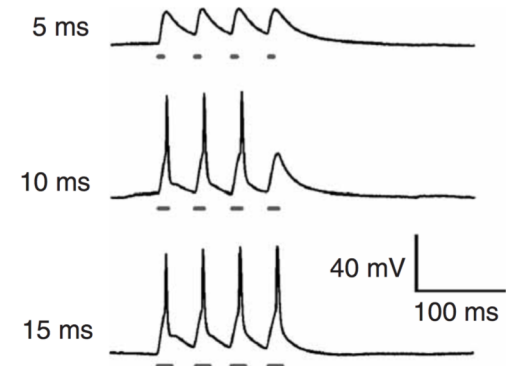
Discovery of bacteriorhodopsin



Chlamyopsin-4 is a cation channel



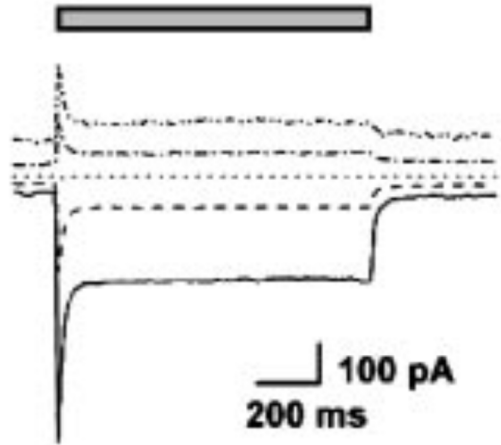
Channelrhodopsin-2 first used in neurons



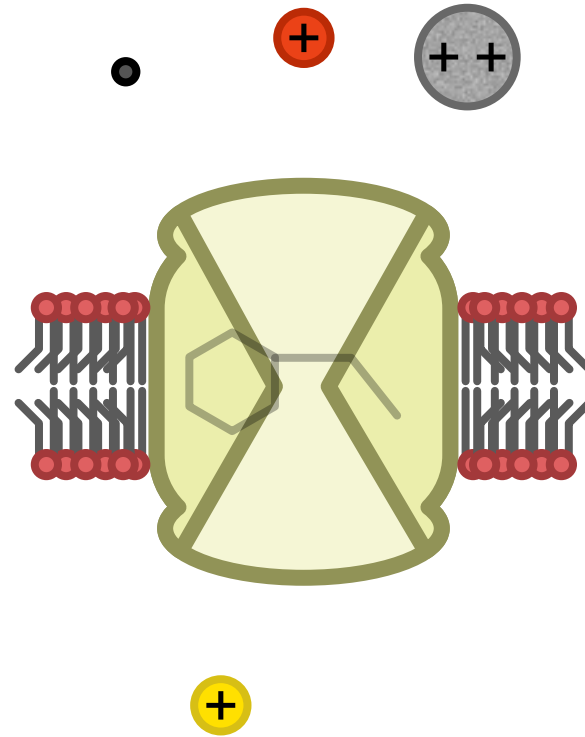
Stoeckenius
1971

Nagel & Hegemann
2003

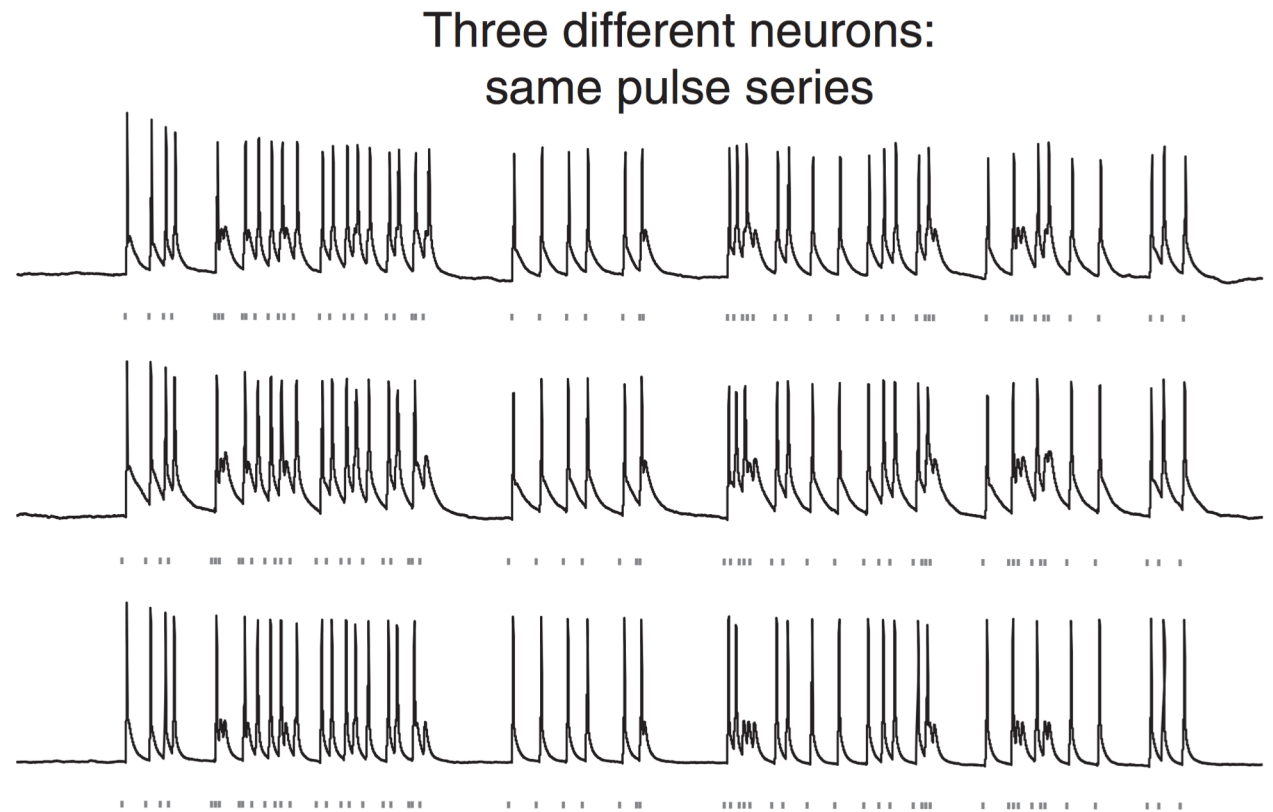
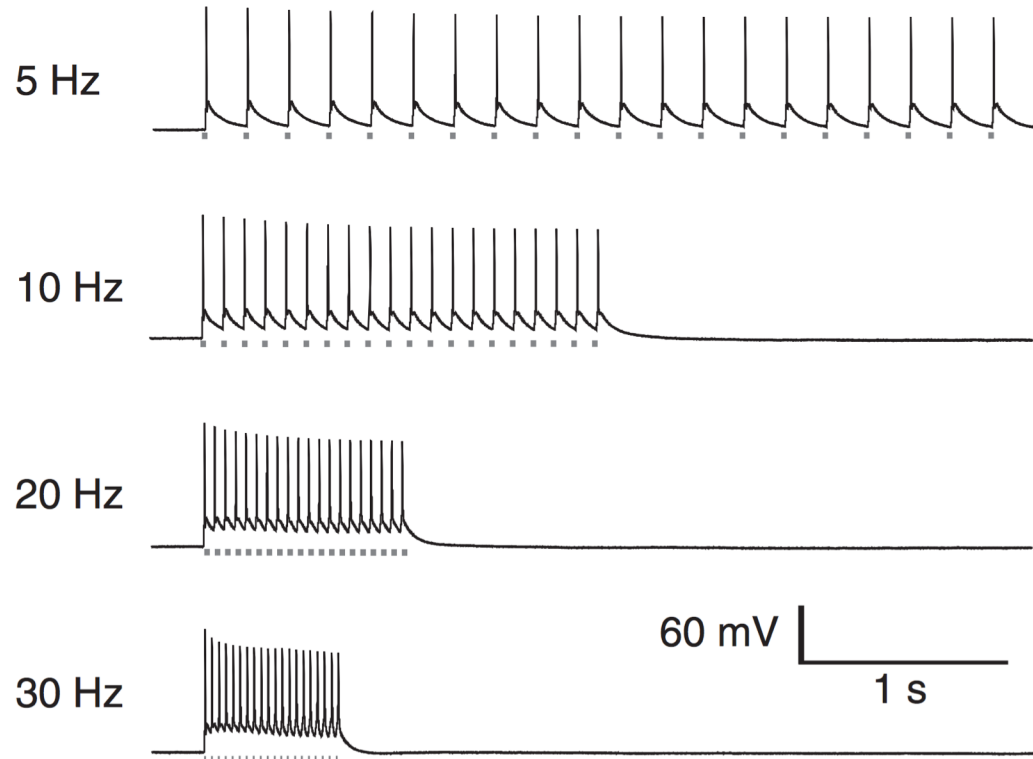
Boyden & Deisseroth
2005



	P_x/P_{Na}
H^+	$\sim 10^6$
Guanidinium ⁺	13 ± 5
$CH_3NH_3^+$	6 ± 2
$(CH_3)_2NH_2^+$	4 ± 2
Li^+	2 ± 0.5
Na^+	1
K^+	0.5 ± 0.3
TMA ⁺	≤ 0.06

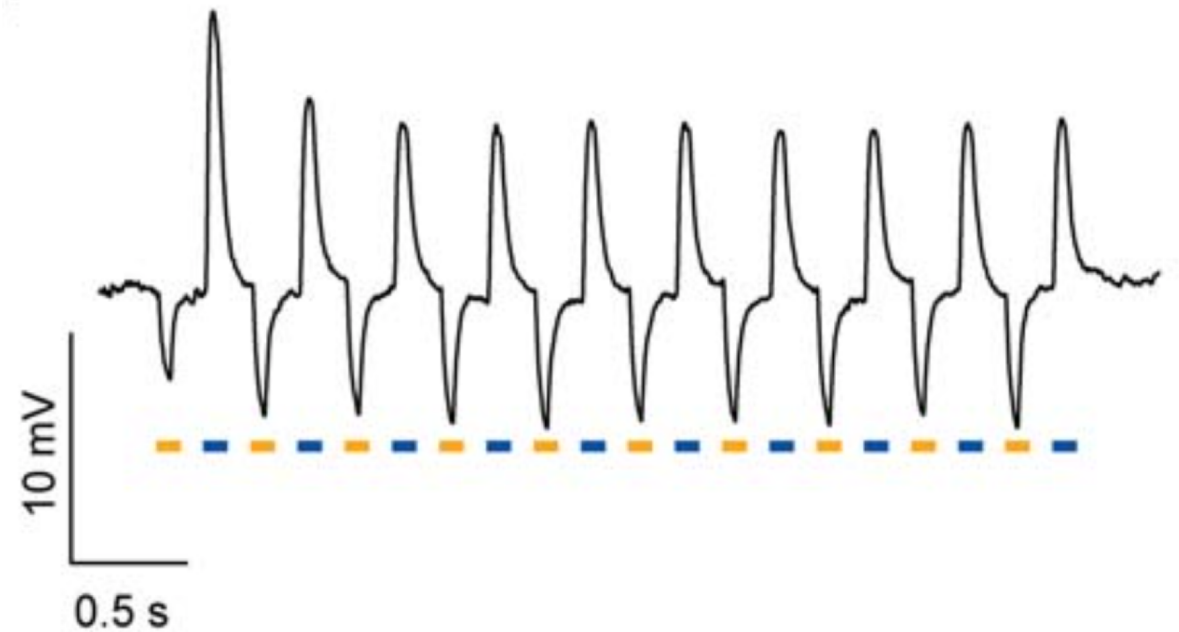
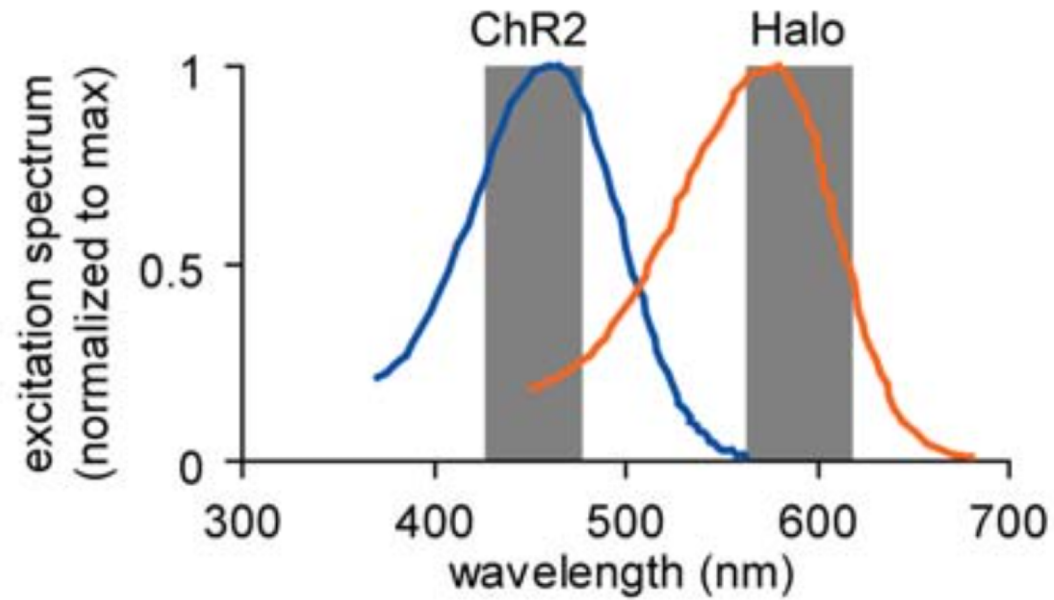


Precise control of spiking with ChR2



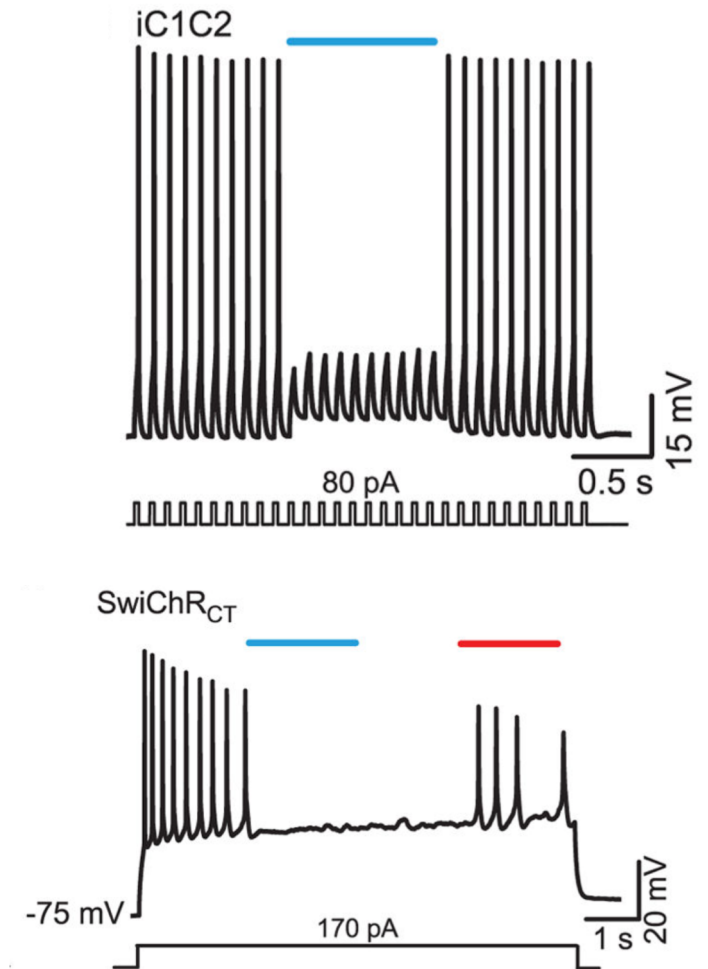
A modern optogeneticist's toolbox

Bidirectional control using halorhodopsin

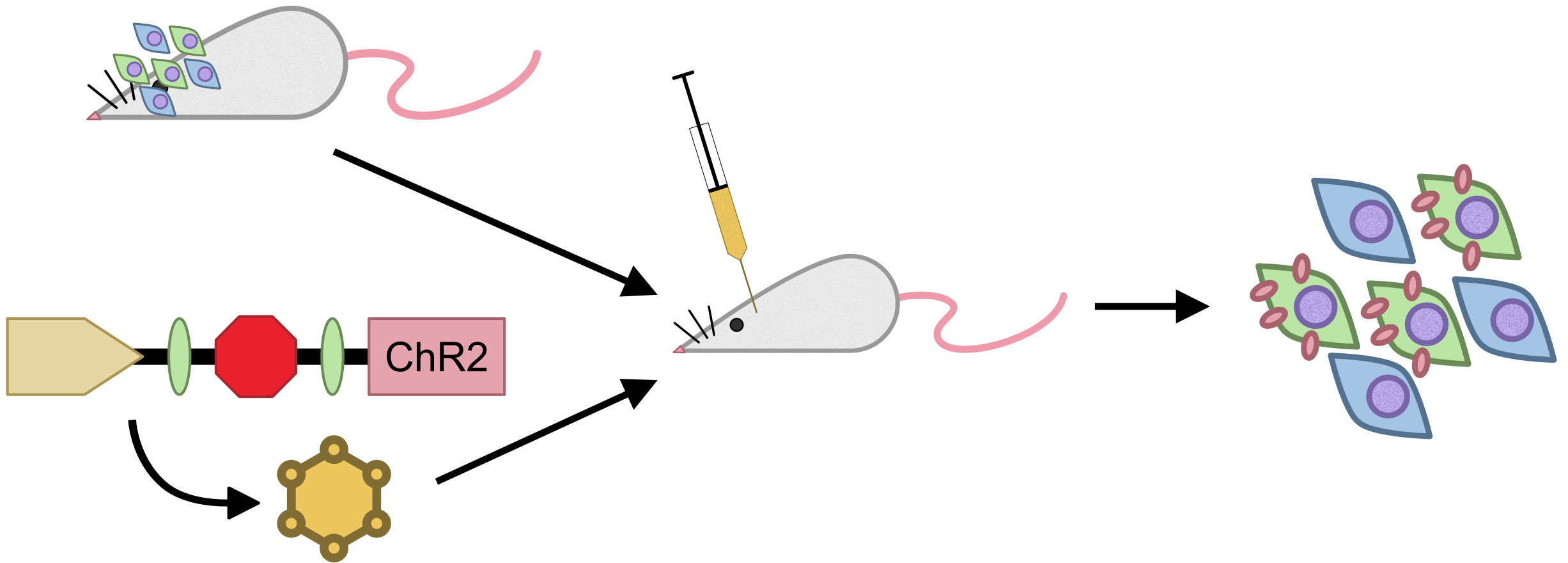


Flavours of channel opsins

- Red-shifted opsins
 - bReaChES
- Faster kinetics
 - ChETA
- Inhibitory channel
 - iC1C2
- Slower kinetics
 - SwiChR

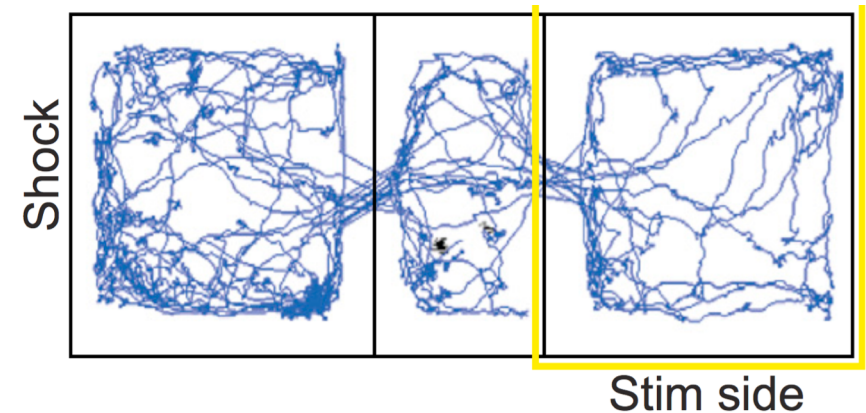
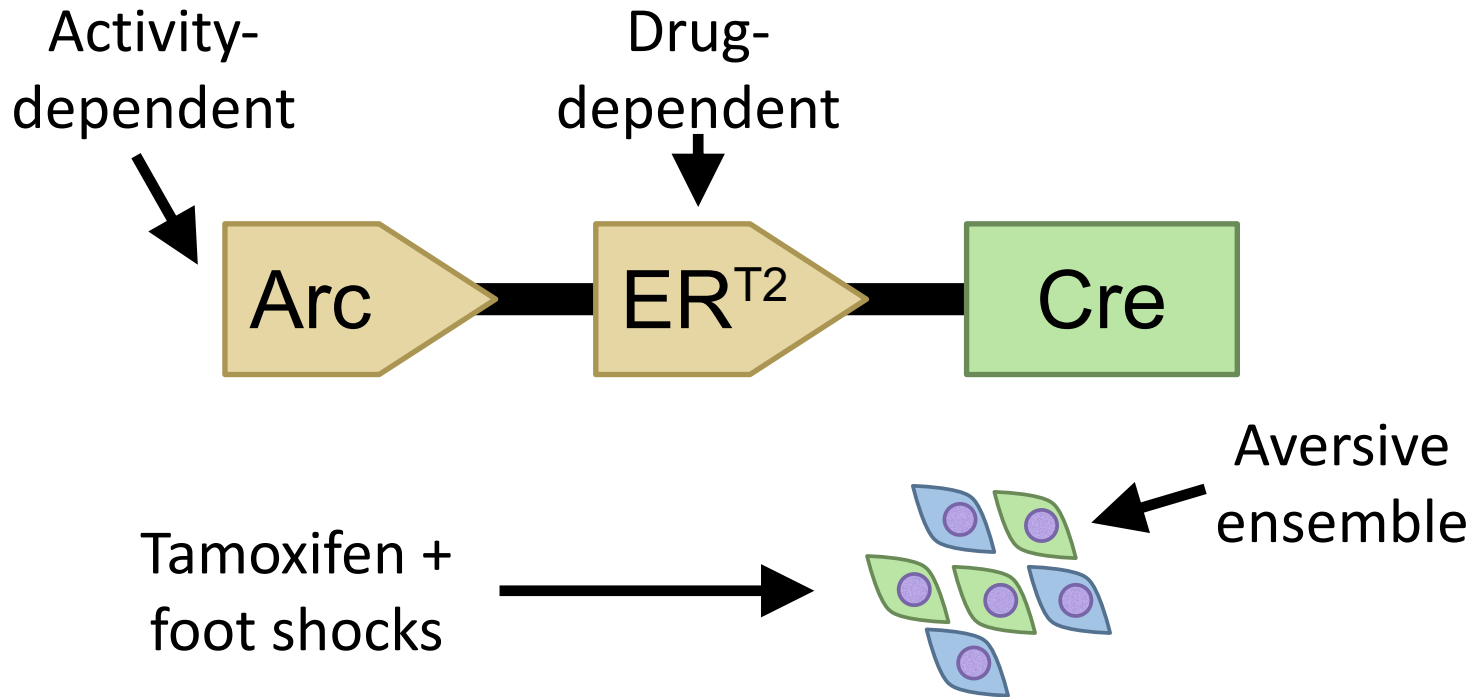


Complex designs using conditional expression



Application

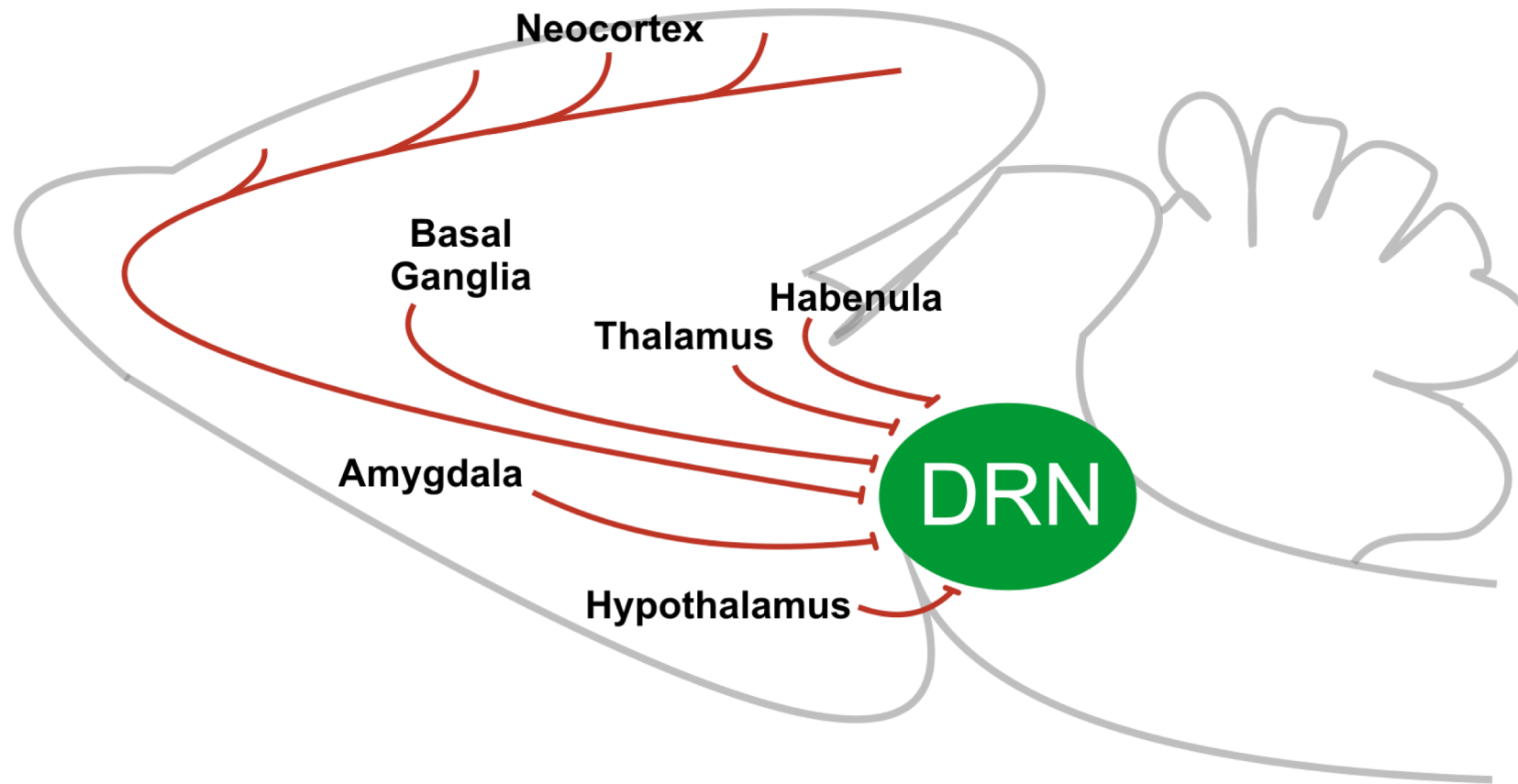
- Activity-dependent expression
 - Manipulate populations activated by reward or punishment



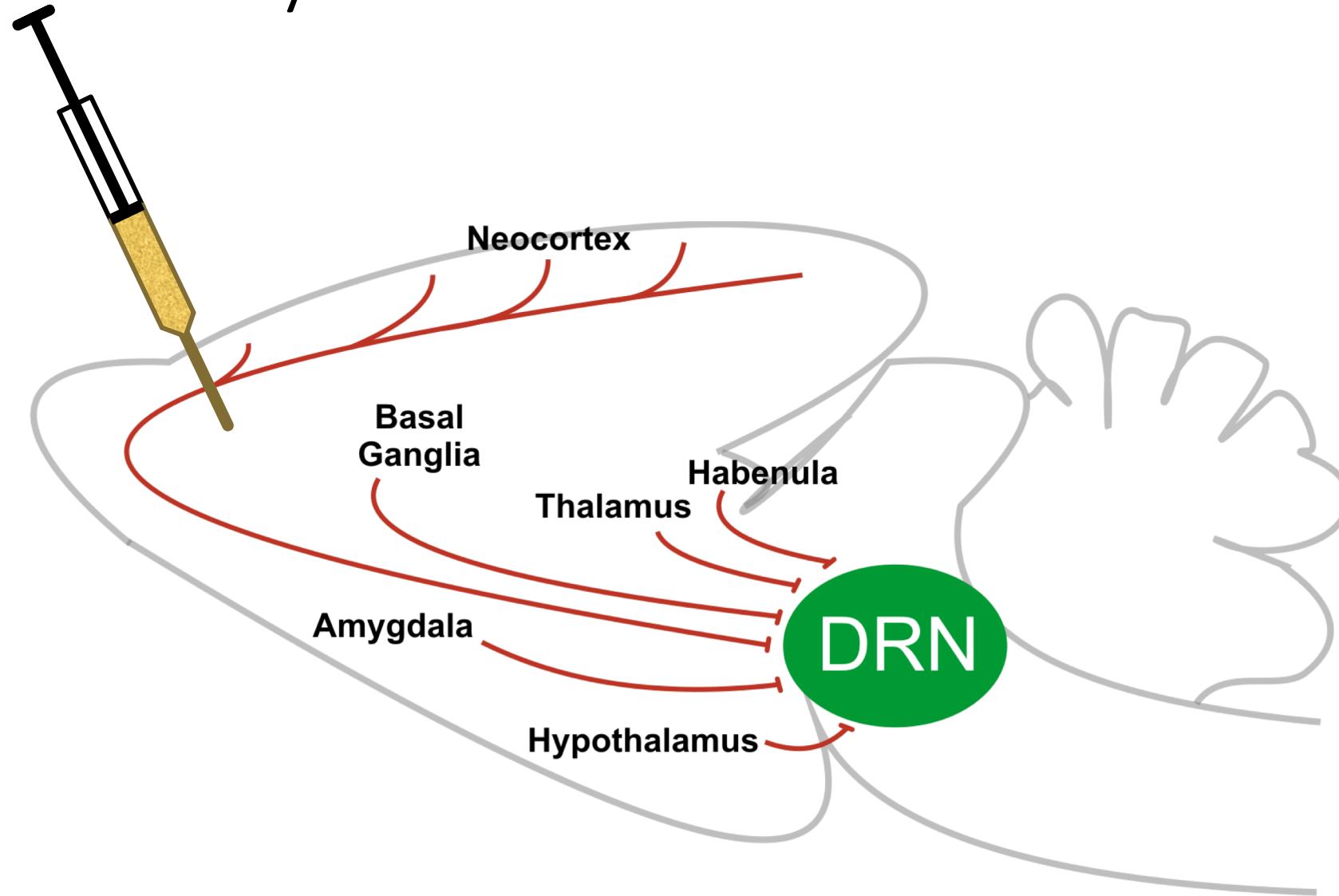
Ye *et al.*, 2016. (Cell)

Case-study: dissecting inputs to
the serotonin system

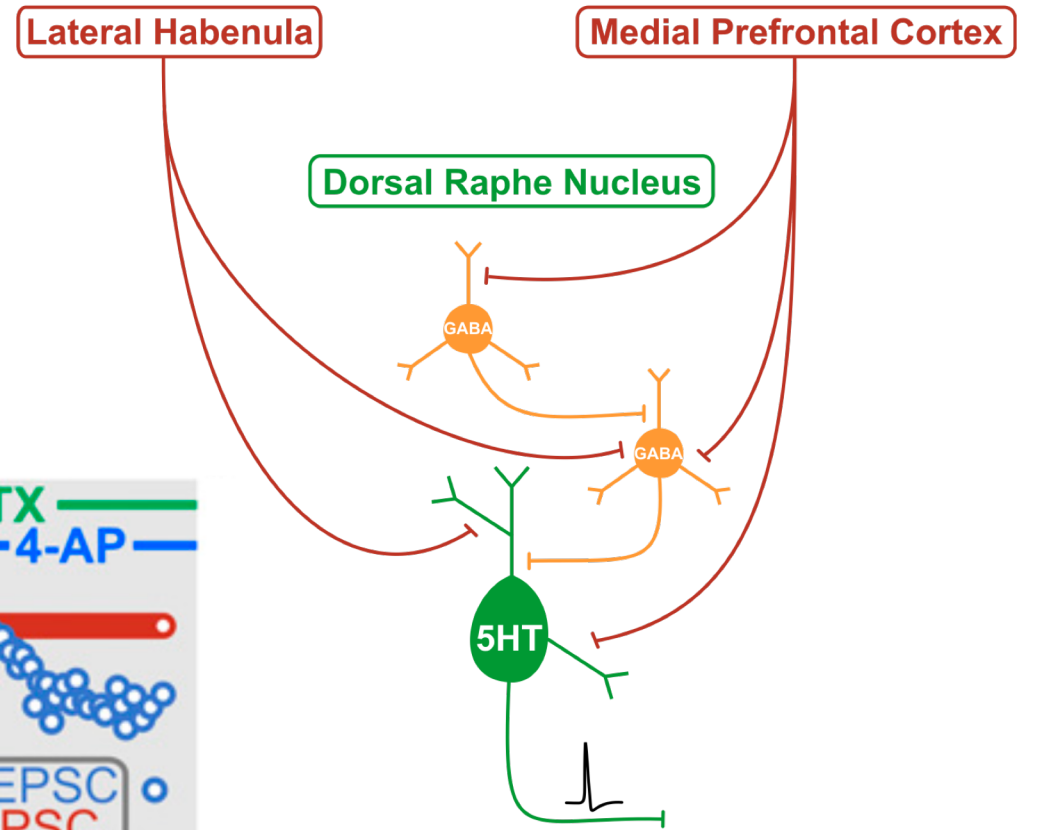
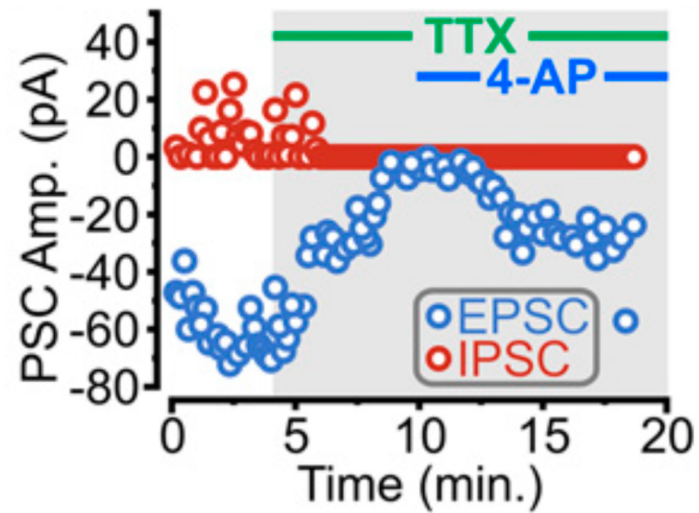
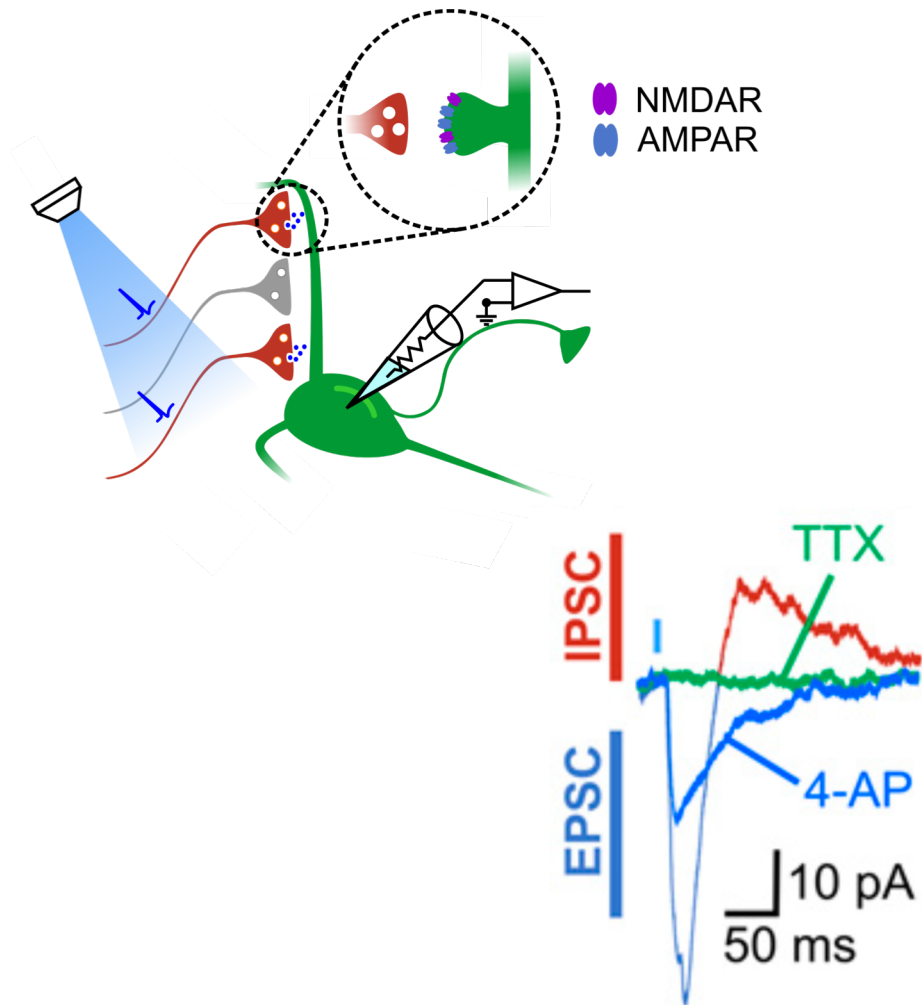
Application: understanding inputs to the serotonin system



Application: understanding inputs to the serotonin system



Focus on mPFC input



Take-home message

Acknowledgements

Supervised by Jean-Claude Béique

Lab members:

- Ginette Hupé
- Sébastien Maillé
- Michael Lynn
- Philippe Vincent-Lamarée
- Éloïse Giraud
- David Lemellin
- Sean Geddes



NSERC
CRSNG



Canada Foundation
for Innovation

Fondation canadienne
pour l'innovation



HEART & STROKE FOUNDATION
**Canadian Partnership
for Stroke Recovery**



CIHR IRSC

 Canadian Institutes of Health Research
Institut de recherche en santé du Canada