Optogenetics

n. *genetics* A science that combines optics and genetics to probe neural circuits
(Wiktionary)

Early origins of optogenetics

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

Selective Photostimulation of Genetically ChARGed Neurons

Neurotechnique

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transmitted optical signal that can be decoded and transduced into electrical activity by only a subset of all illuminated neurons. The "receiver" of the optical signal is encoded in DNA, and the responsive subset of neurons can therefore be restricted genetically (Crick, 1999; Zemelman and Miesenböck, 2001) to certain cell types (through cell-type specific promoters) or circuit ele-

Expression of fly arrestin in vertebrate neurons

Cell, Vol. 121, 141–152, April 8, 2005, Copyright ©2005 by Elsevier Inc. DOI 10.1016/j.cell.2005.02.004

Remote Control of Behavior through Genetically Targeted Photostimulation of Neurons

Resource

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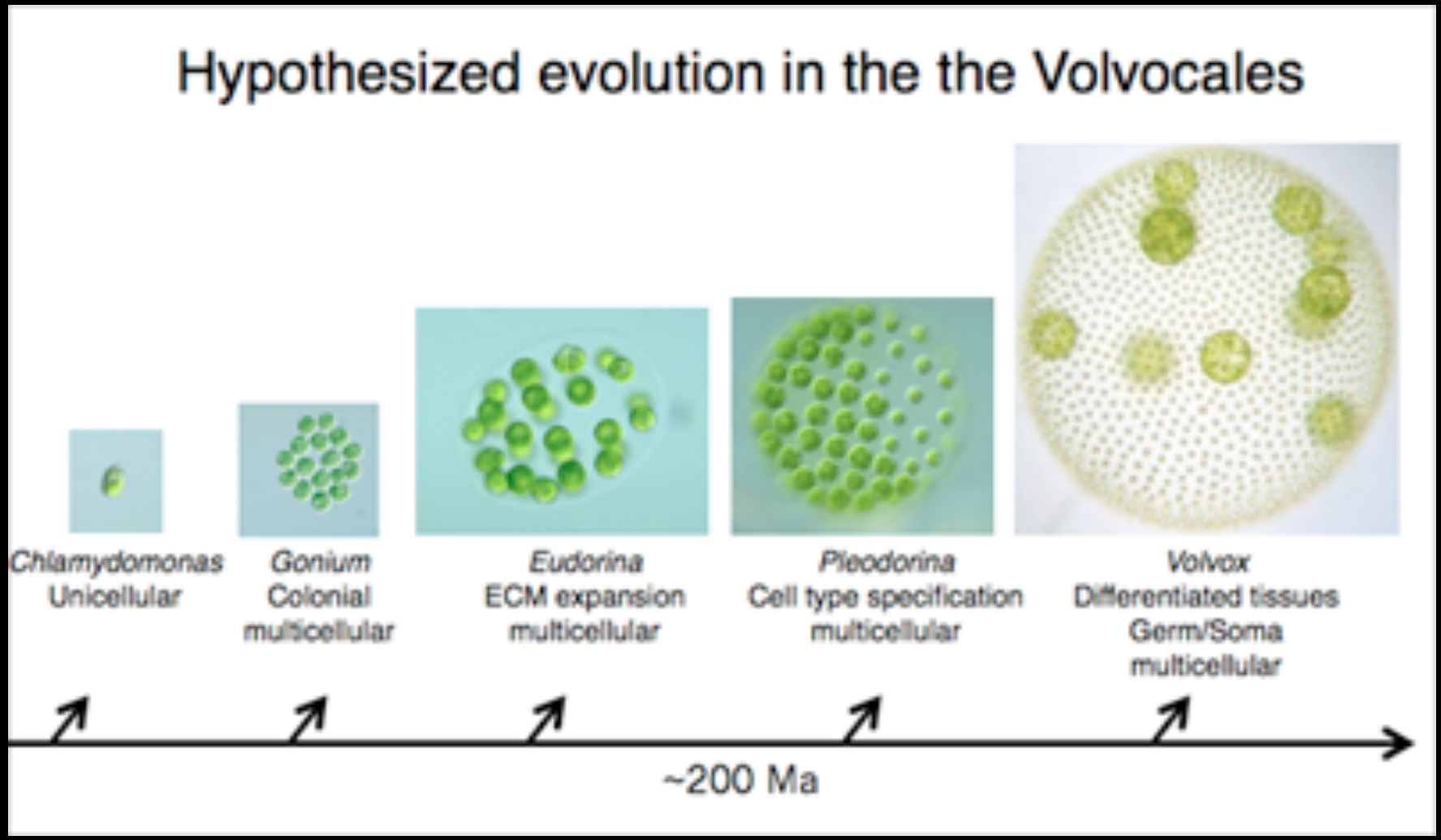
ity patterns are correlated with a given behavior?—to active and predictive manipulation of behavior.

We report experiments in *Drosophila* that realize this scenario. Unfocused laser light played the part of the publicly broadcast stimulus; genetically encoded "pho-

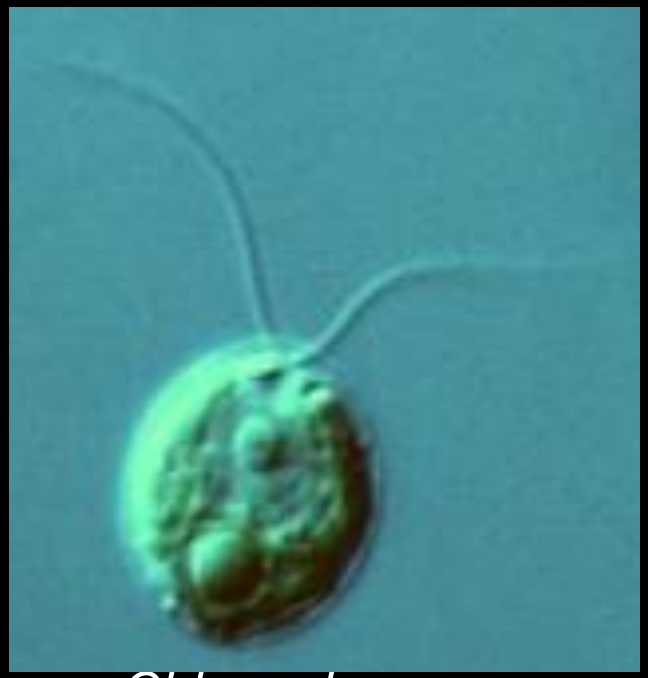
Purinoreceptor (must inject caged ATP)

Really early origins of optogenetics

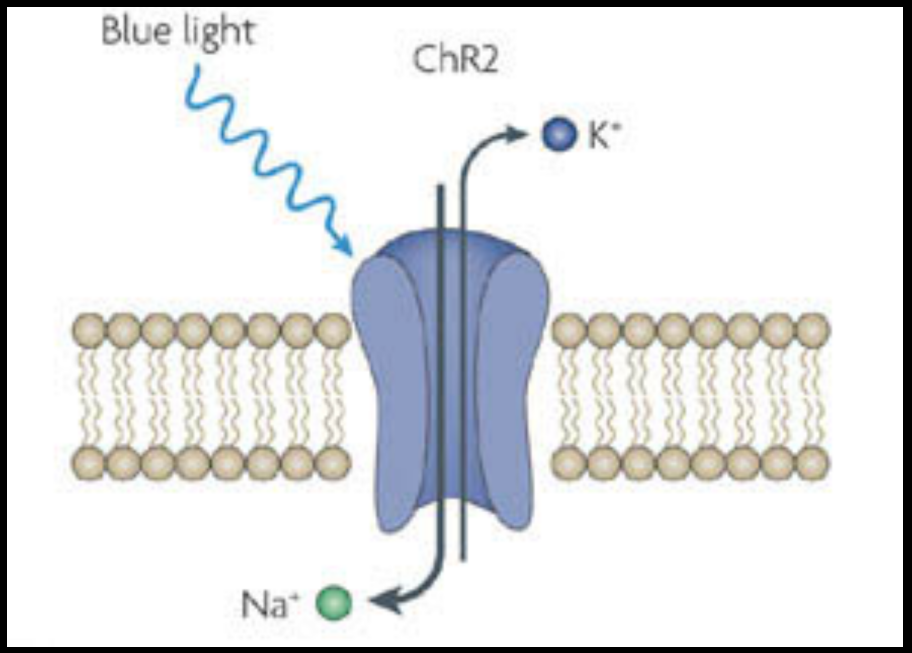


Brad Olsen

Suddenly, neuroscientists are interested in algae



Chlamydomonas reinhardtii



Thank you, green C. reinhardtii

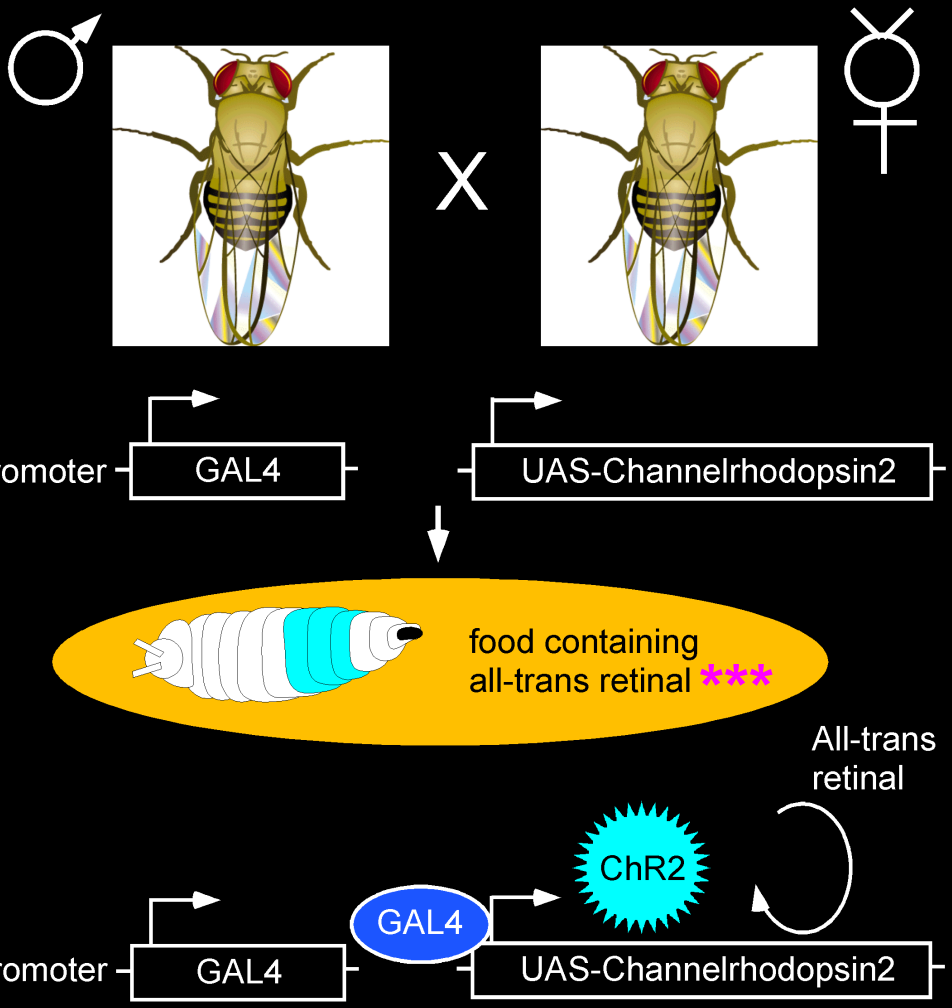
Nagel, Szellas, Huhn, Kateriya, Adesshvill, Berthold, Ollig, Hegemann, Bamberg (2003) PNAS
(ChR2 is directly light-gated, depolarizes cells when expressed in cultured cells)

Boyden, Zhang, Bamberg, Nagel, Dessiroth (2005) Nat. Neuro.
(ChR2 can be expressed in vertebrate neurons and can control activity on ms time scales)

Nagel G, Brauner M, Liewald JF, Adeishvili N, Bamberg E, Gottschalk A (2005) Curr. Biol.
(ChR2 can be used to remotely activate neurons in freely behaving nematodes)

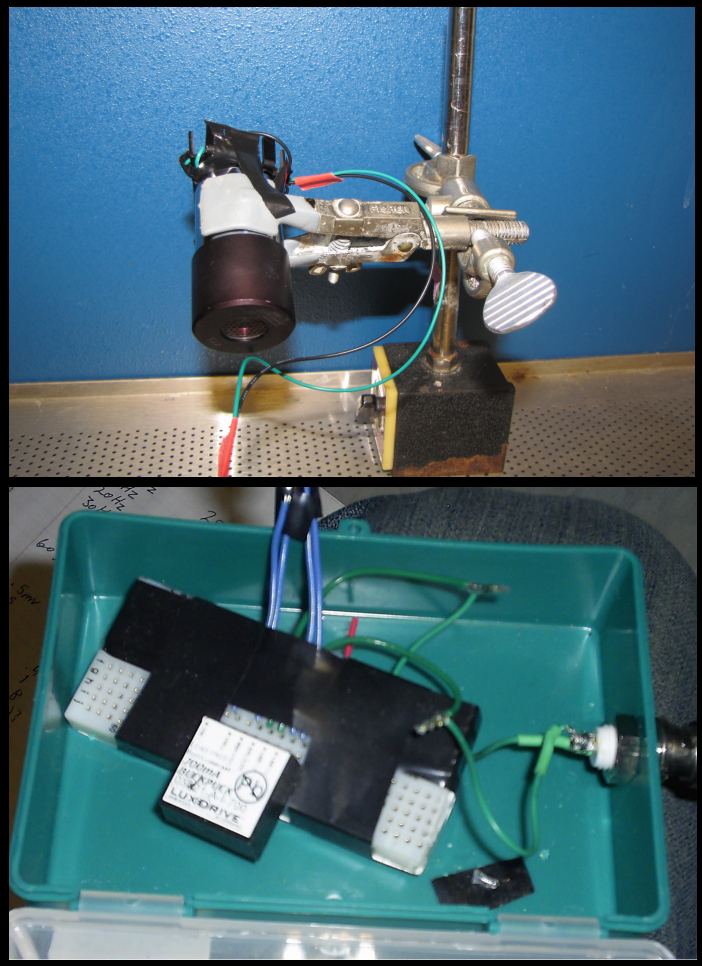
What do you need to do basic optogenetic experiments in flies?

Transgenic flies (freely available)

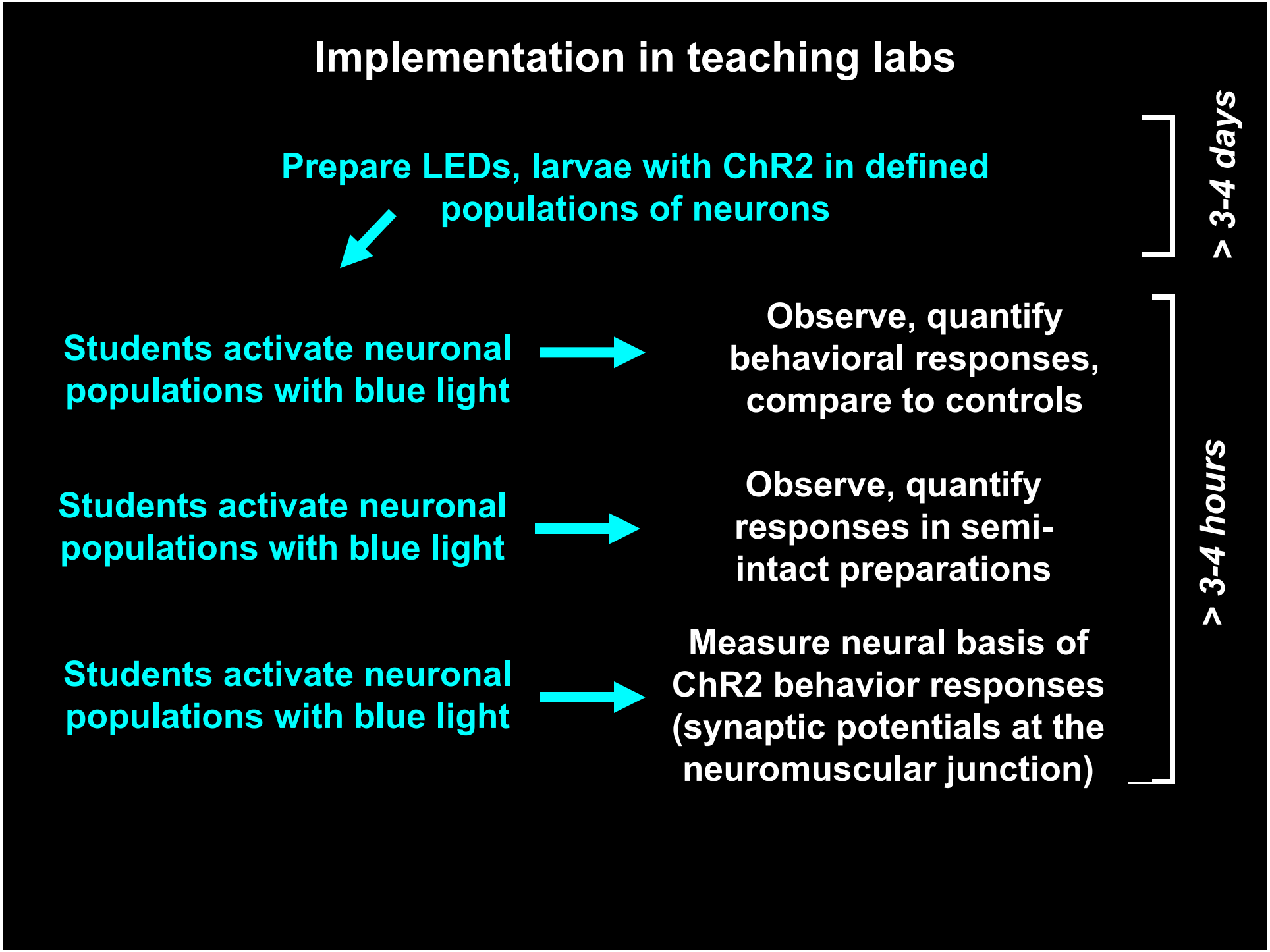


***Expensive

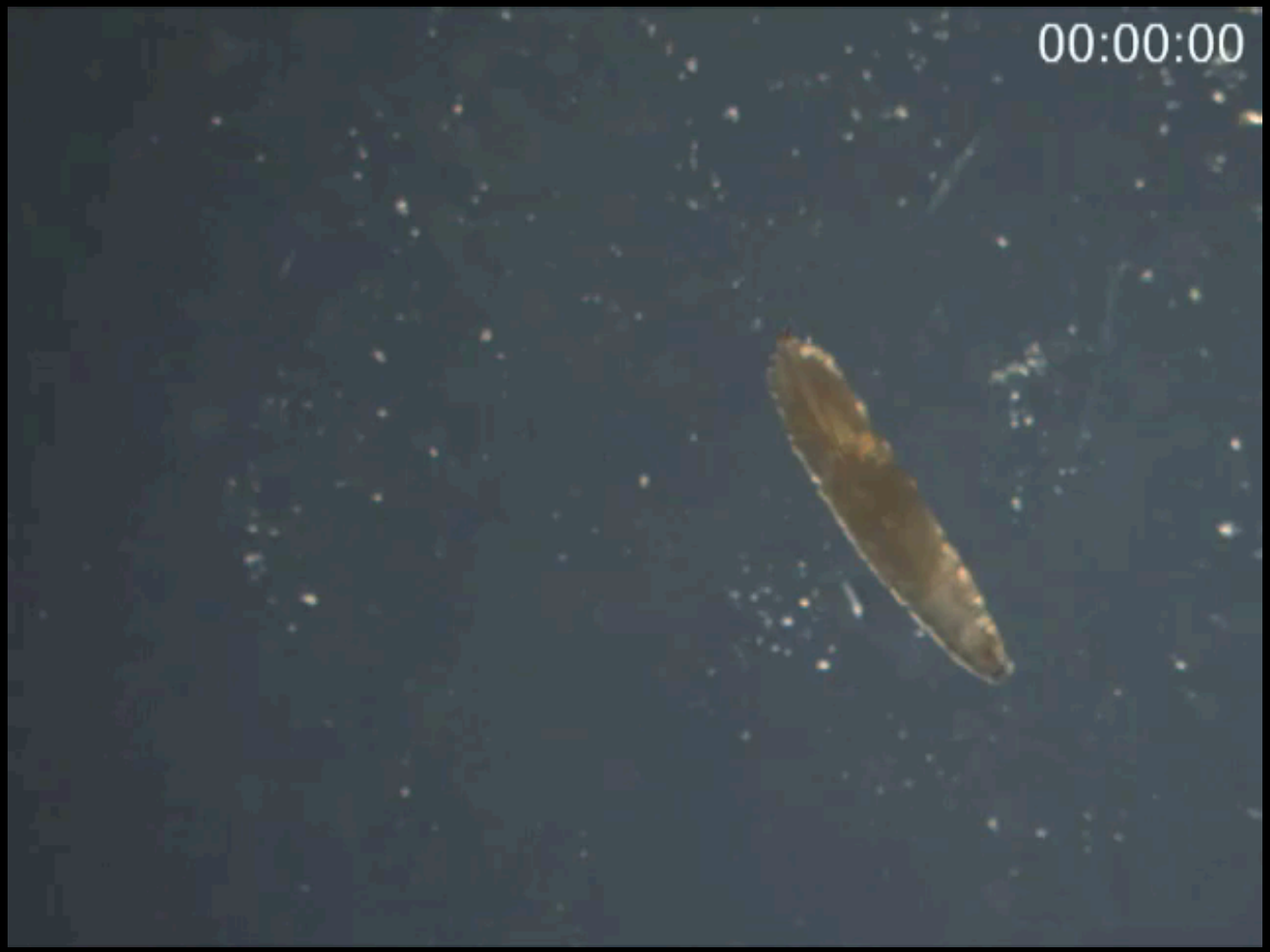
Inexpensive blue light source



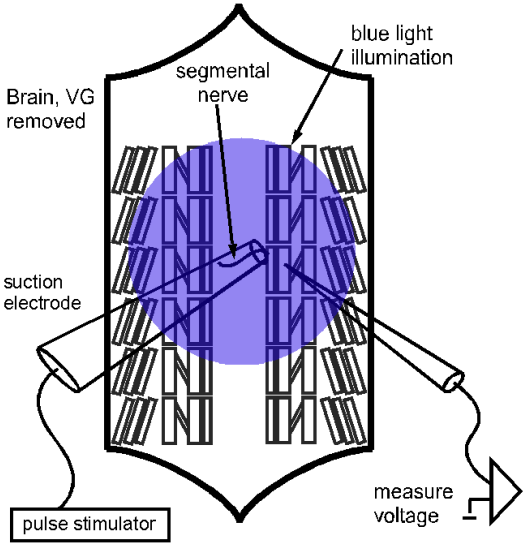
Pulver et al., 2011, *Adv. Physiol. Edu.*
Hornstein et al., 2009, *J. Vis. Exp.*

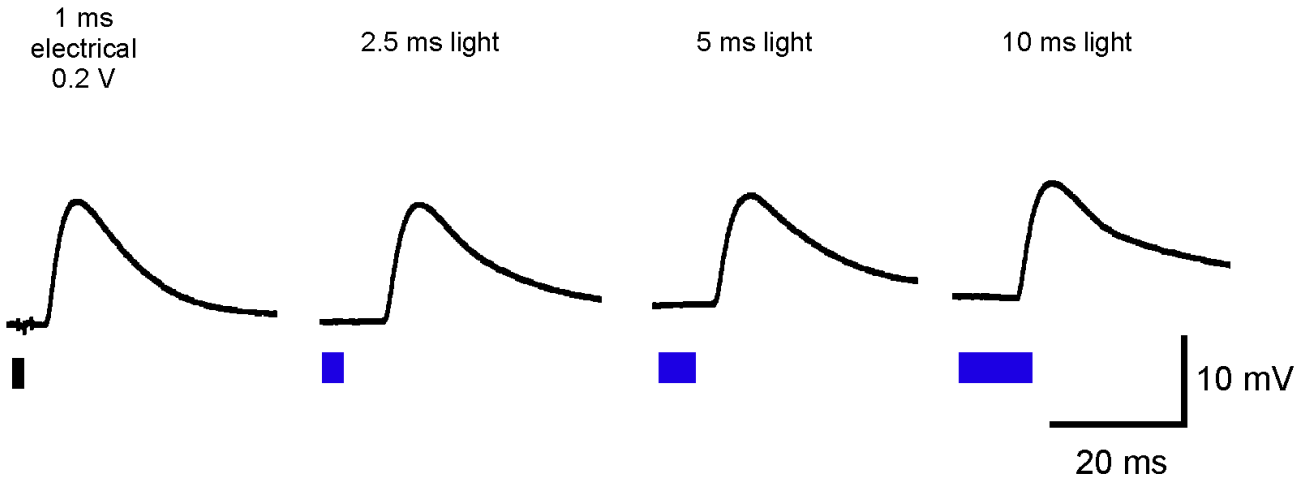

Implementation in teaching labs
Prepare LEDs, larvae with ChR2 in defined populations of neurons
> 3-4 days
Students activate neuronal populations with blue light
Observe, quantify behavioral responses, compare to controls
Students activate neuronal populations with blue light
Observe, quantify responses in semi-intact preparations
Students activate neuronal populations with blue light
Measure neural basis of ChR2 behavior responses (synaptic potentials at the neuromuscular junction)
> 3-4 hours

What will students see when all motor neurons are stimulated at once?



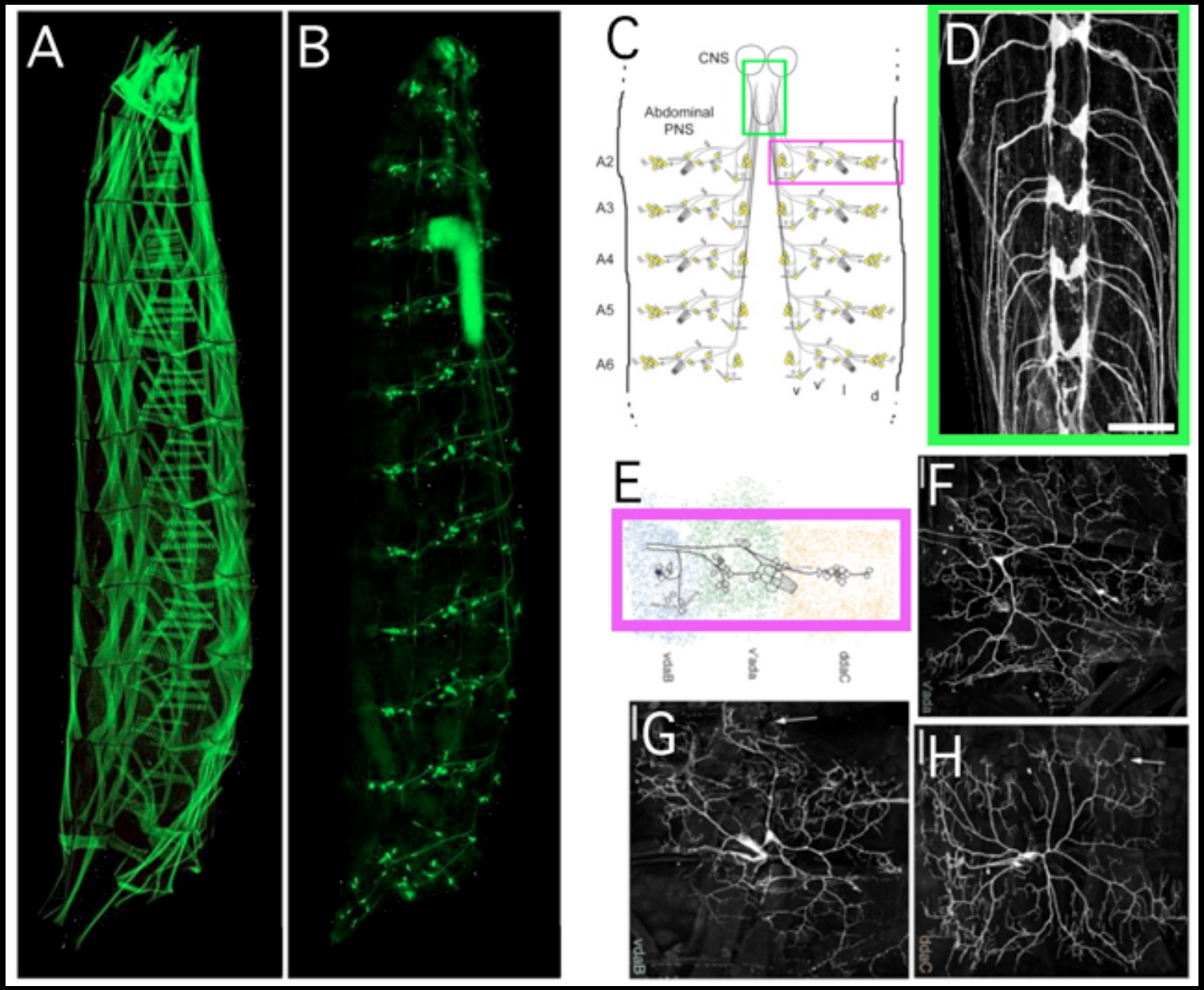
Light-evoked synaptic potentials at the larval neuromuscular junction





***Nuts and bolts: before poking anything, check for visible contractions in response to light

Pickpocket-GAL4 expresses in larval nociceptive neurons



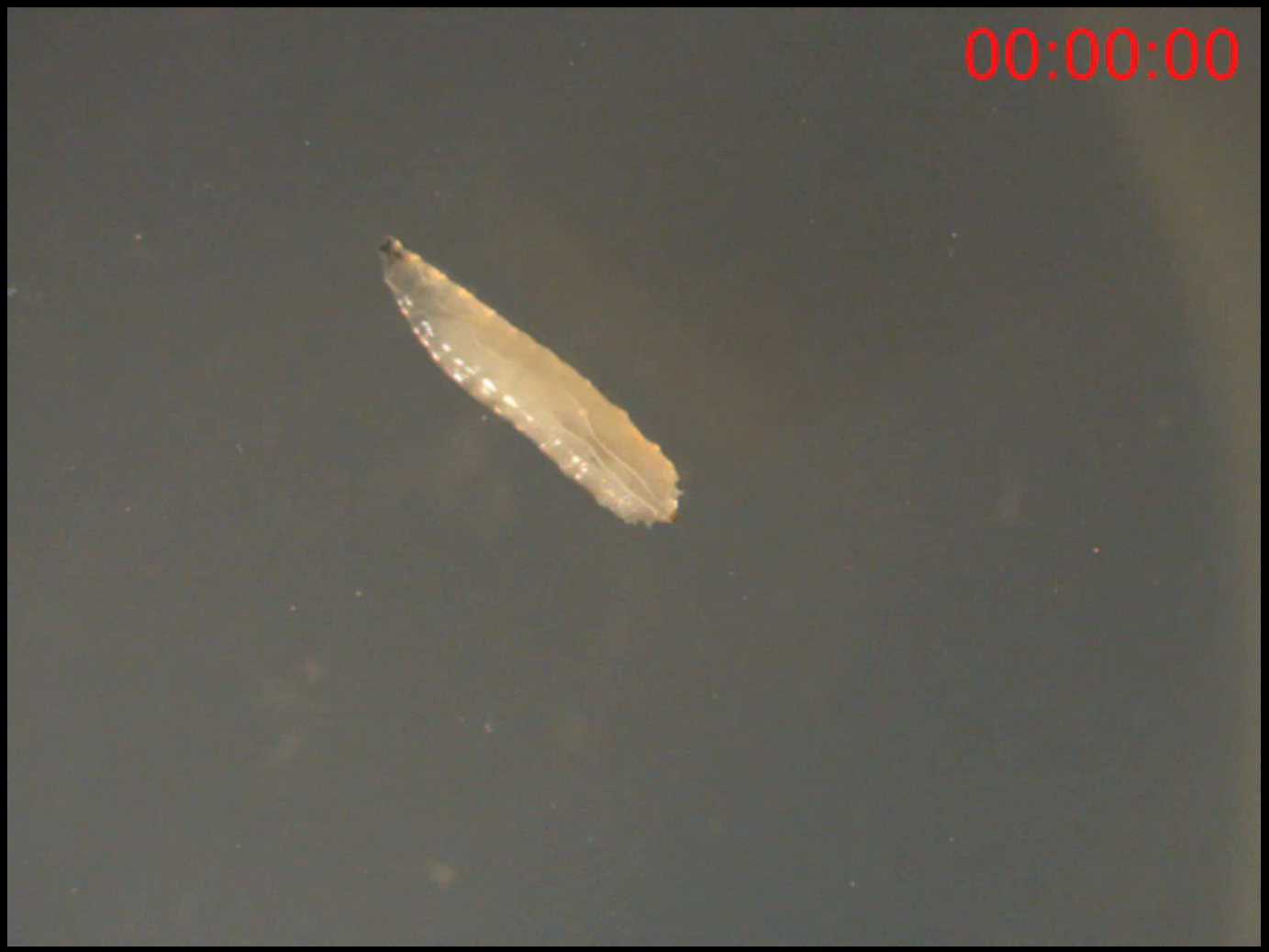
PPK neurons are necessary and sufficient for evoking a larval ‘nocifensive’ behavior

Movies in

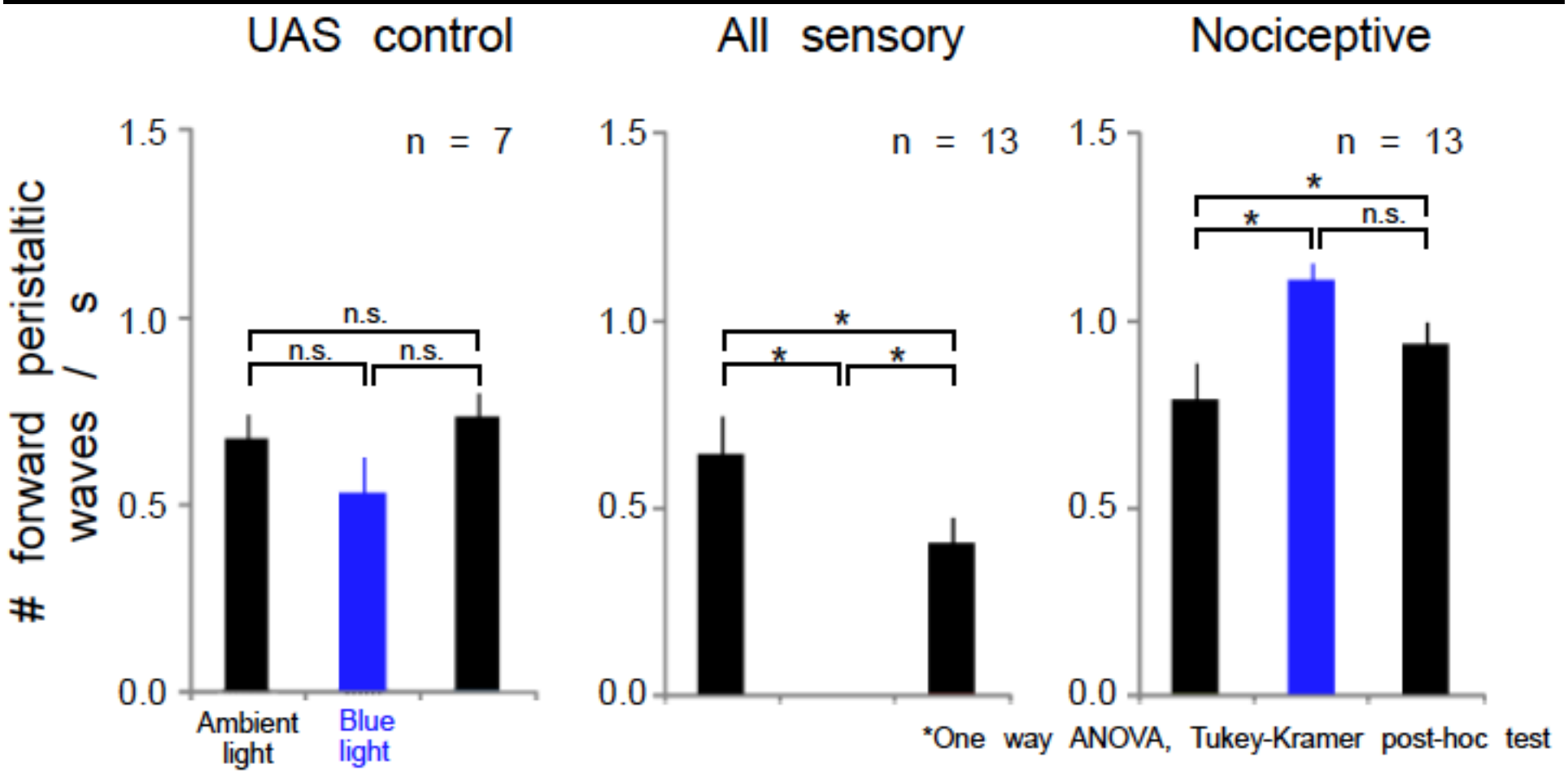
Hwang et al., 2007, *Curr. Biol.*

Stimulation of sensory neurons in teaching labs

ChR2 expressed in ‘nociceptive’ neurons

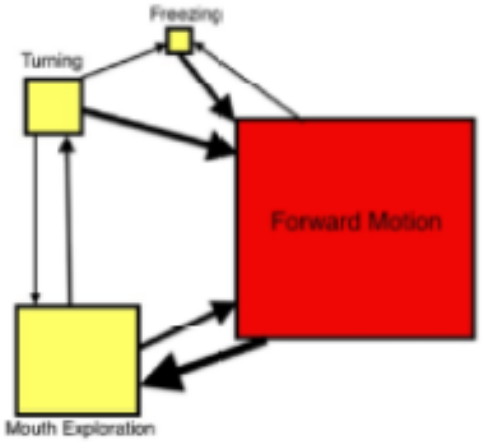


Student-initiated analysis of behavior

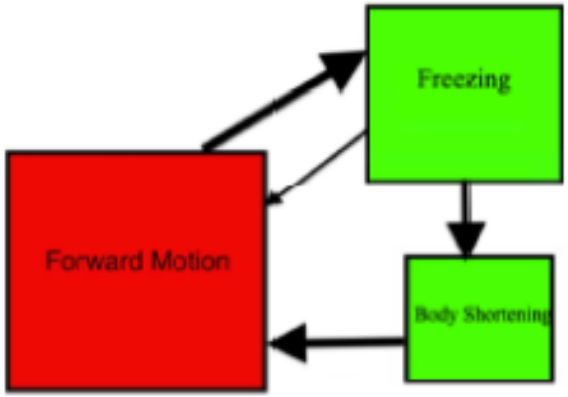


Student-initiated analysis of behavior

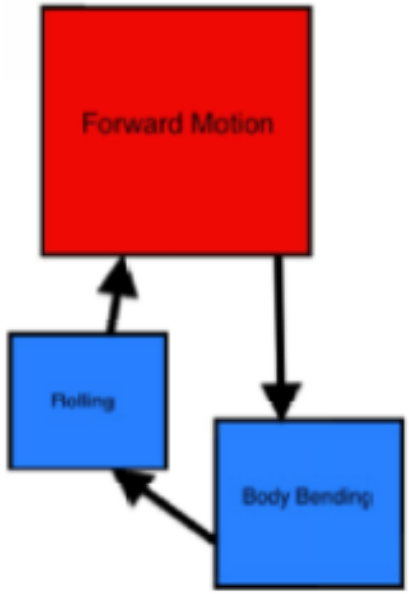
All genotypes under white light & wild type under blue light



All sensory under blue light

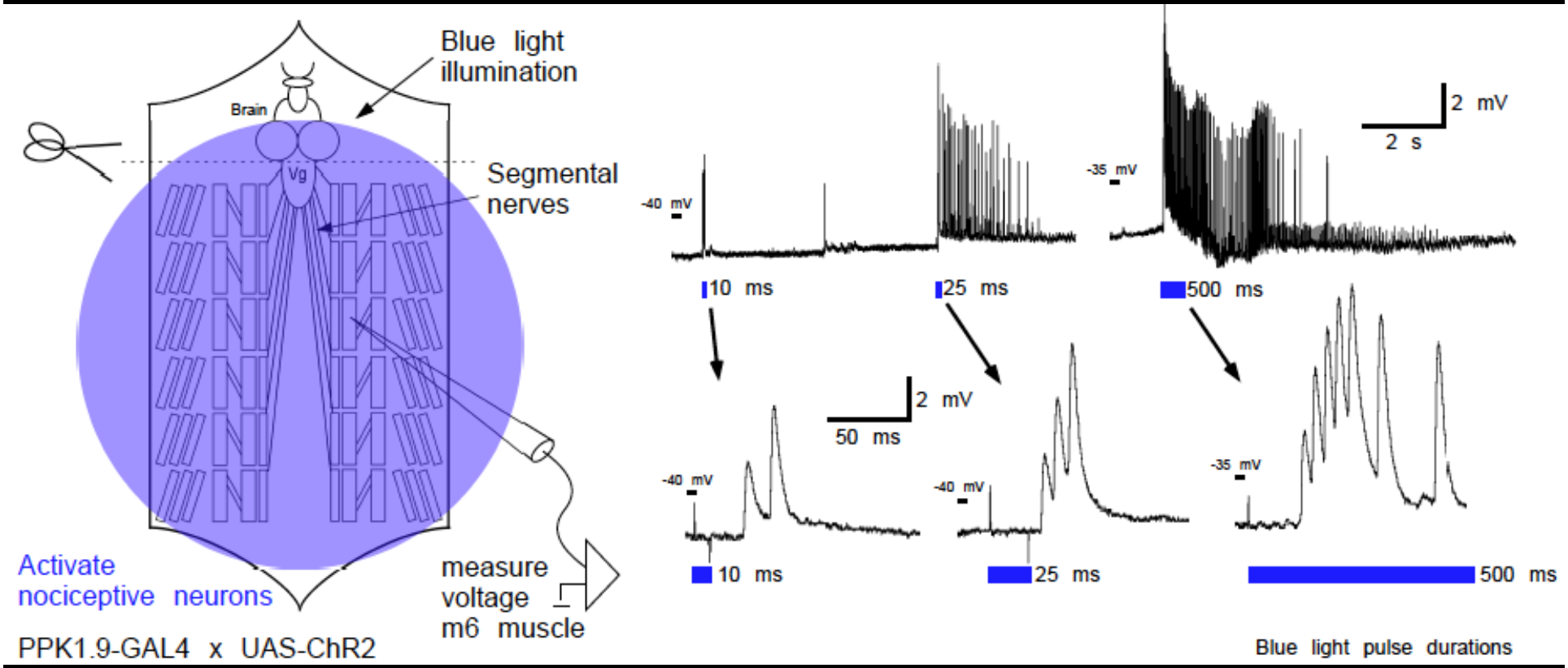


Nociceptive under blue light



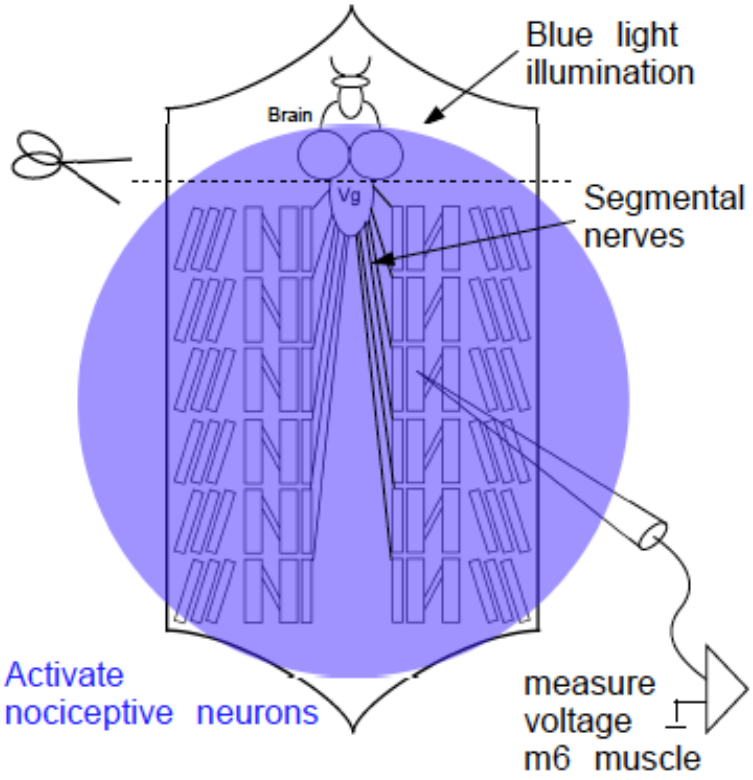
*Size of boxes represents proportion of time spent in given behavior. Thickness of arrows indicates relative probabilities of transitions from one behavior to another.
Analysis by S. Albers and Z. Lorsch.

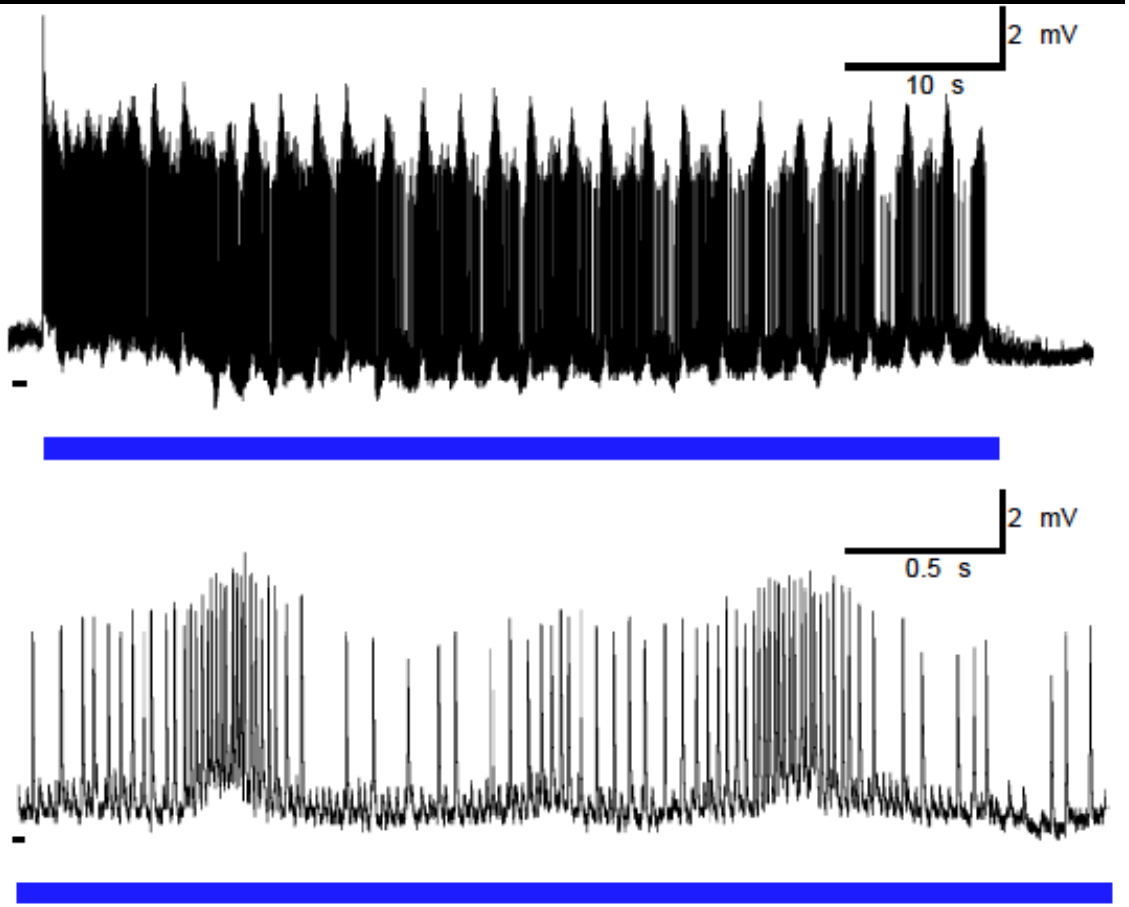
Activation of sensory neurons triggers EJPs at NMJ



***Specific mission: compare delay to first EJP in motor neuron vs sensory

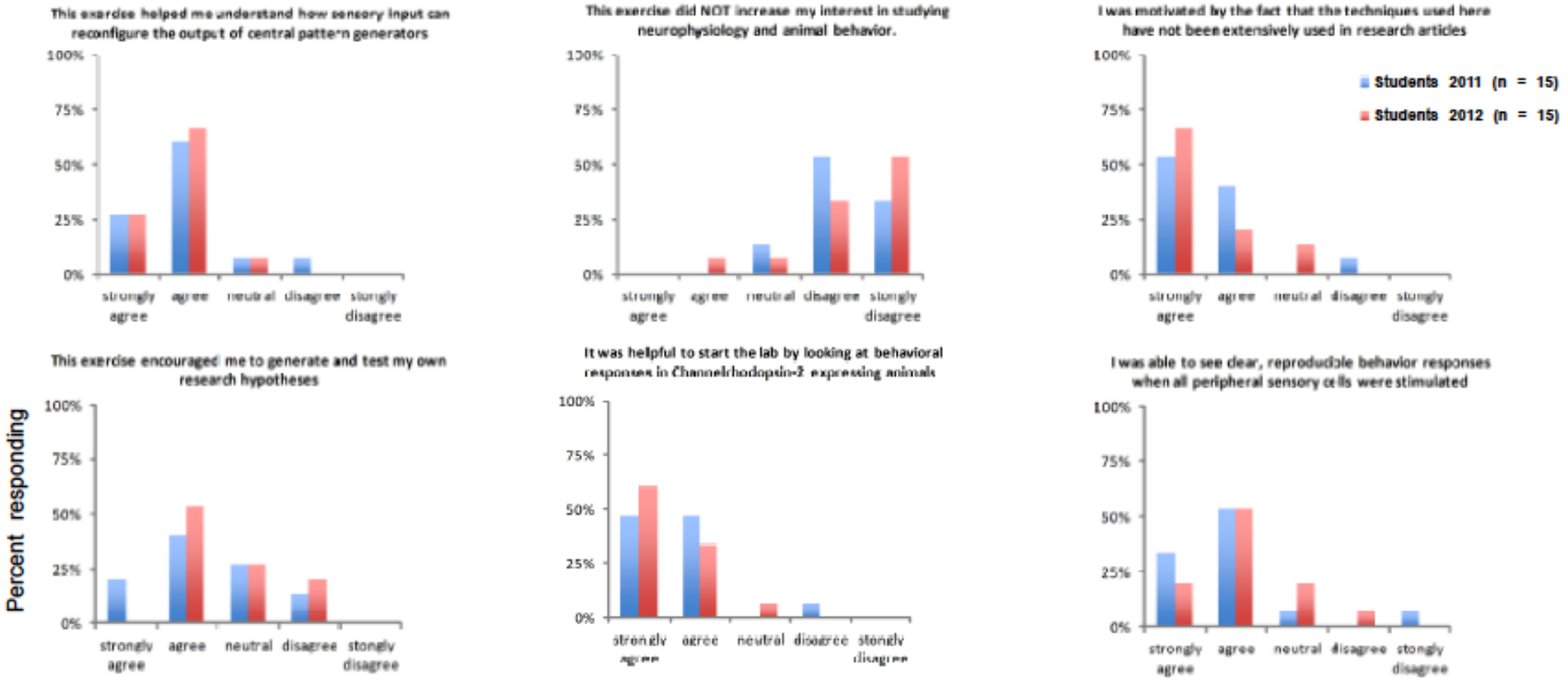
Rhythmic bursts of EJPs with constant stimulation



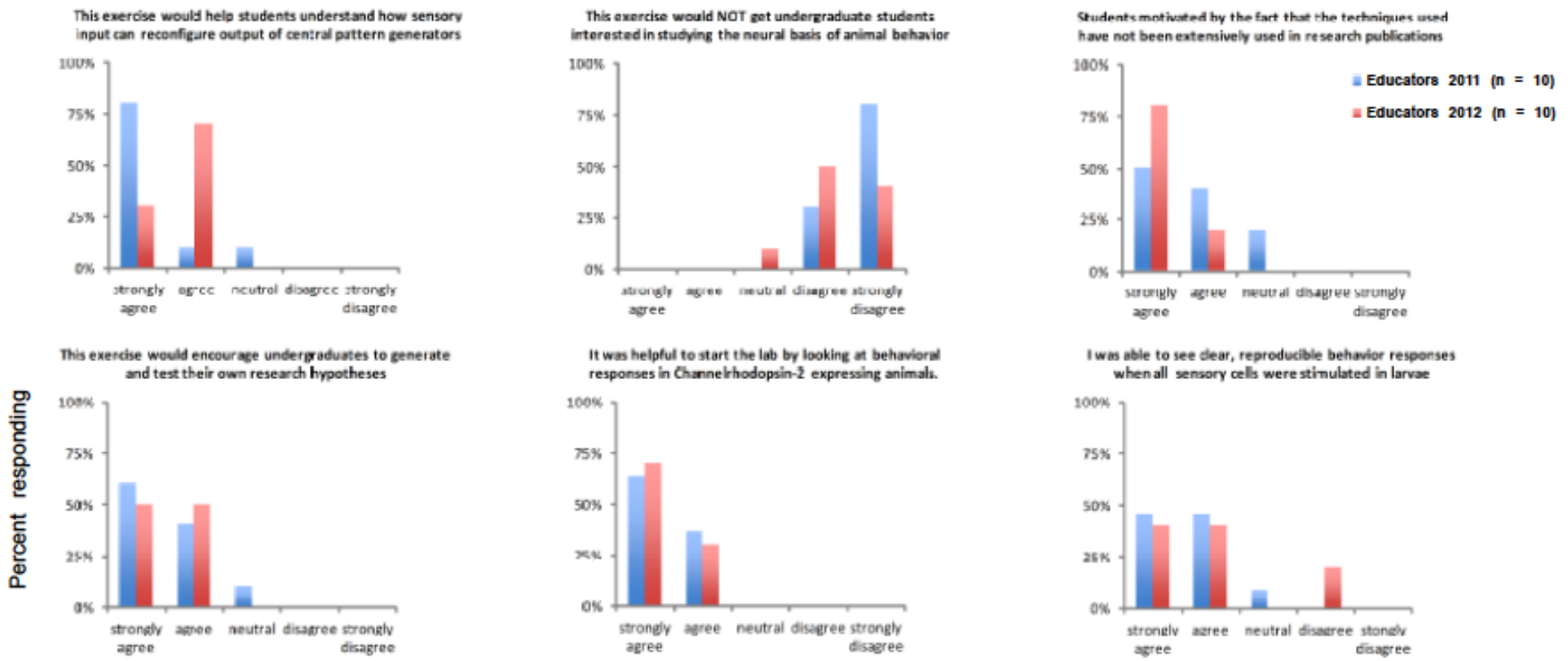


PPK1.9-GAL4 x UAS-ChR2 (n=4)	cycle period [s]	inst burstfreq [Hz]	burst duration [s]	dutycycle	interburst interval [s]	#spikes in burst	spikefreq in burst [Hz]
Ambient light	0	0	0	0	0	0	0
60 sec blue light	1.7 ± 0.5	0.58 ± 0.1	1.12 ± 0.4	0.49 ± 0.1	1.08 ± 0.2	39.4 ± 15.4	35.1 ± 4.7

Students: Are these exercises actually effective?



Educators: Are these exercises actually effective?



DISCUSSION POINTS

- What is it about this technology that is so helpful?
- When isn't it helpful? What are the limitations?
- Who made this discovery?
- Why do we have this new technology?