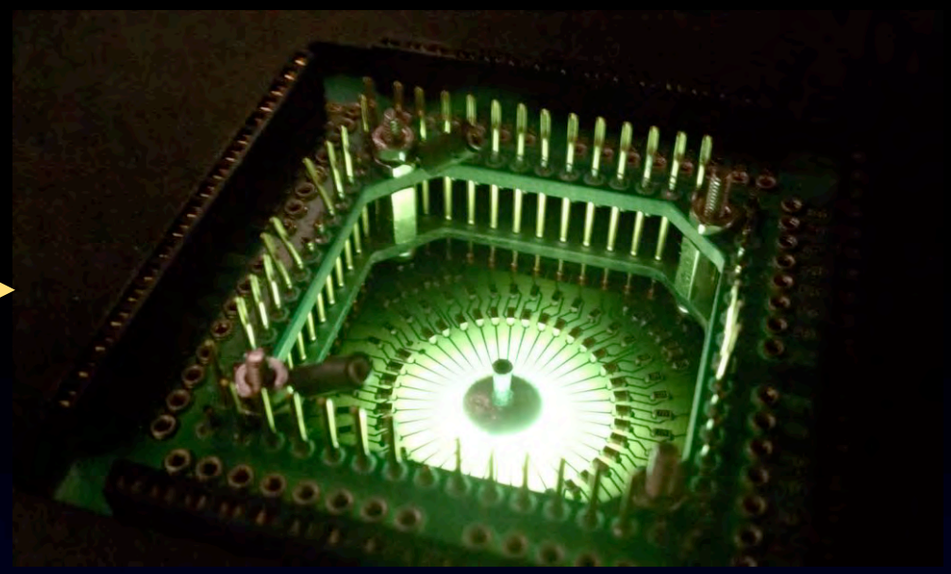


Hybrid Systems

Combining Wetware and Hardware

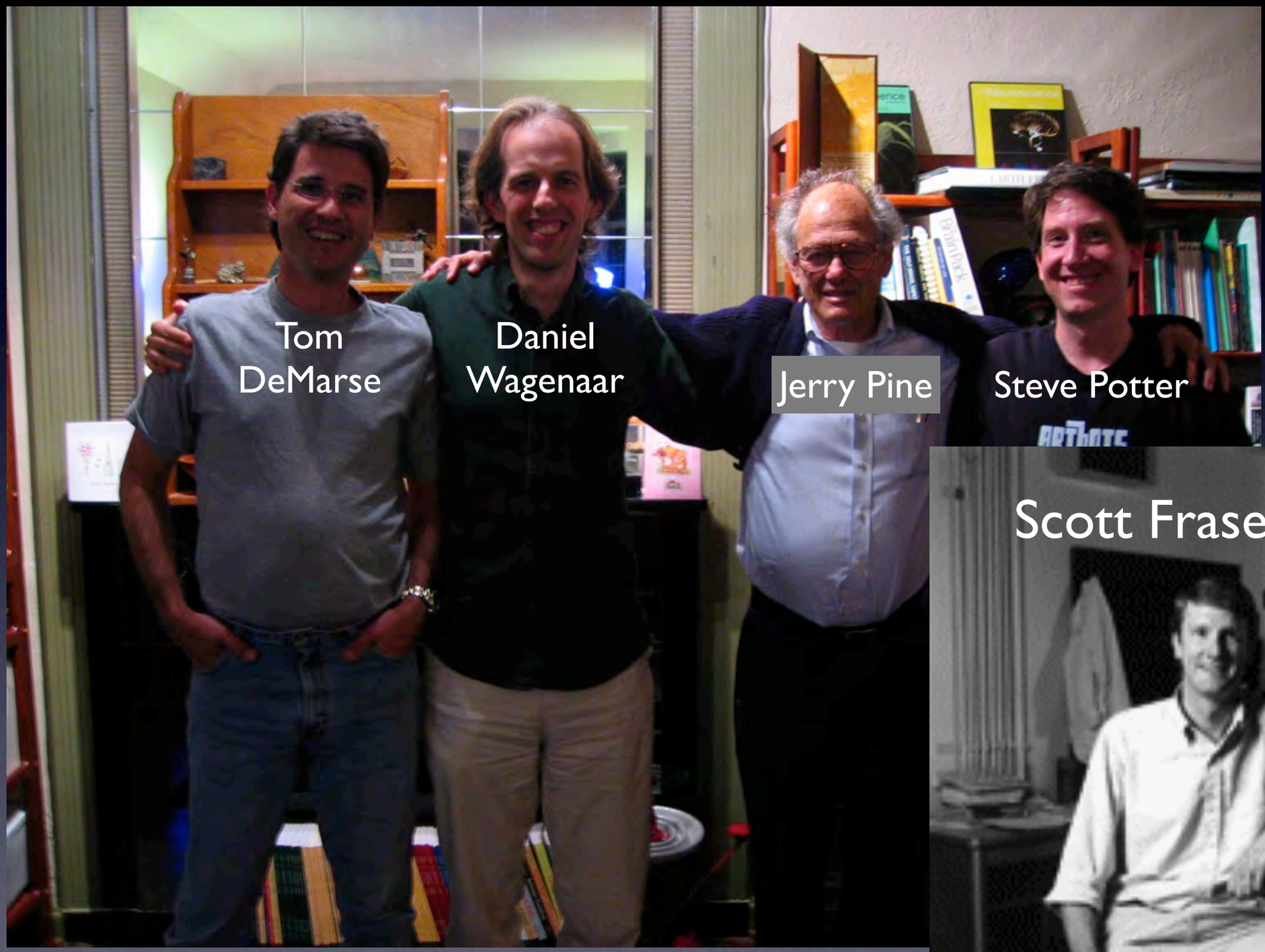
Steve M. Potter, PhD
Adjunct Associate Professor
Department of Biomedical Engineering
Georgia Institute of Technology and
Emory University School of Medicine

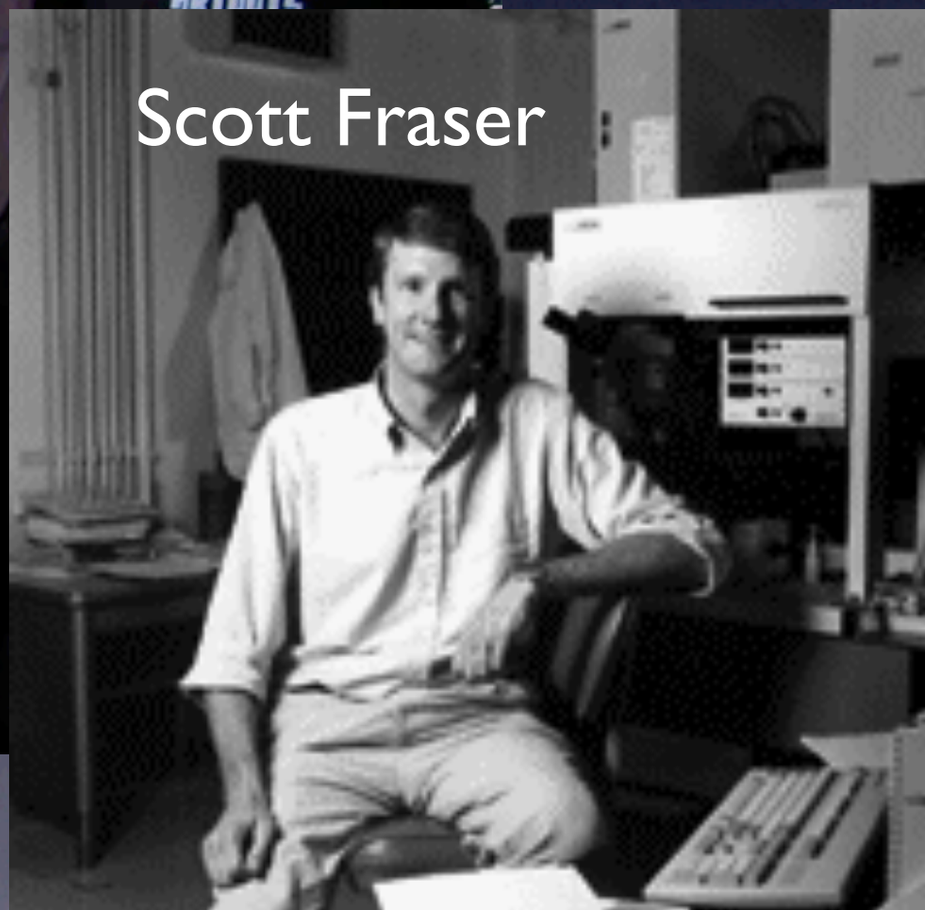
About me...

- BA in biochemistry from UC San Diego
- PhD in neurobiology from UC Irvine
- 8 years as research faculty at Caltech
- 13 years as professor at Georgia Tech
- I moved to Ireland in 2016 to become a freelance AI consultant and writer.
- All our papers are available at http://potterlab.gatech.edu

At Caltech

as Senior Research Faculty (1994-2002)

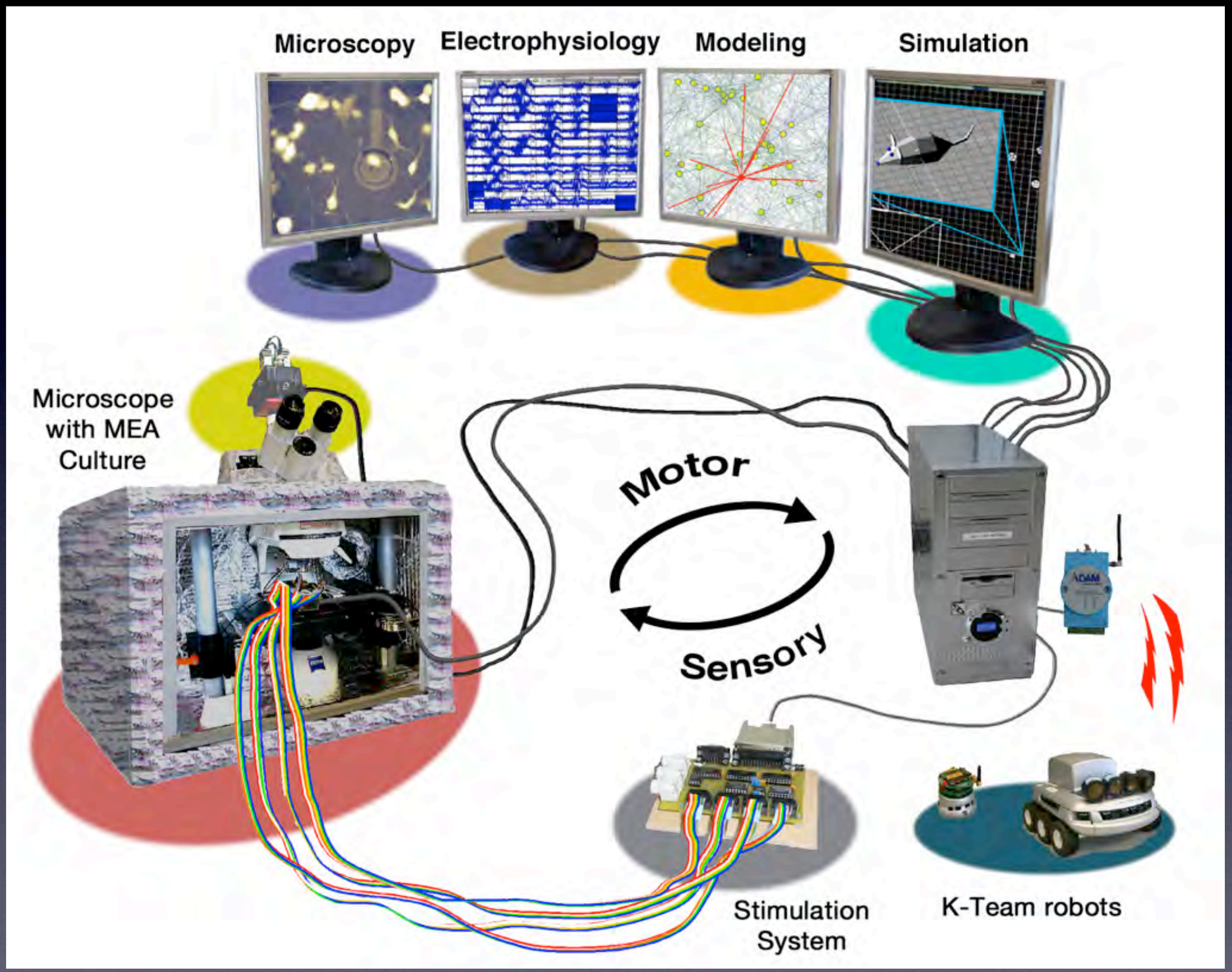




Caltech (1994-2002)

- Invented high-speed camera for neural activity imaging (with Jerry Pine, US patent #6,633,331)
- Built one of the first 2-photon microscopes for imaging living neural tissue. (with Scott Fraser)
- First to image GFP in living animals.
- Invented systems for keeping neural cultures alive over 2 years. (US patent #6,521,451)
- Built first many-electrode stimulators and closed-loop neurophysiology systems. (with DeMarse, Wagenaar)
- Developed first embodied cultured networks.

Embodied Cultured Networks



At the Georgia Institute of Technology

as tenured Professor (2002-2015)

At Georgia Tech

- Developed closed-loop neuromodulation systems
- Used embodied cultured networks to study learning in vitro
- Developed seizure control using multi-electrode stimulation
- Developed optogenetic neuromodulation system
- Use OptoClamp to study homeostatic plasticity

Open-Source

16-wire MEA for chronic implantation and headstage preamp with stimulation multiplexor

in vivo

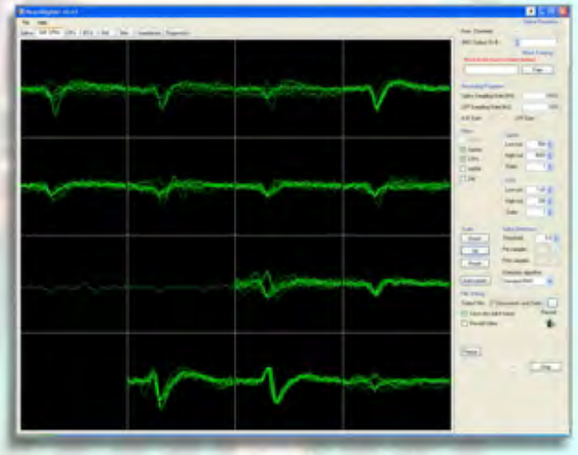
in vitro

Recorded LFPs & action potentials
(motor output, neural state)

Closed-Loop Hybrid System

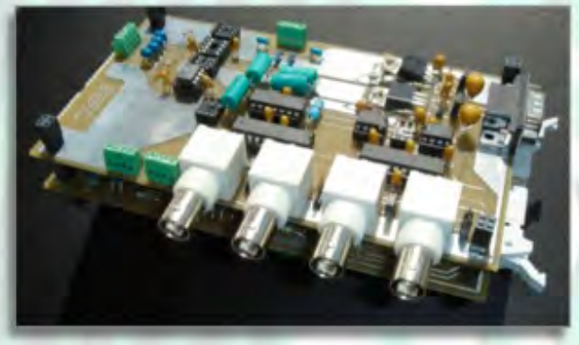
For brain research

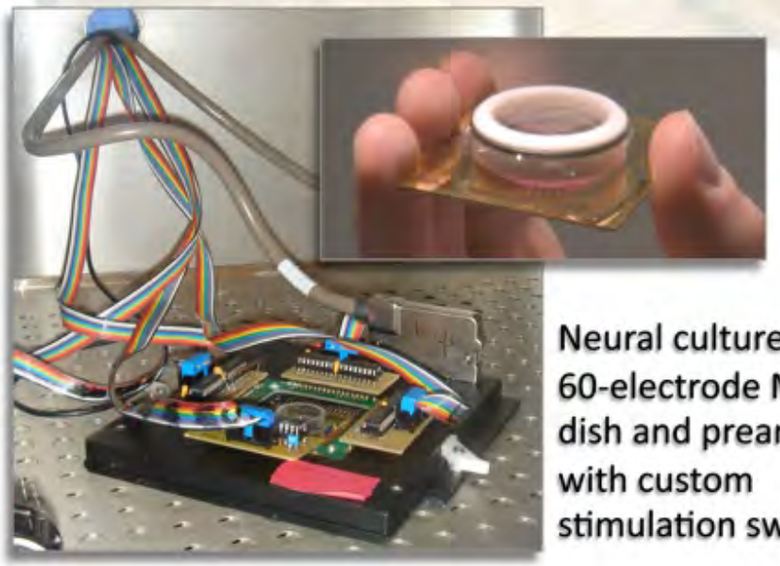
Electrical stimuli
(sensory input, modulation, training)



NeuroRighter GUI

Workstation and interface boards





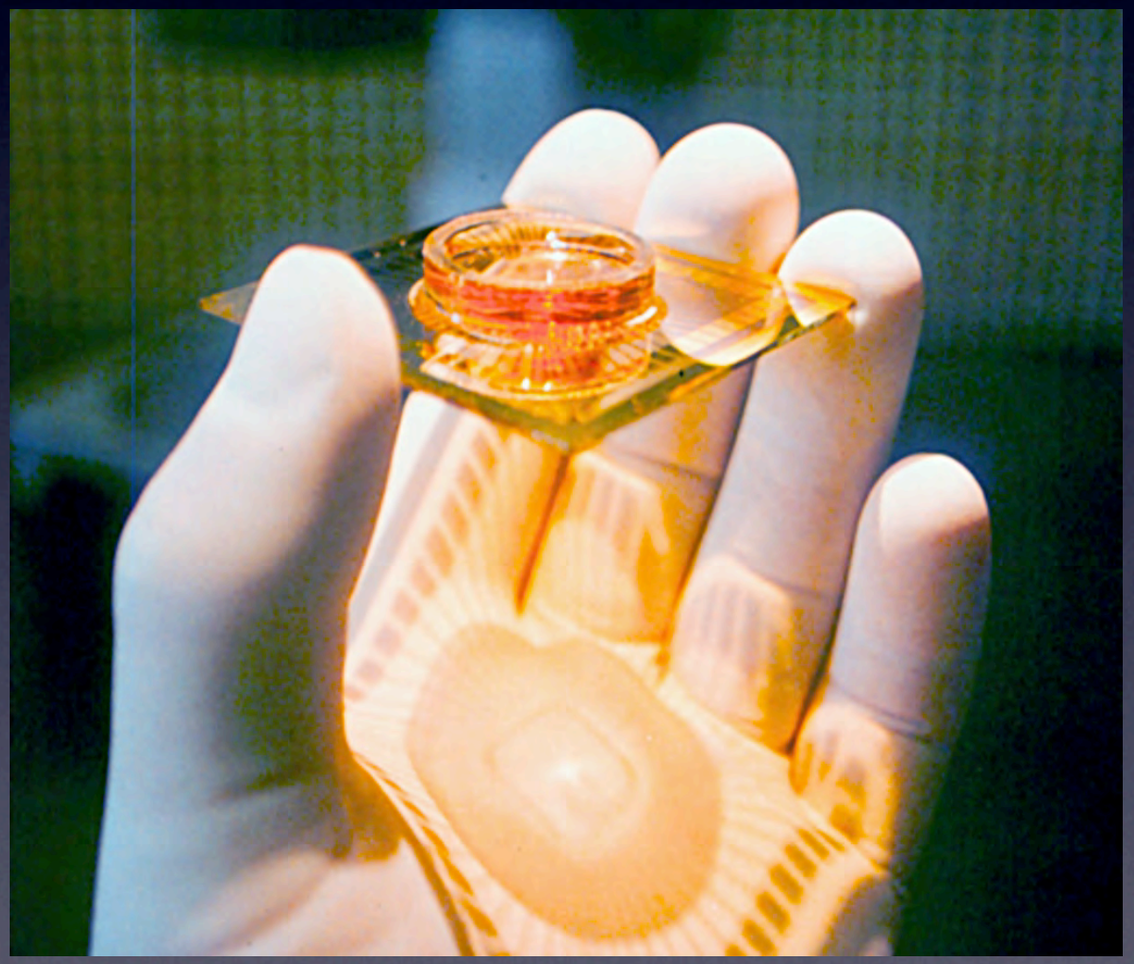
Neural culture in 60-electrode MEA dish and preamp, with custom stimulation switches

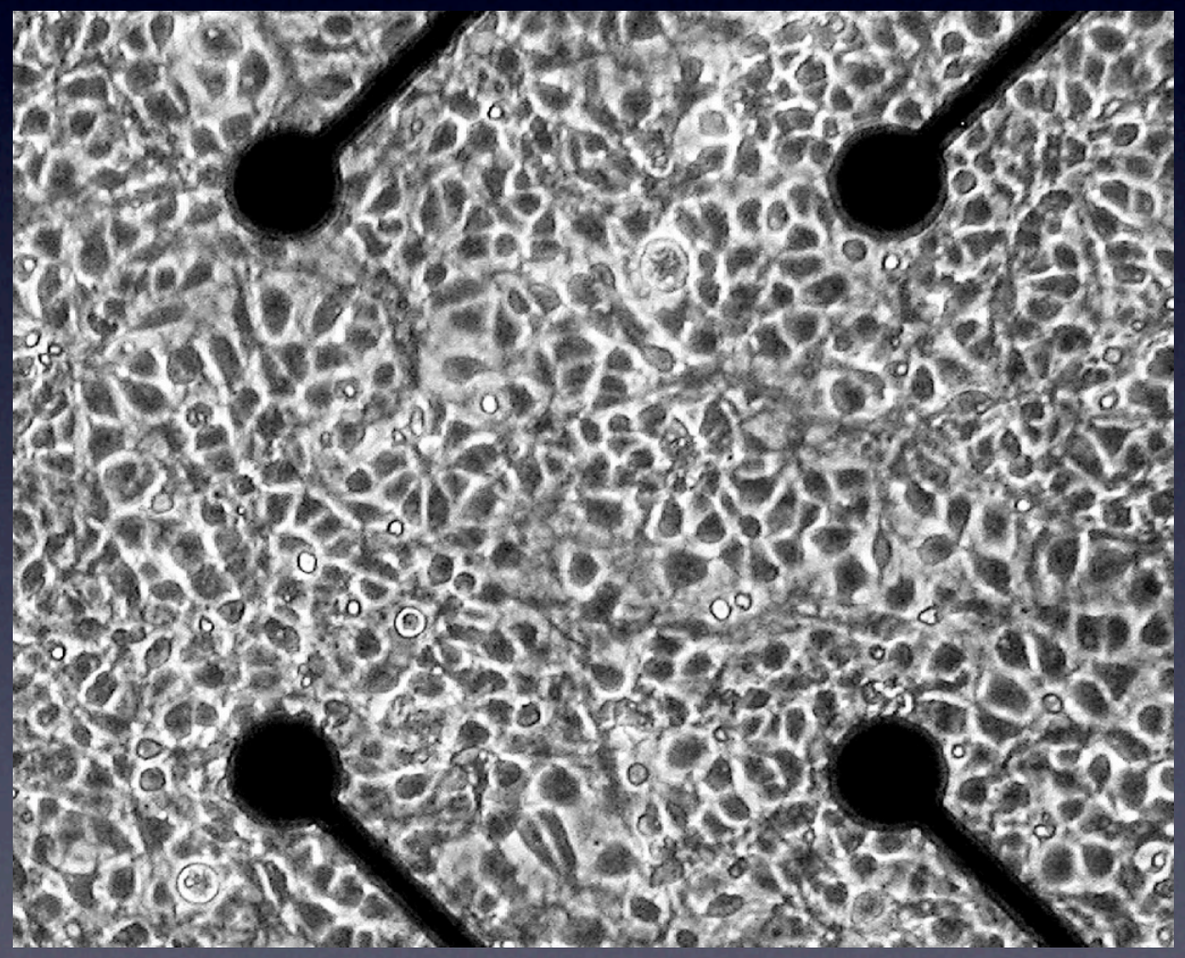
ADC, DAC and digital interface card

MeaBench

NeuroRighter

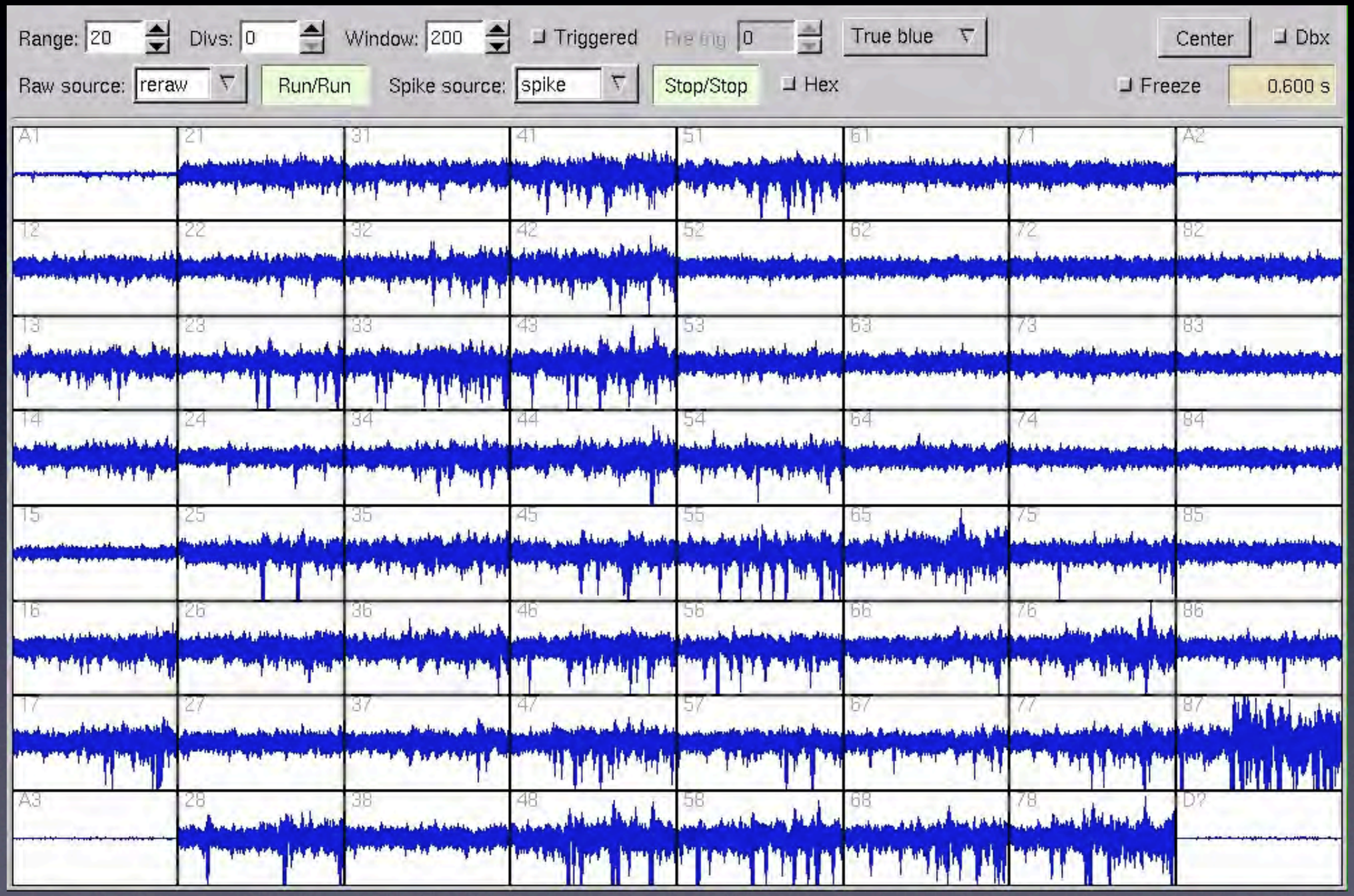
Using closed-loop hybrid systems for basic neuro research



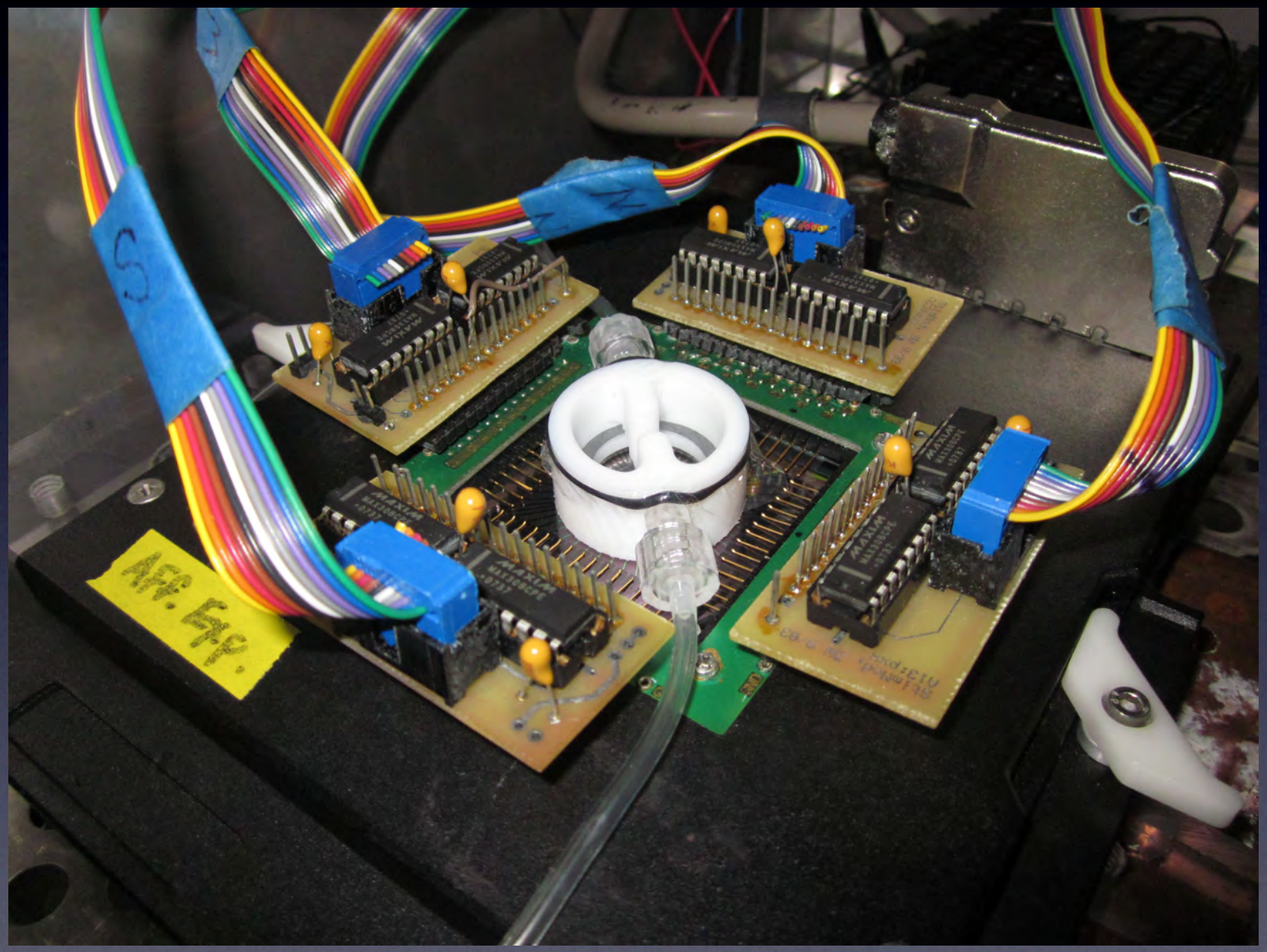


MEA with rat cortical culture

Dish-wide bursts resemble epileptic seizures



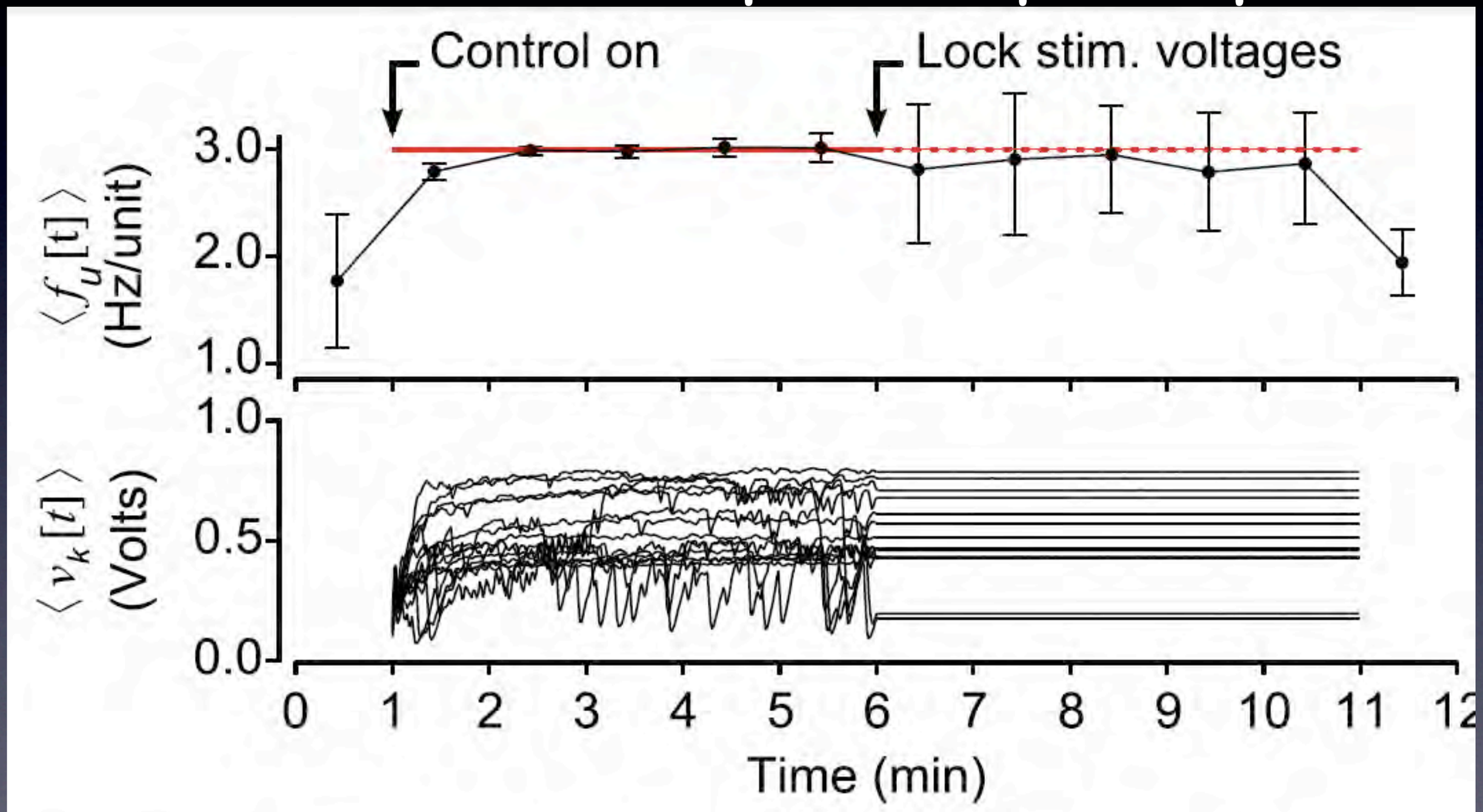
Closed-loop interface to a living neural culture



Wagenaar, D. A. and Potter, S. M. (2004).
A versatile all-channel stimulator for electrode arrays, with real-time control.
Journal of Neural Engineering 1: 39-45.

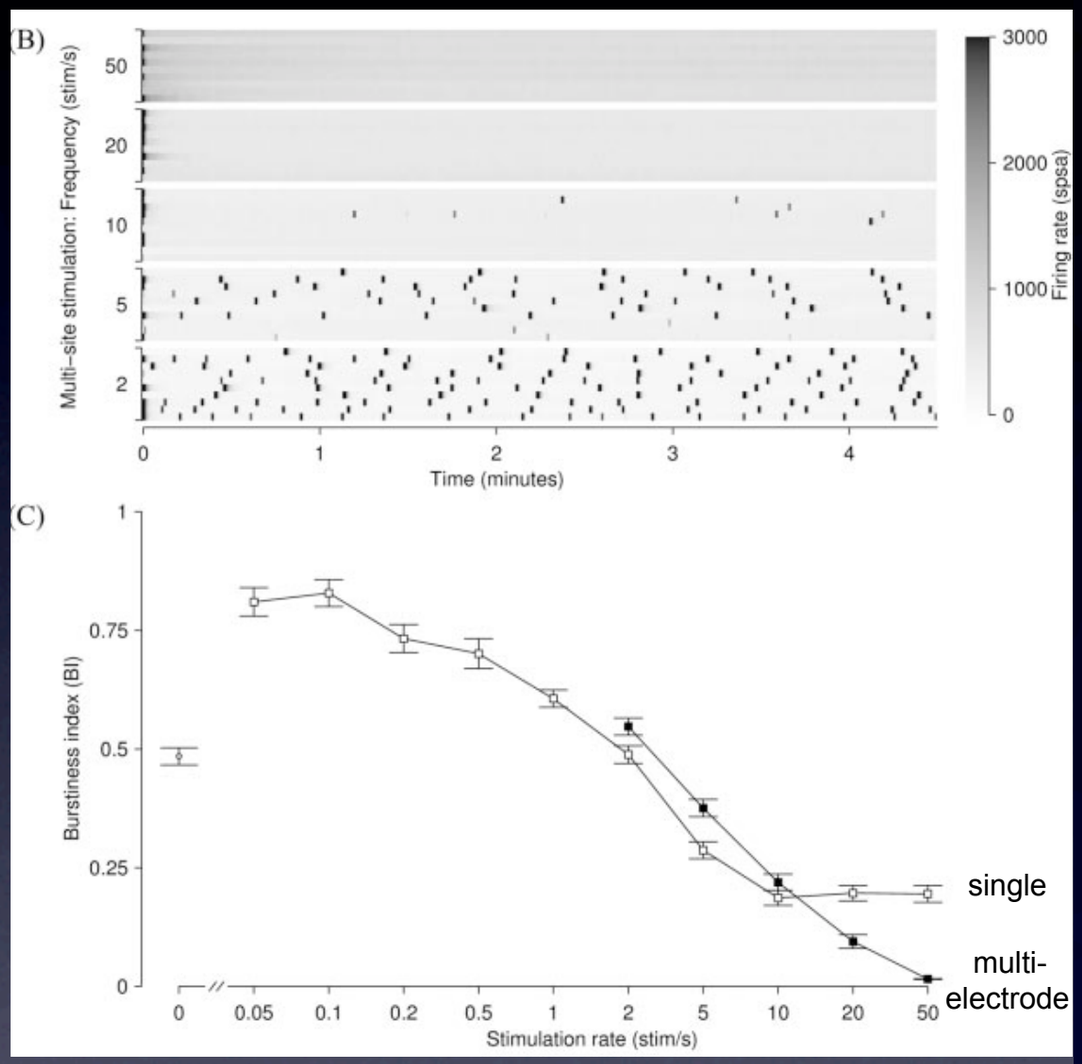
Electrical clamping of network firing rate using NeuroRighter

closed loop open loop



Newman et al. (2013) “Closed-loop, multichannel experimentation using the open-source NeuroRighter electrophysiology platform,” Frontiers in Neural Circuits 6:98

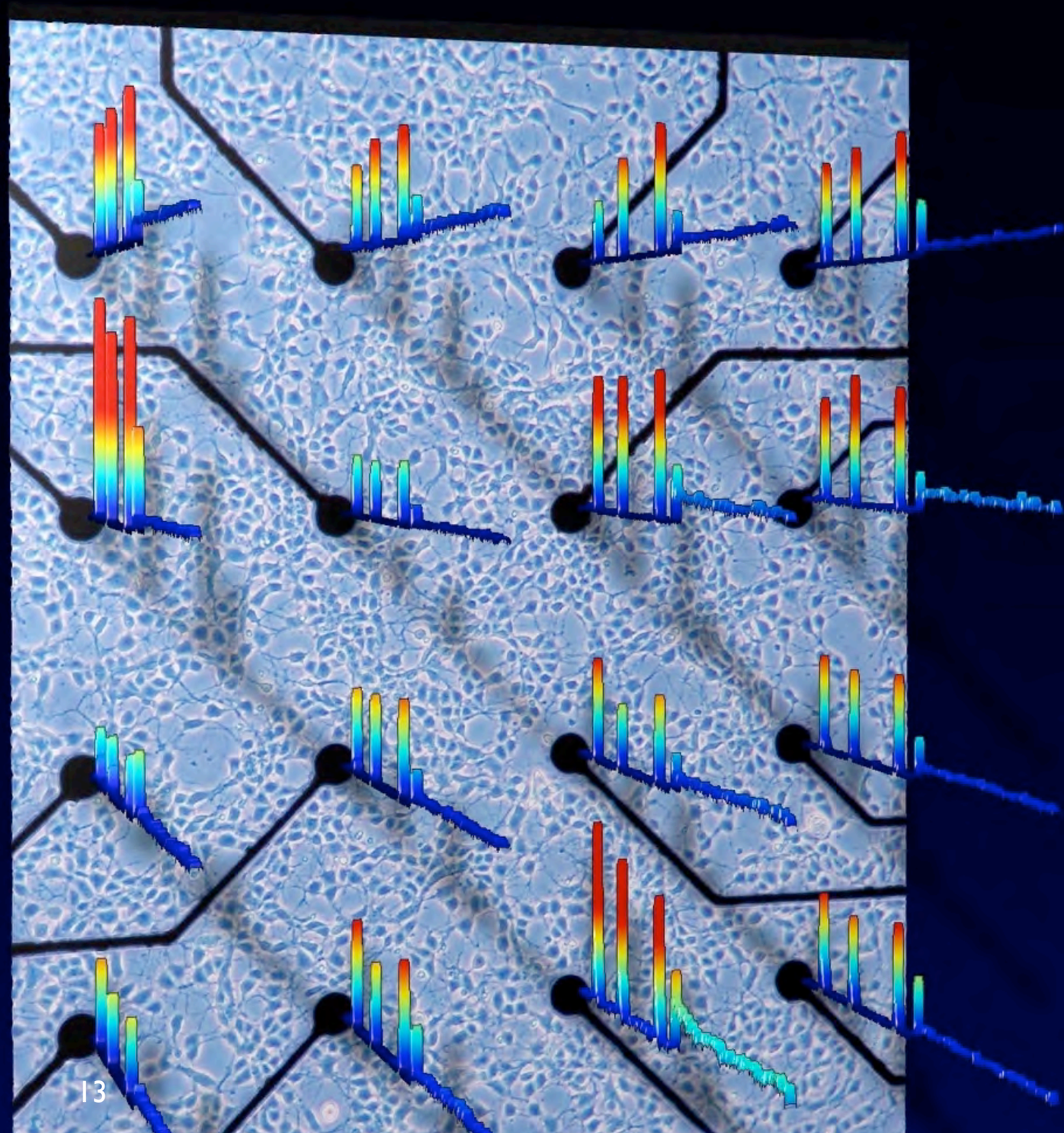
Multisite stimulation as a potential cure for epilepsy



single

multi-electrode

Wagenaar, D. A., Madhavan, R., Pine, J., & Potter, S. M. (2005). Controlling bursting in cortical cultures with closed-loop multi-electrode stimulation. *J. Neuroscience*, *25*, 680-688.



Success in rats:
Desai, S. A., Rolston, J. D., McCracken, C. E., Potter, S. M., & Gross, R. E. (2016). Asynchronous distributed multielectrode microstimulation reduces seizures in the dorsal tetanus toxin model of temporal lobe epilepsy. Brain Stimulation, 9, 86-100.

Note!

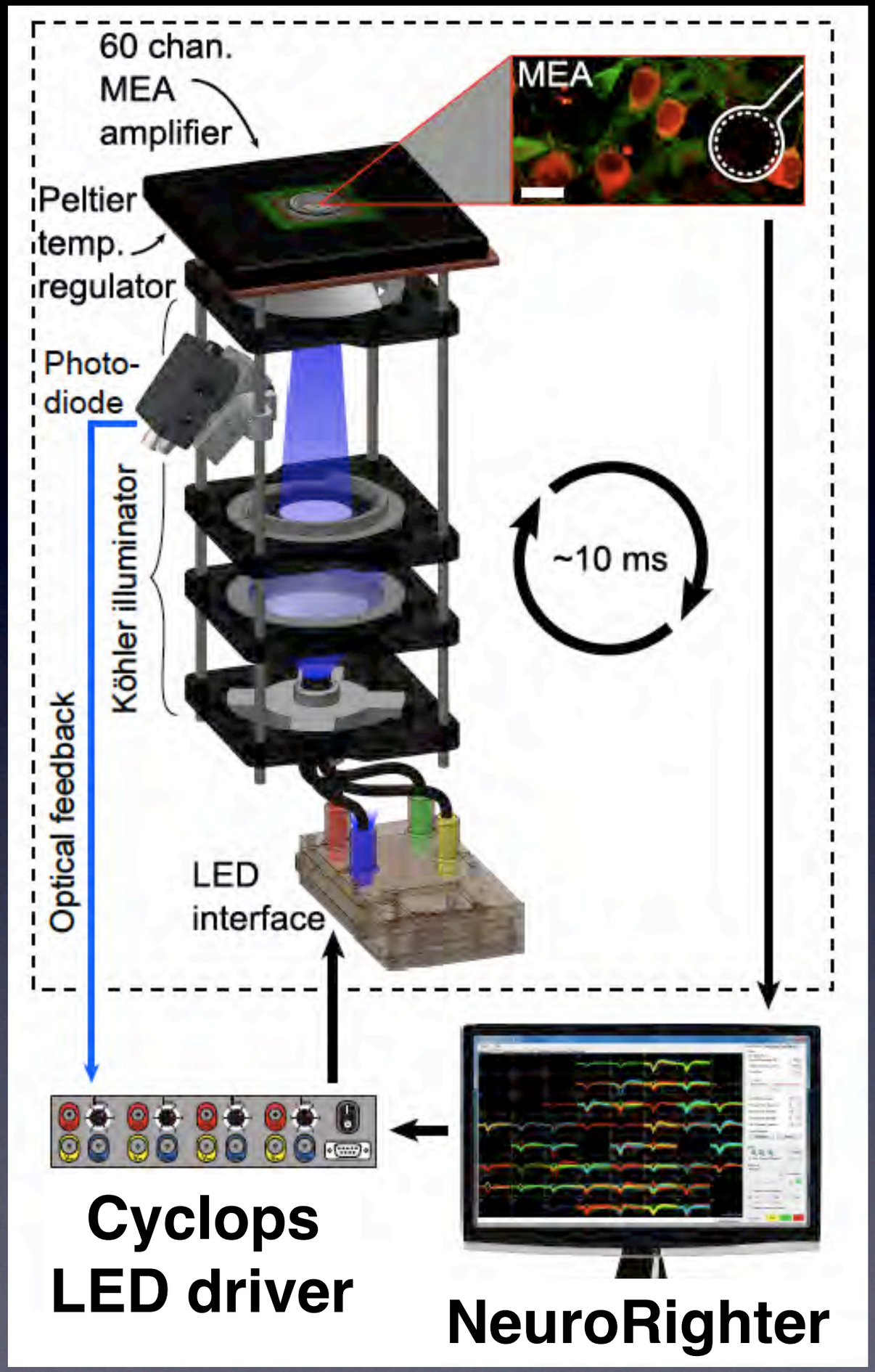
This is not stimulating when a seizure is beginning, as most closed-loop approaches do.

This is closed-loop *state control*, **keeping the neural tissue continuously in a state where it is less inclined to have a seizure, based on its current total firing rate.**

The OptoClamp: optogenetic neuromodulation

Using light AND electricity to close the loop around neural circuits

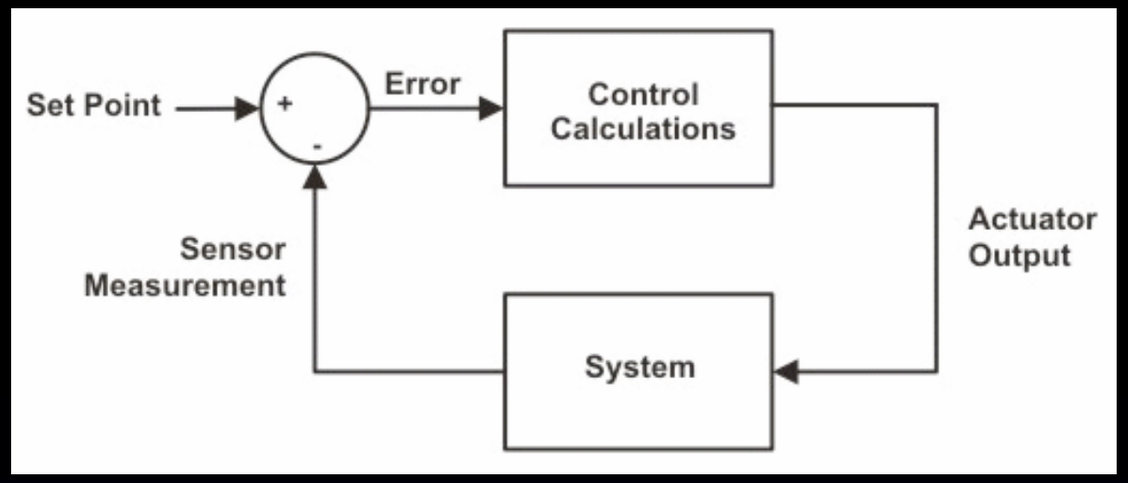
The OptoClamp



Closed-loop Optogenetic setup for modulating neural activity with light

- Adeno-associated virus vector
- Channelrhodpsin for depolarizing currents. Blue light sensitive
- Halorhodopsin for inhibitory currents. Yellow light sensitive
- CaMKIIa promoter: expressed in excitatory neurons only.

Jonathan Newman



The OptoClamp

NeuroRighter platform

Experimenter sets desired activity set point

Real-time software comparison

MEA extracellular multi-unit recording

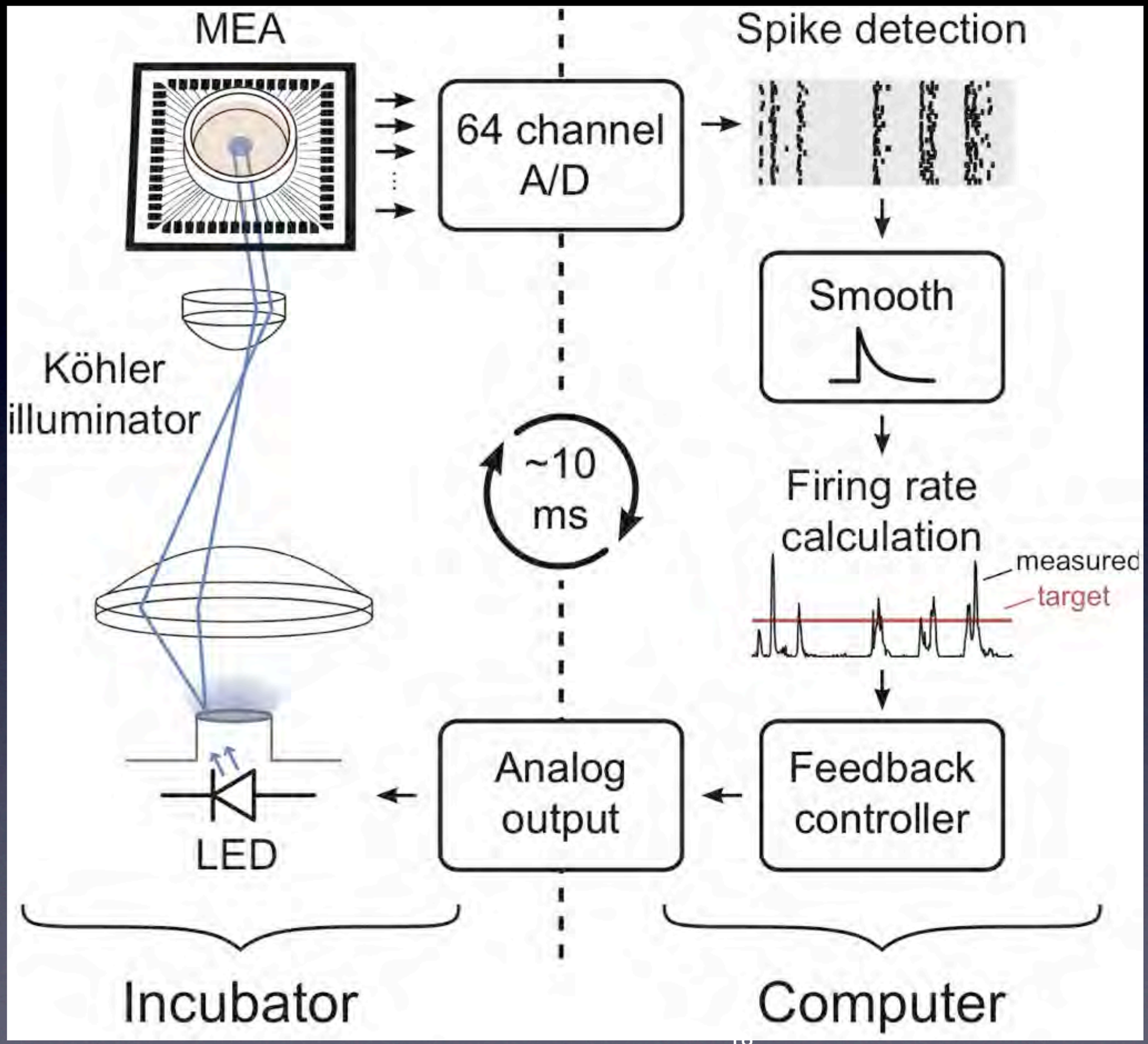
High-speed LED controller

Light control feedback

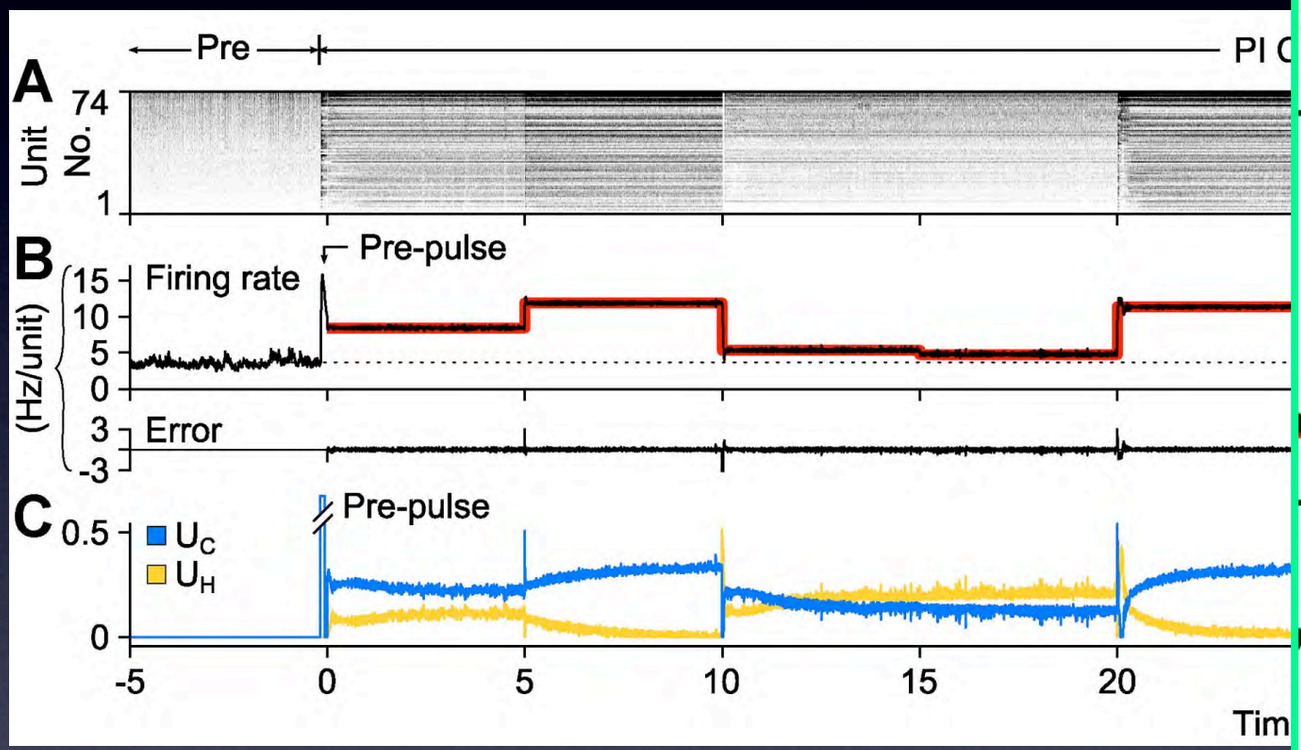
Blue & Yellow high-power LEDs, fiber optics, and collimating optics

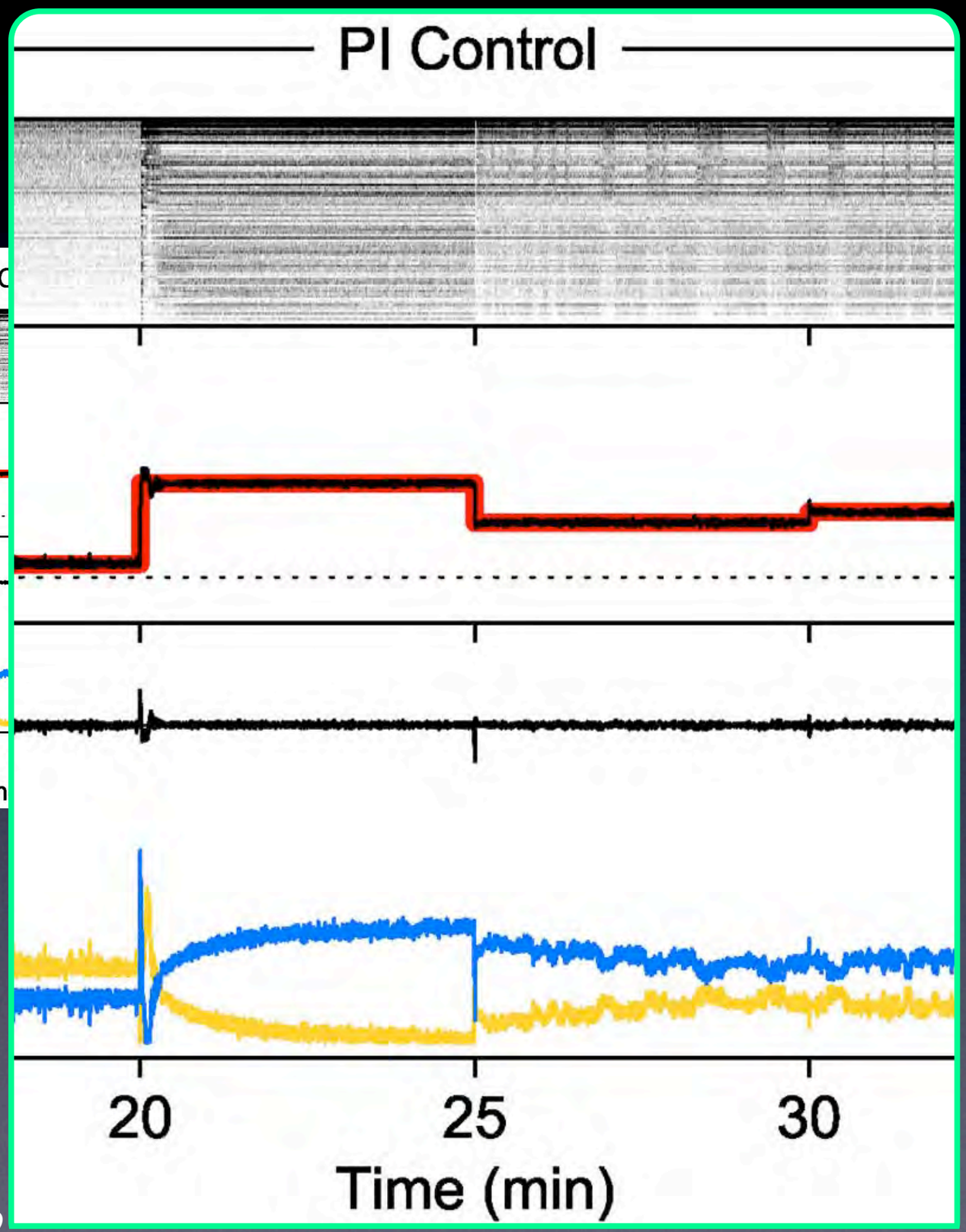
light-sensitive cortical culture on MEA

MEA spikes as feedback signal for closed loop control



50-min Proportional-Integral (PI) feedback control





OptoClamp used to study homeostatic plasticity

nature COMMUNICATIONS

ARTICLE

Received 8 Feb 2014 | Accepted 21 Jan 2015 | Published 9 Mar 2015

DOI: 10.1038/ncomms7339

OPEN

Upward synaptic scaling is dependent on neurotransmission rather than spiking

Ming-fai Fong[1,2,3], Jonathan P. Newman[2,3], Steve M. Potter[2] & Peter Wenner[1]

Homeostatic plasticity encompasses a set of mechanisms that are thought to stabilize firing rates in neural circuits. The most widely studied form of homeostatic plasticity is upward synaptic scaling (upscaling), characterized by a multiplicative increase in the strength of excitatory synaptic inputs to a neuron as a compensatory response to chronic reductions in firing rate. While reduced spiking is thought to trigger upscaling, an alternative possibility is that reduced glutamatergic transmission generates this plasticity directly. However, spiking

OptoClamp in vivo

(from my collaborator Garrett Stanley's lab)

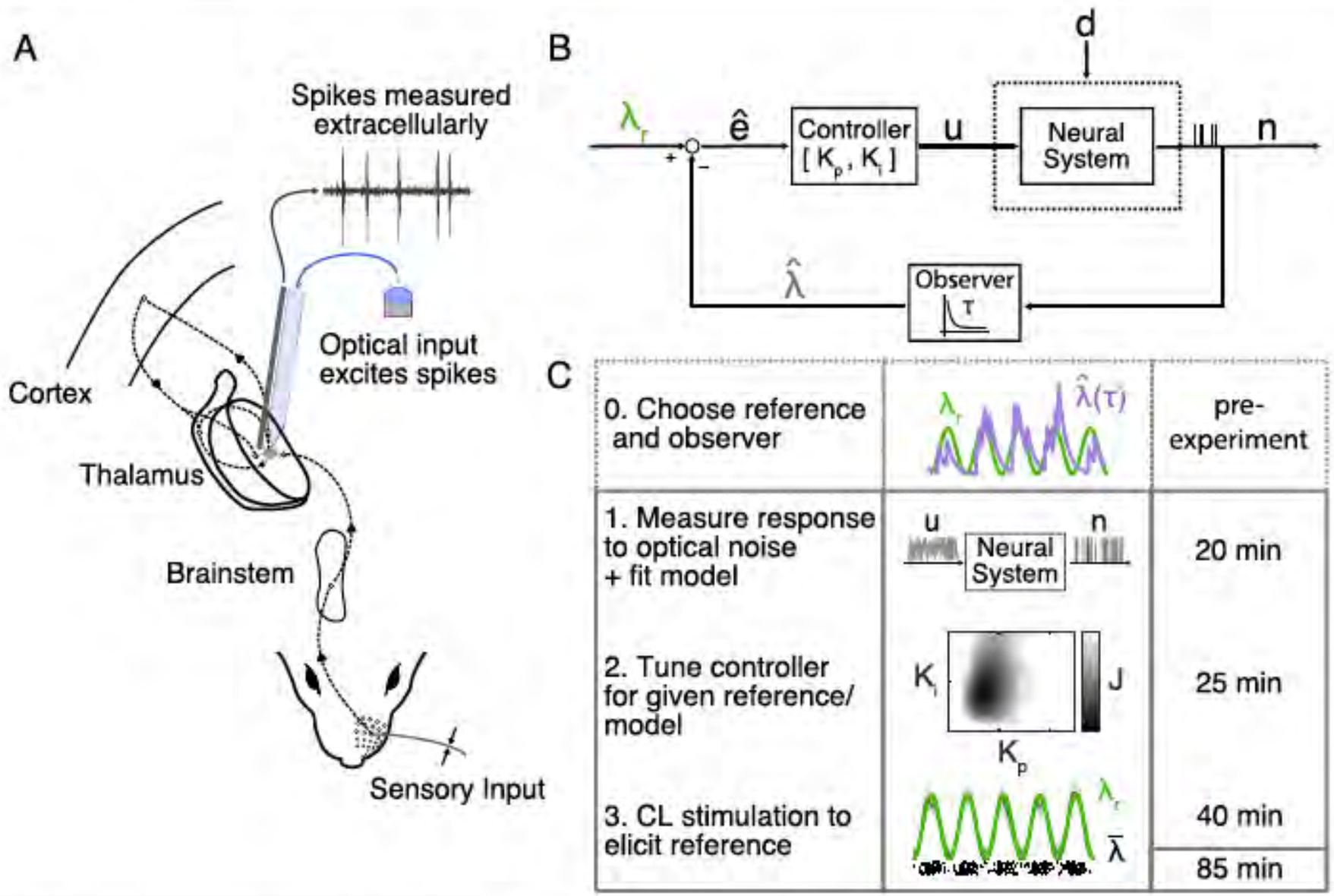
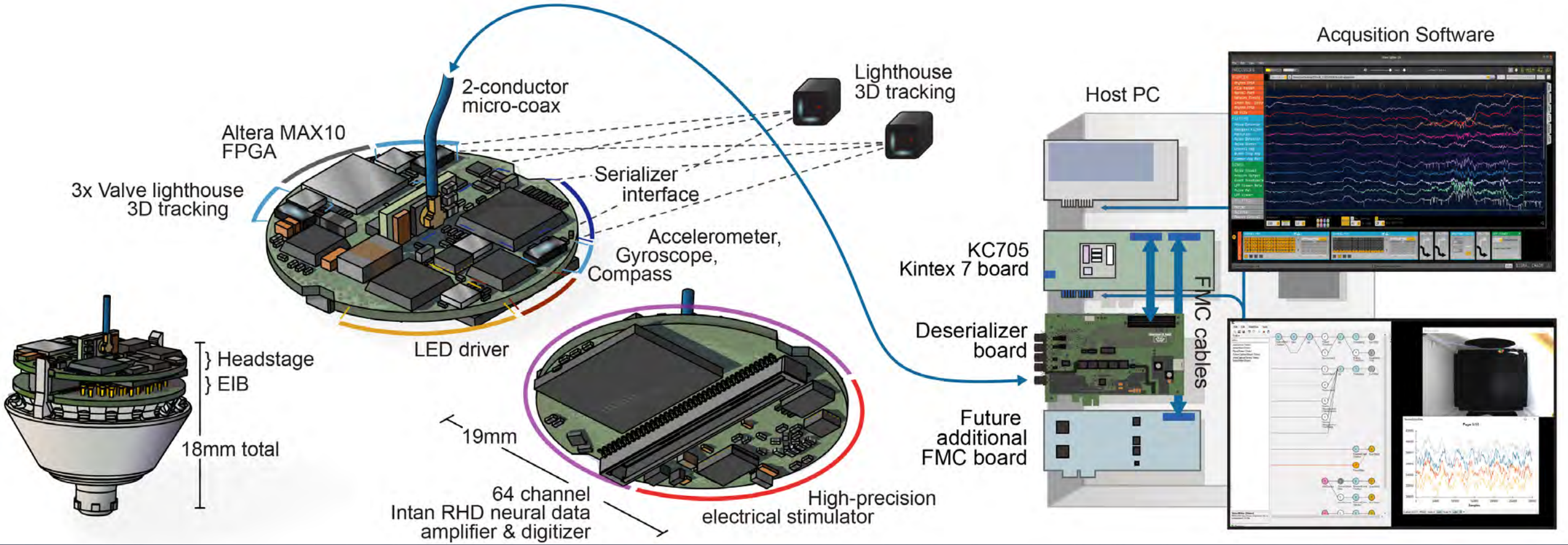


Figure 1. Closed loop optogenetic control of firing rate. (A) Physical diagram. (B) System block flow diagram. (C) Procedure for closed-loop stimulation experiments. The observer was designed for a given reference firing rate pattern previous to experiments. A model was fit to data recorded for system identification during the experiment. Using this model, controller gains were optimized in simulation. These

New standard for closed-loop neuroscience



On Github

Open Ephys++ Communication Protocol and API Specification
Version 0.0

Jonathan P. Newman, Wilson Lab, MIT

August 29, 2018

Abstract

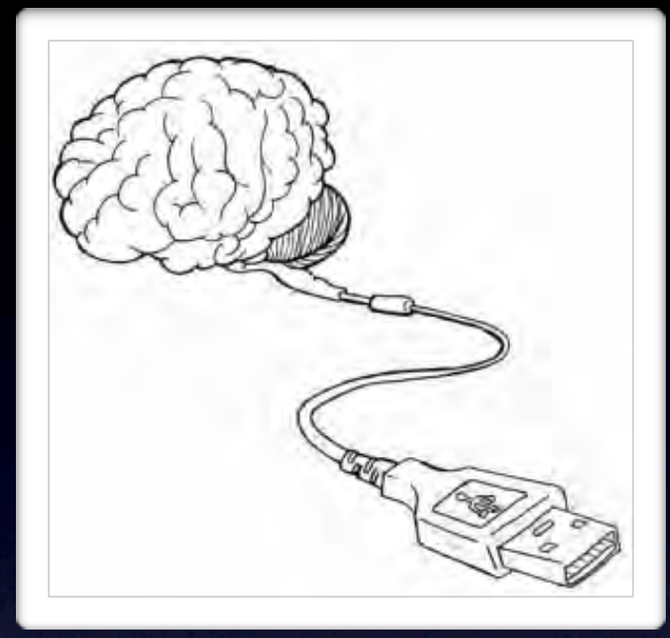
This document specifies requirements for implementing the Open Ephys++ data acquisition system. This specification entails two basic elements: (1) Communication protocols between acquisition firmware and host software and (2) an application programming interface (API) for utilizing this communication protocol. This document is incomplete and we gratefully welcome criticisms and amendments.

Contents

Other types of hybrid systems

- Neural Prostheses
  - Sensory – cochlear & retinal implants
  - Motor – FES for moving paralyzed limbs
  - Sensory-motor – prosthetic hand with tactile feedback
  - (future) Cognitive
- Neuromodulators
  - Deep brain stimulators (DBS)
  - Spinal stimulators for chronic pain
- Diagnostic, e.g. electrocorticography array
- (future) Computers with living neuron processors

More *brain-like* computing



- Extremely complex dynamical system
- Especially good for real-time control
- Analog not digital, or a mix of the two
- Sparse, distributed memory – No CPU or system clock
- Lots of feedback
- Delays are part of the computation
- Computation depends on connectivity and morphology
- Adaptive at every level

Note!

We don’t need to completely understand the brain’s mechanisms to use more brain-like computing in our AI.

I predict...

- Hybrid systems for research will lead to new insights about the brain that will help us design better hybrid systems for AI.
- Better 2-way (closed-loop) interfaces will revolutionize neuromodulation for diseases & disabilities, AND for cognitive enhancement.
- Less invasive closed-loop neural interfaces will become commonplace as they are refined and made more inexpensive:
  - EEG and MEG
  - Transcranial current and magnetic stimulation
  - fMRI and Near-IR recording
- Optical interfaces will make electrical ones obsolete.

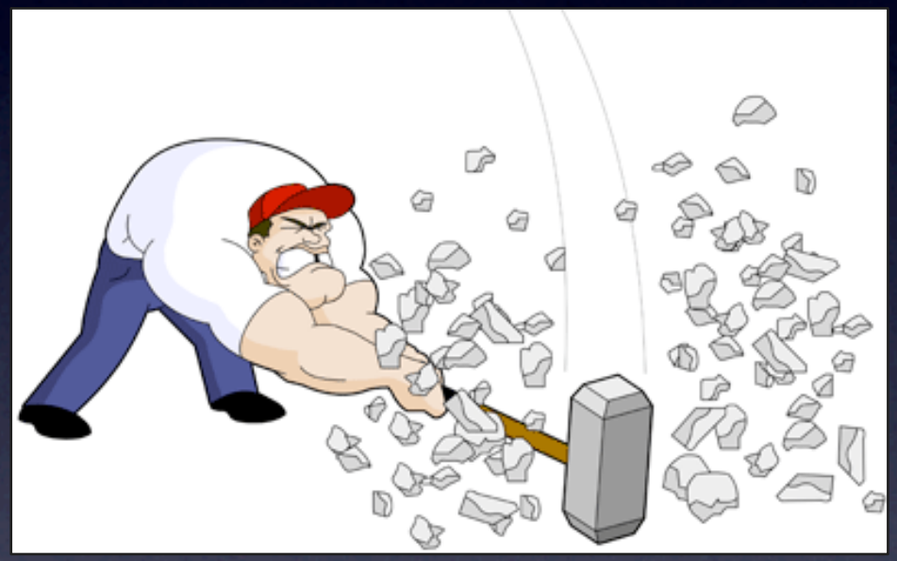
If you take home only one message:

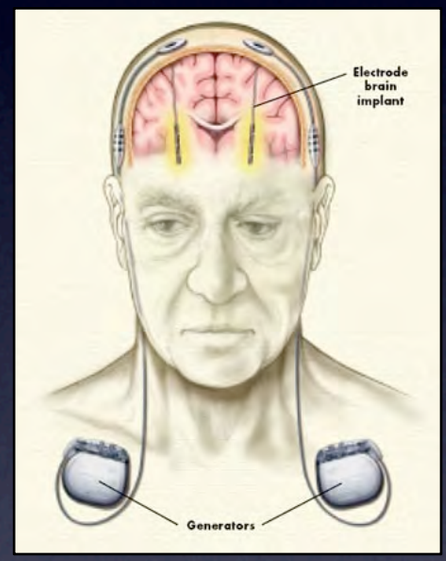
Closed-loop hybrid systems are the future

Close the Loop!

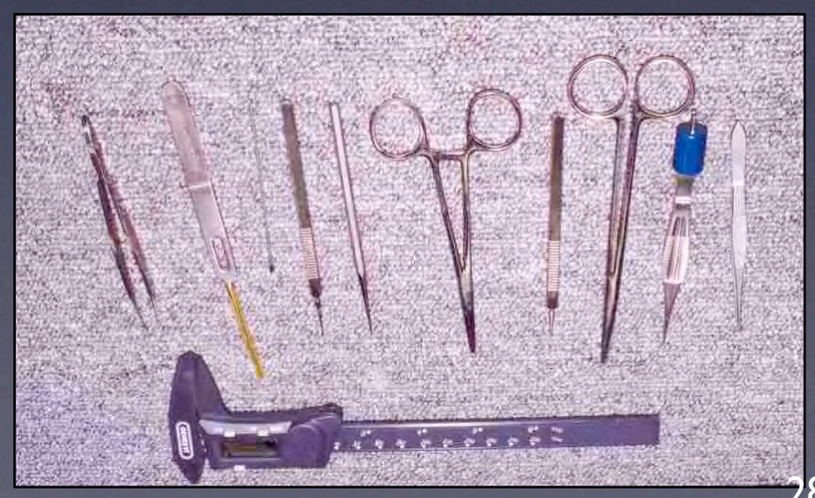
- Some day all brain stimulation, whether electrical or optical, will be controlled in real time by recordings.
- Open-loop stimulation will be considered barbaric.

Open Loop





Closed Loop



Fiber-optic implants for research, therapy and enhancement

Justin Wood

They will all be CLOSED-LOOP

For example,
Optogenetic Approaches for Controlling Seizure Activity
Tung, Berglund & Gross
Brain stimulation 2016, Vol. 9(6), p.801-810

Thanks

Sharanya Arcot Desai, Ethan Craig, Eric Eisner, Candace Law, Ushnik Ghosh, Silvia Vaca, Nathan Killian, Alex Calhoun, **Jon Newman**, Riley Zeller-Townson, **Ming-fai Fong**, Marc Powell, Michelle Kuykendal

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Tom DeMarse

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Coulter Foundation
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Epilepsy Research Foundation

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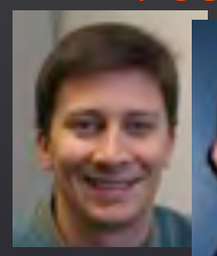
Former Postdocs



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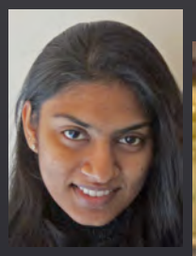
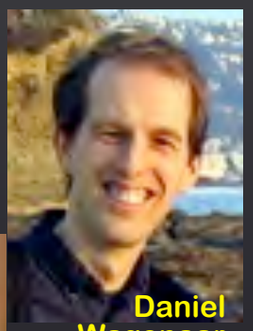
Sharanya Arcot Desai





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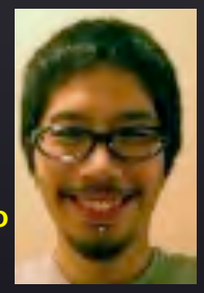

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Radhika Madhavan

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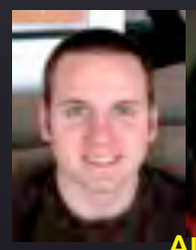
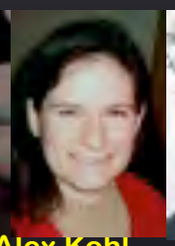
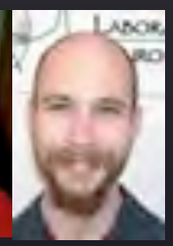
Former Technicians







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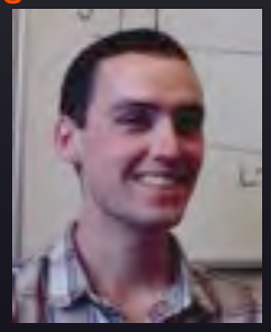
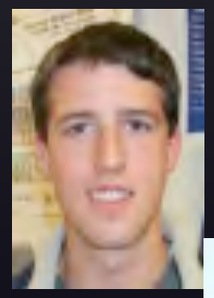
Sarah Davis
Douglas Swehla

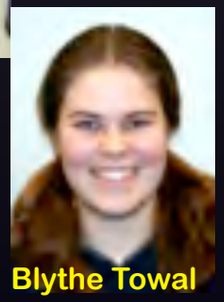
Former Georgia Tech and Emory Undergrads



Matthew MacDougall

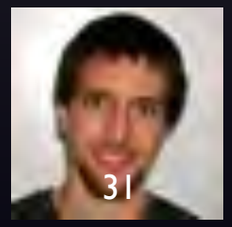


John Brumfield



Blythe Towal

Alec Shkolnik



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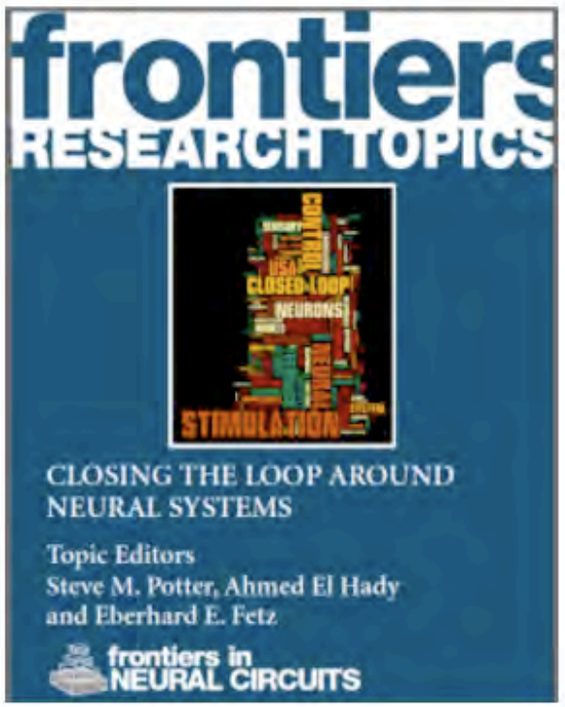

Closing the Loop Around Neural Systems

Edited by: Steve M Potter, Eberhard E Fetz, Ahmed El Hady

Publisher: Frontiers Media SA

Frontiers Research Topic FREE Ebook

Potter, S. M. (2007). **What can Artificial Intelligence get from Neuroscience?** In book "50 Years of Artificial Intelligence: Essays Dedicated to the 50th Anniversary of Artificial Intelligence," M. Lungarella, J. Bongard, & R. Pfeifer (eds.) (pp. 174-185). Berlin: Springer-Verlag.

Potter, S. M., (2017) **"The Future of Computing and Neural Interfacing: Wetware-Hardware Hybrids,"** Future Now: Reconfiguring Reality, Institute for the Future – Issue 3, pp. 57-59.

Potter, S. M. (2013). **Better Minds: Cognitive Enhancement in the 21st Century.** In D. Bulatov (Ed.), Evolution Haute Couture: Art and Science in the Post-biological age, Part 2 – Theory. (pp. 304-319). Kalingrad: National Center for Contemporary Arts.

- All our papers are available at http://potterlab.gatech.edu