Resources for Open Collaboration at the Allen Brain Institute

July 23, 2015

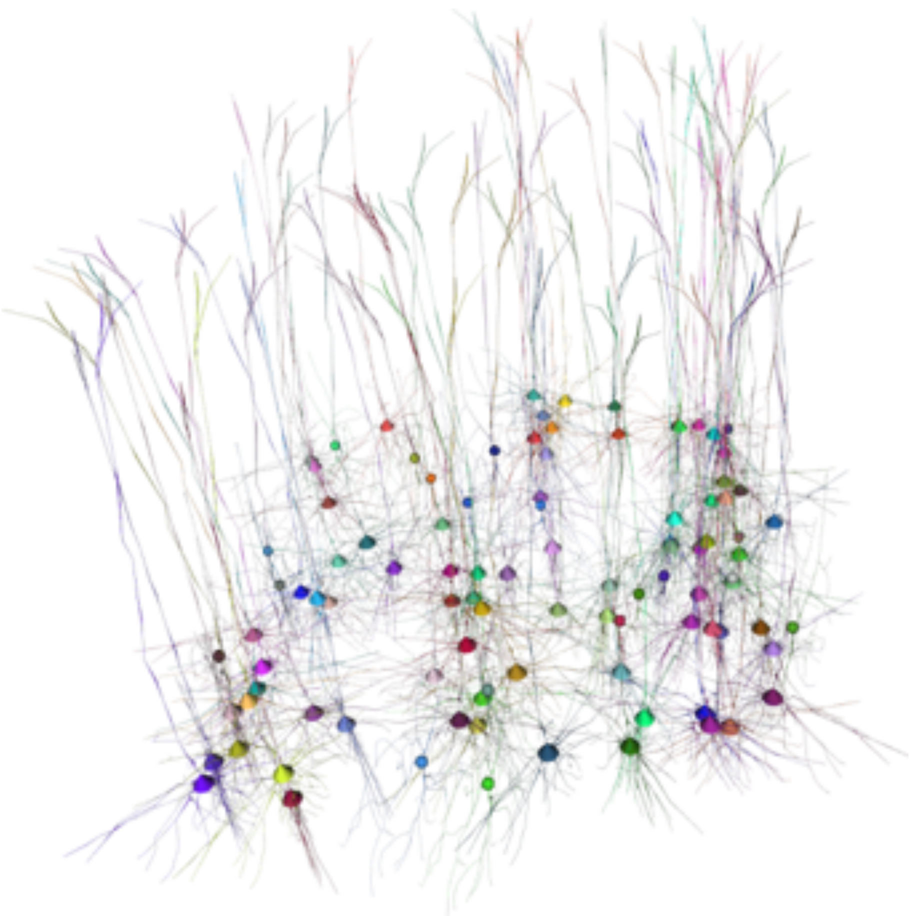
Nicholas Cain: Scientist 1, Allen Institute for Brain Science

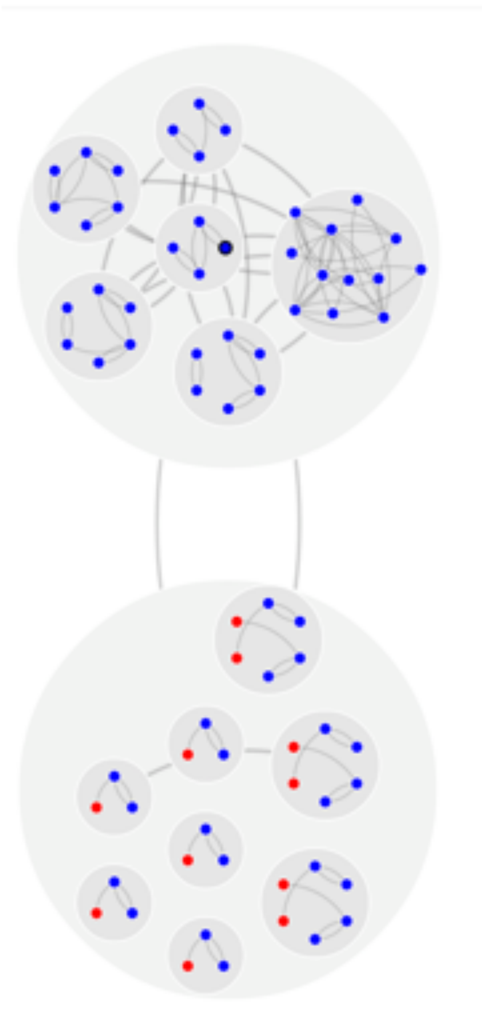
Corinne Teeter, Ram Iyer, Nathan Gouwens, David Feng, Stefan Mihalas

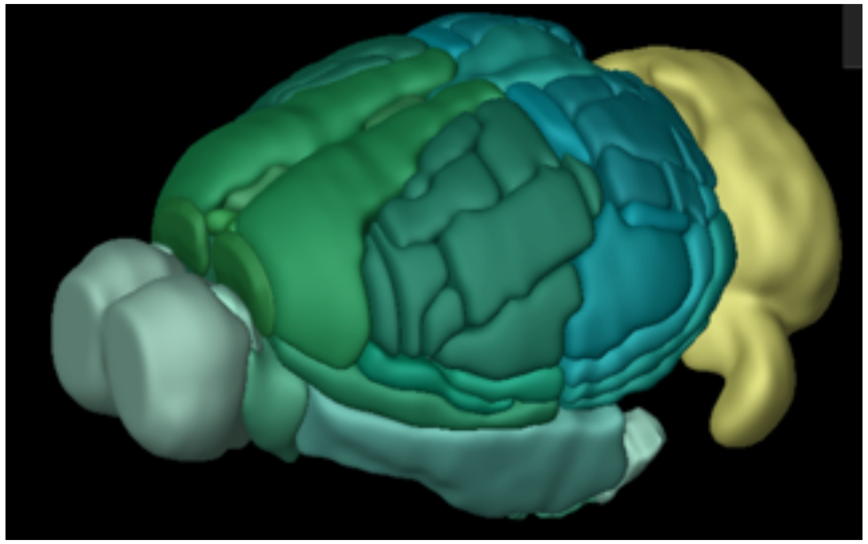
This talk at: https://goo.gl/Xpxce3

ALLEN INSTITUTE *for* BRAIN SCIENCE
Fueling Discovery

Three Levels of Abstraction







Biophysically detailed models

Point-neuron models

Population-statistic models

Overview

- Introduction
- **Allen Cell Types Database** (http://celltypes.brain-map.org/)
- Allen SDK (http://alleninstitute.github.io/AllenSDK/)
- DiPDE (http://alleninstitute.github.io/dipde/)

Allen Cell Types Database: http://celltypes.brain-map.org/

Goal: characterize, in a systematic and standardized fashion, Neurons in the mouse LGN and V1:

- Intrinsic electrophysiology
- Neuron morphology
- Point-neuron models: hierarchy of GLIF parameterization
- Biophysicially detailed computational models

Comprehensive whitepapers available online

Search and Filter Options

Cell Positions in Common Coordinate Framework

Summary of Cell Characteristics (*Click for additional details*)

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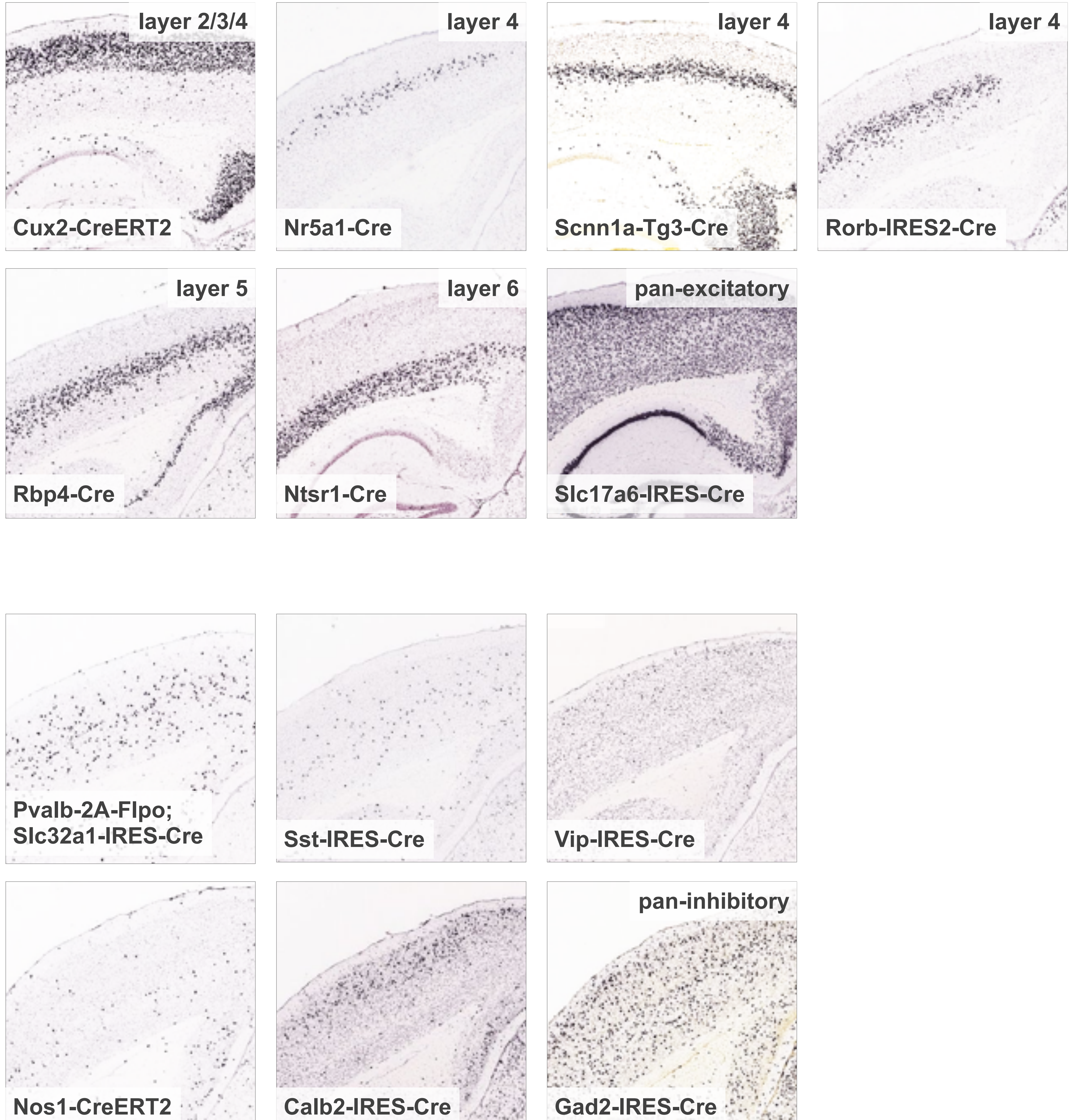
Genetic Markers via Cre Lines

Excitatory neurons

Inhibitory neurons



Cre-drive/LoxP (floxed) reporter Recombinase Binary System:

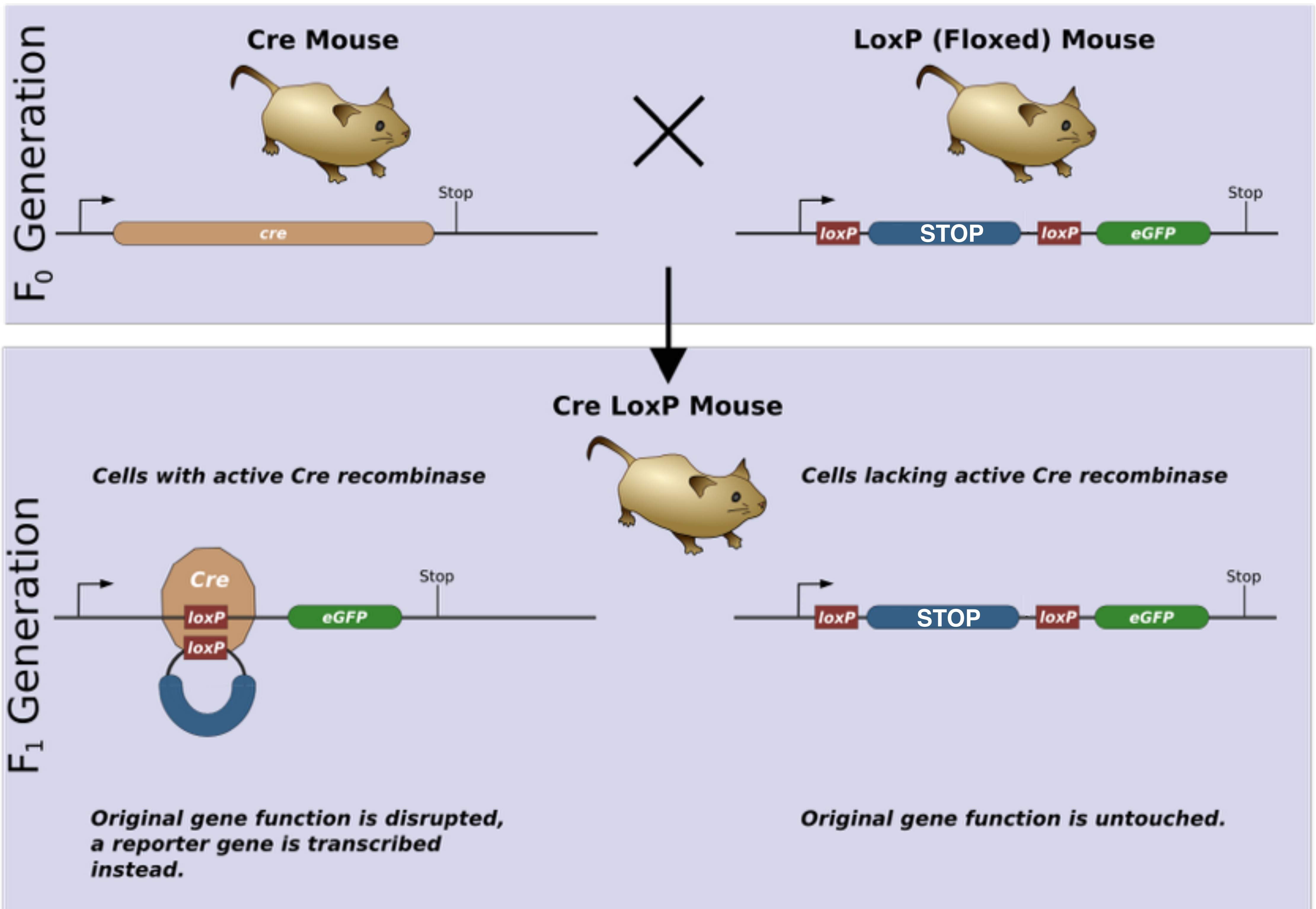


Image by Matthias Zepper via Wikipedia (modified)

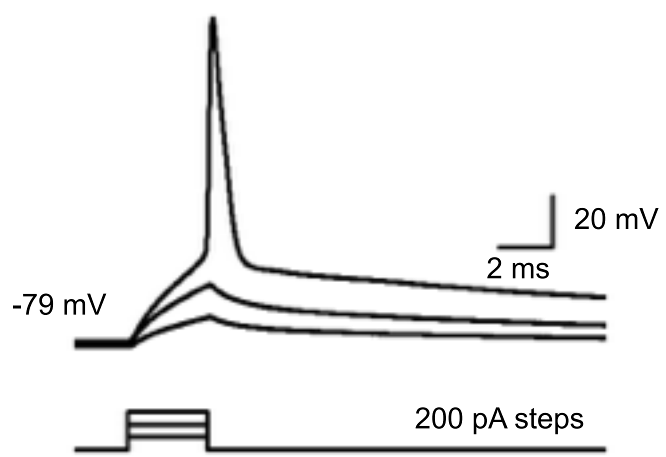
Electrophysiology Protocol

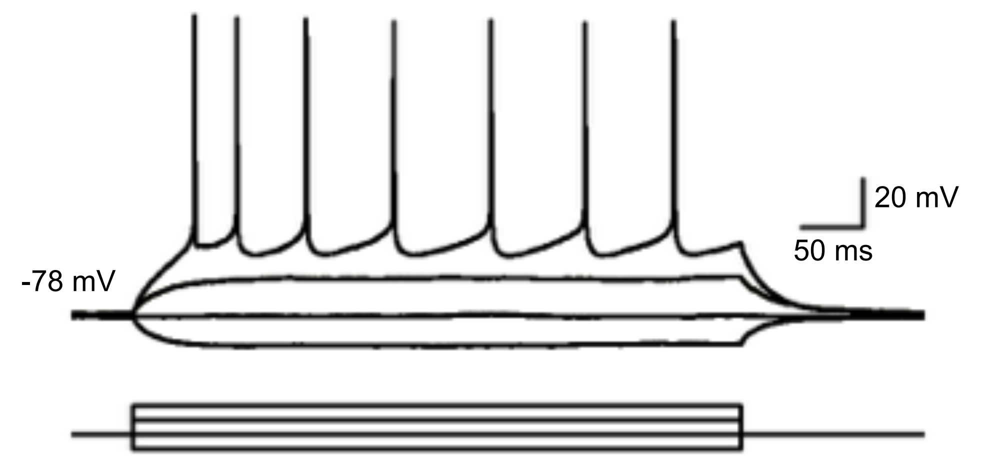
Instantaneous threshold

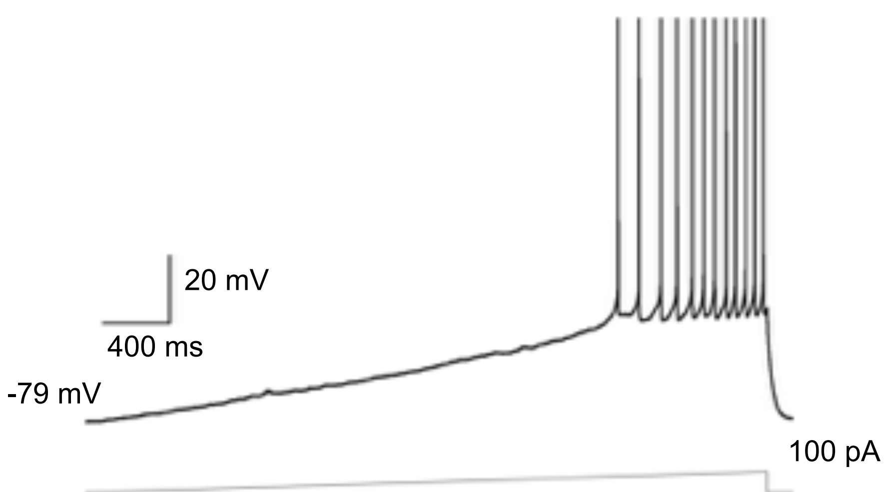
Adaptive threshold

Subthreshold, Rheobase & Suprathreshold

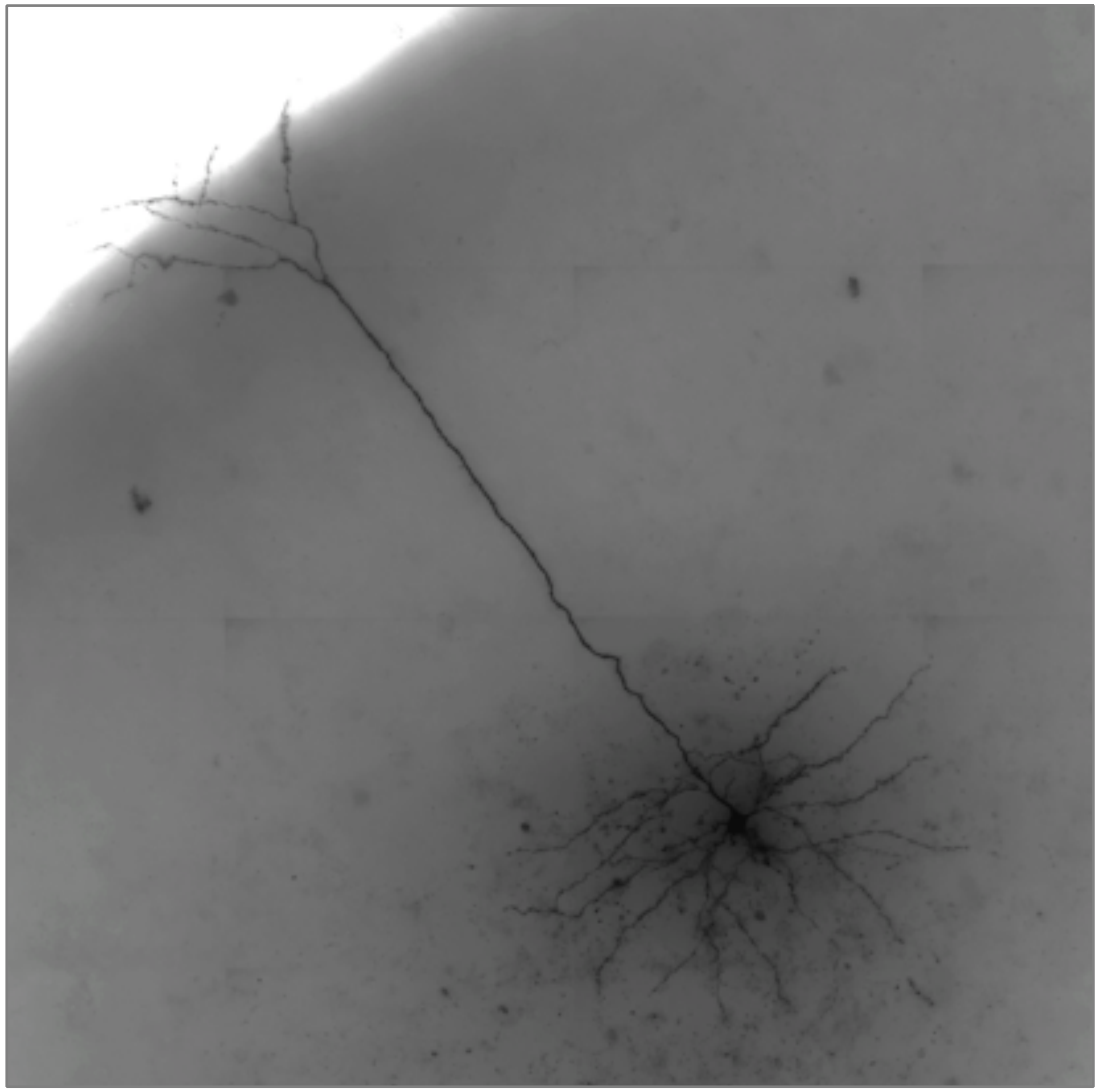
Naturalistic response



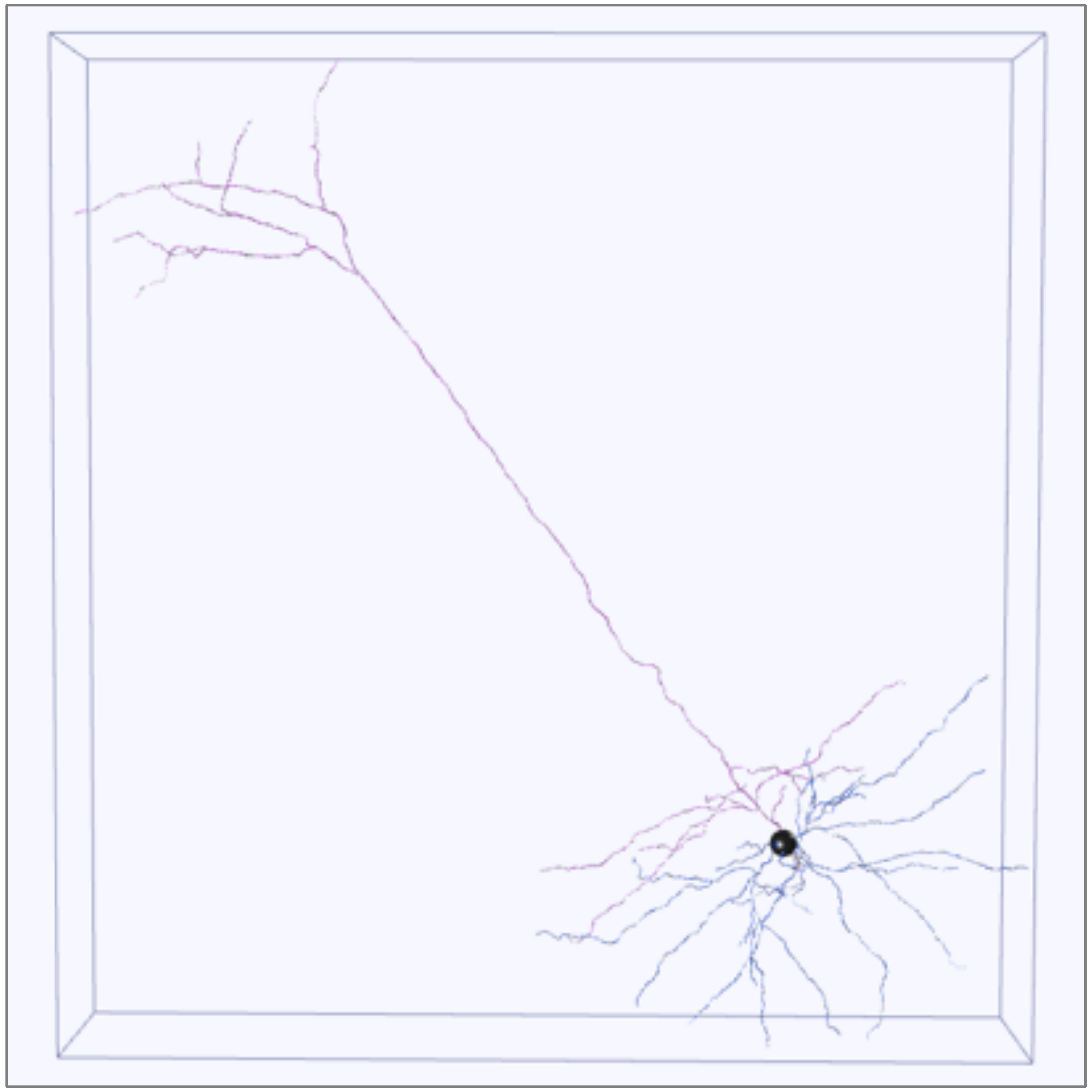




Reconstruction of Morphologies

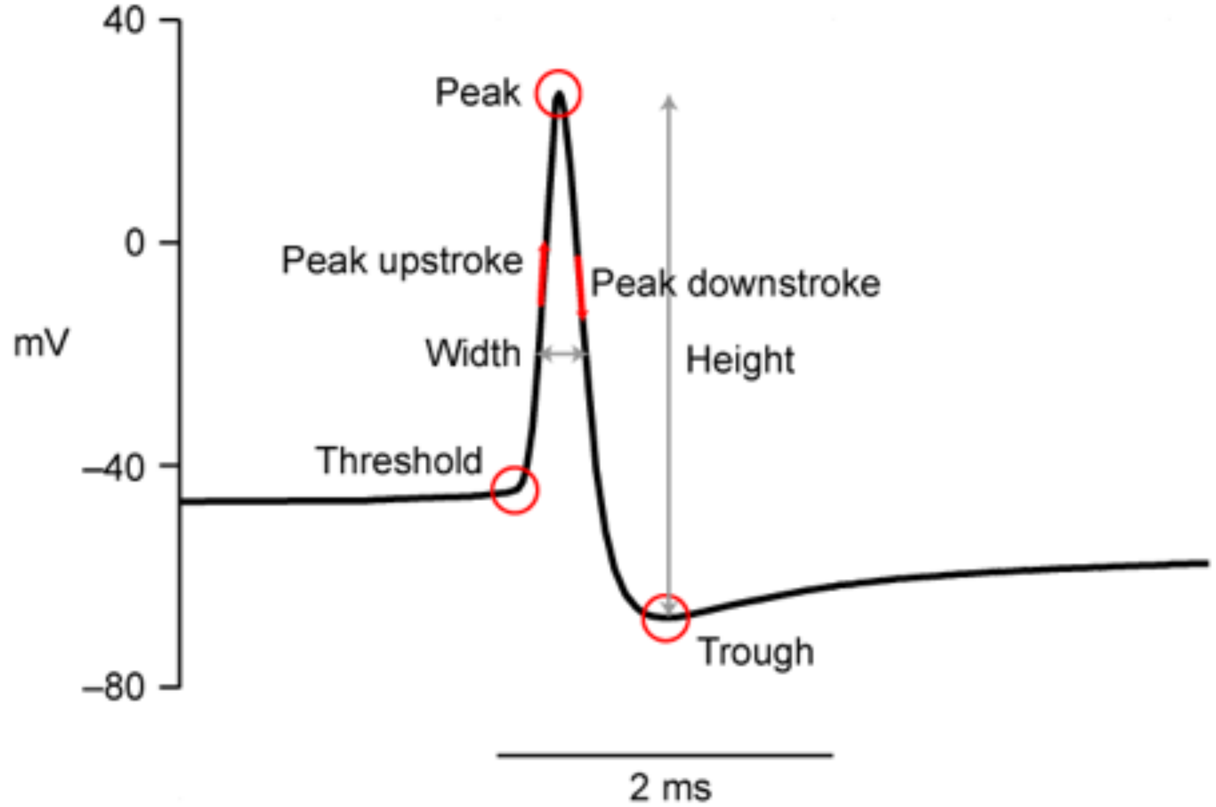


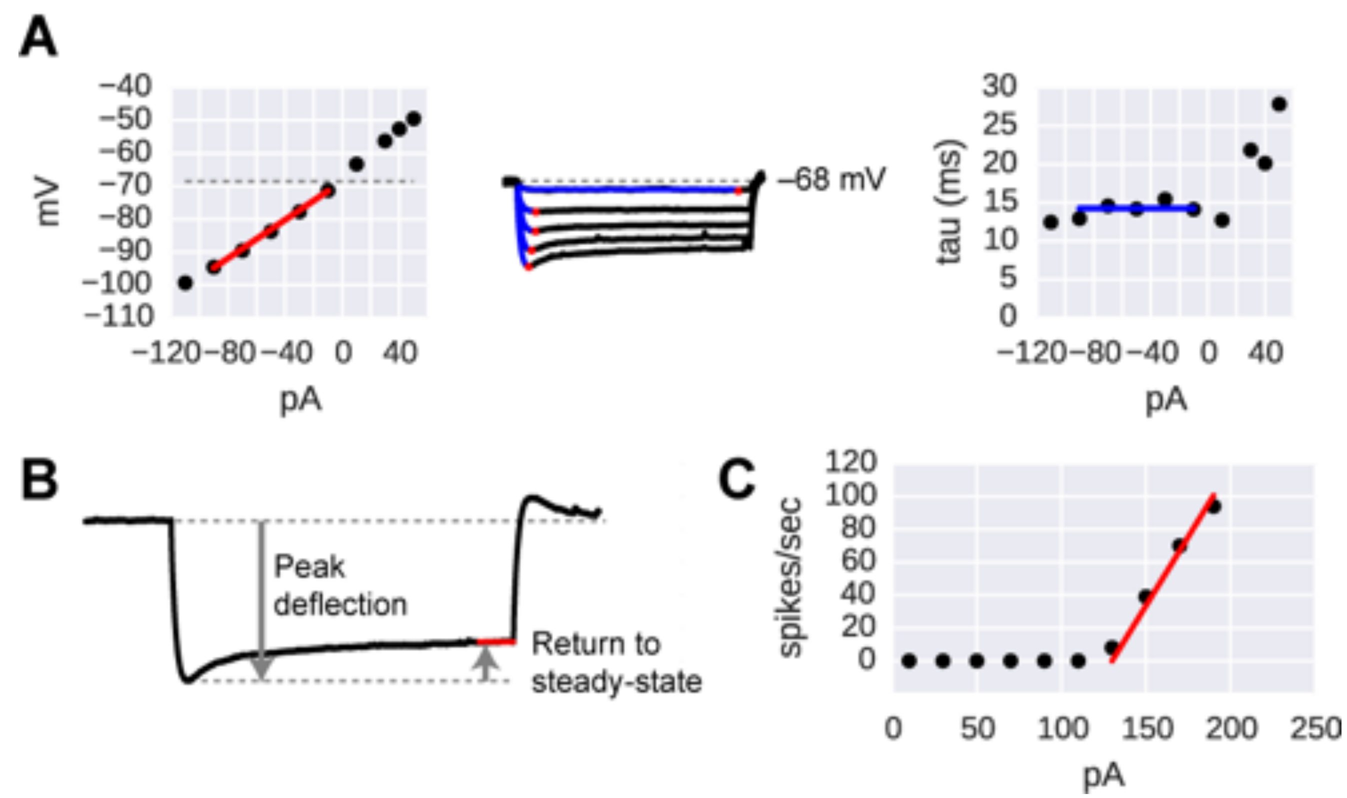
Staining and imaging of biocytin-filled cell

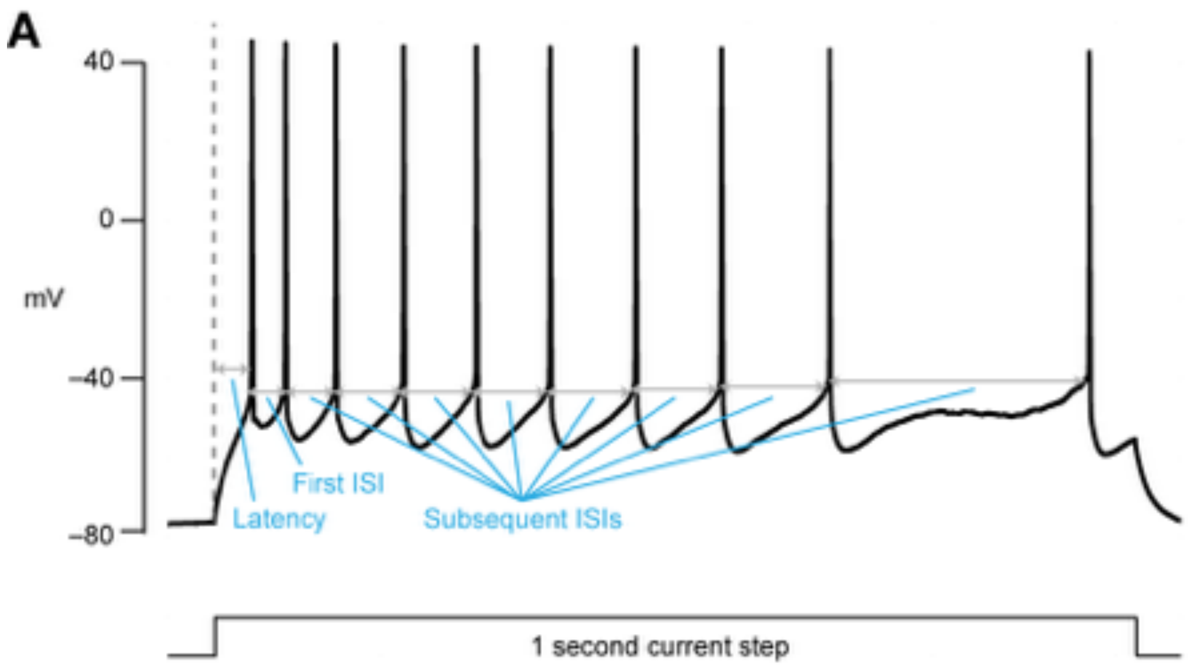


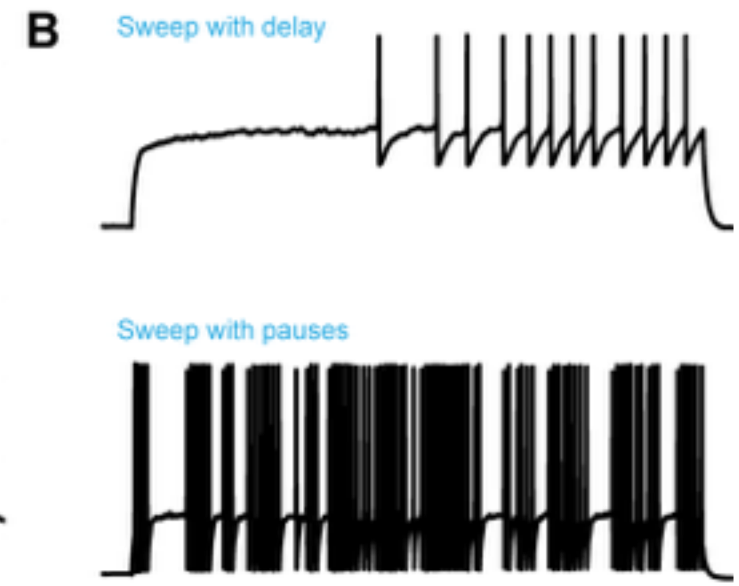
Enhancement of image and auto-trace, followed by manual curation

Electrophysiological Features





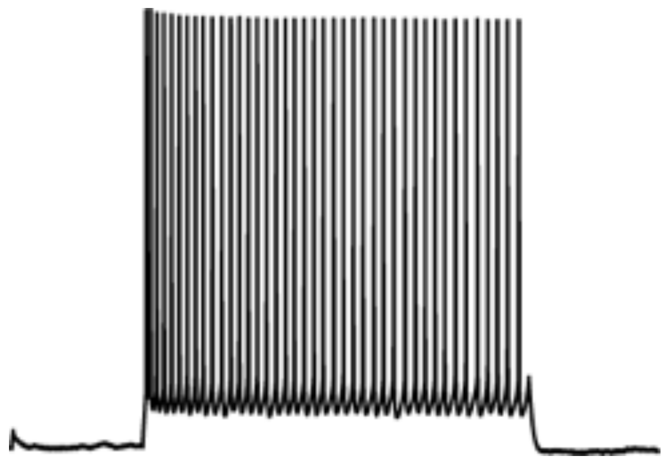


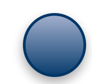


From Slice Data to Neuronal Models

IVSCC

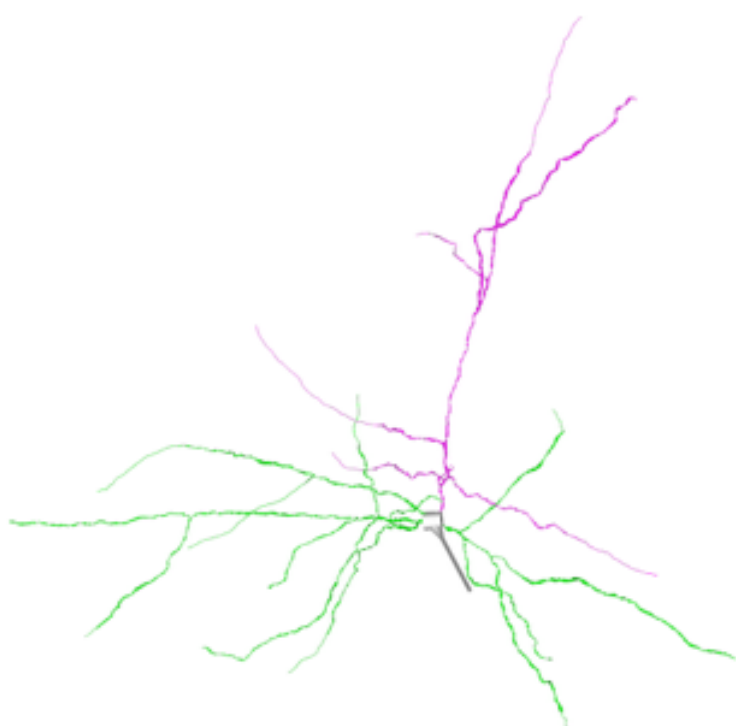
Electrophysiology

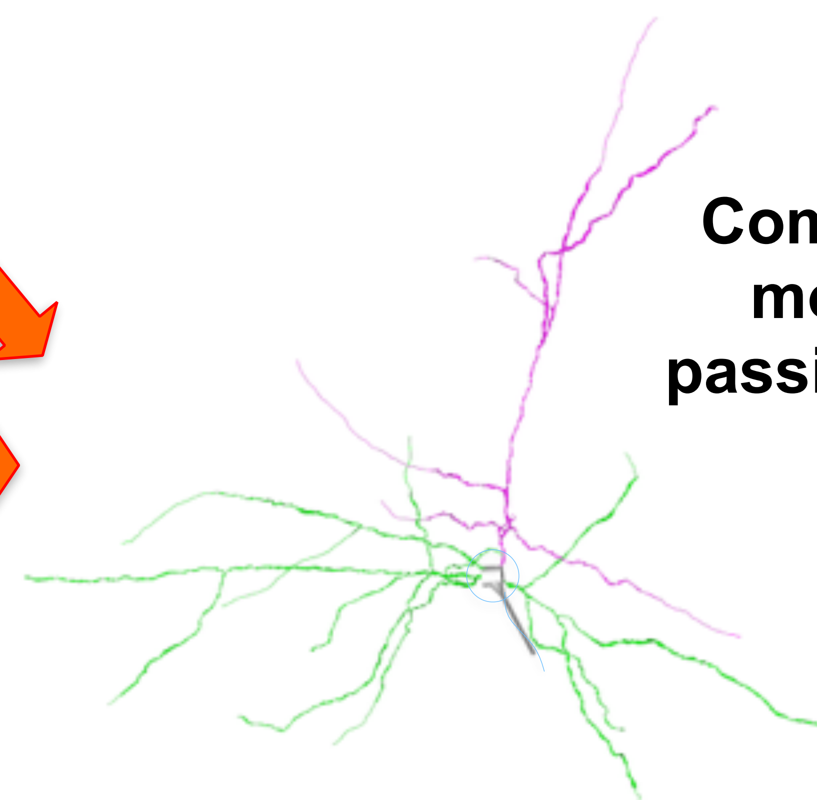




Point models (GLIF)

Morphology



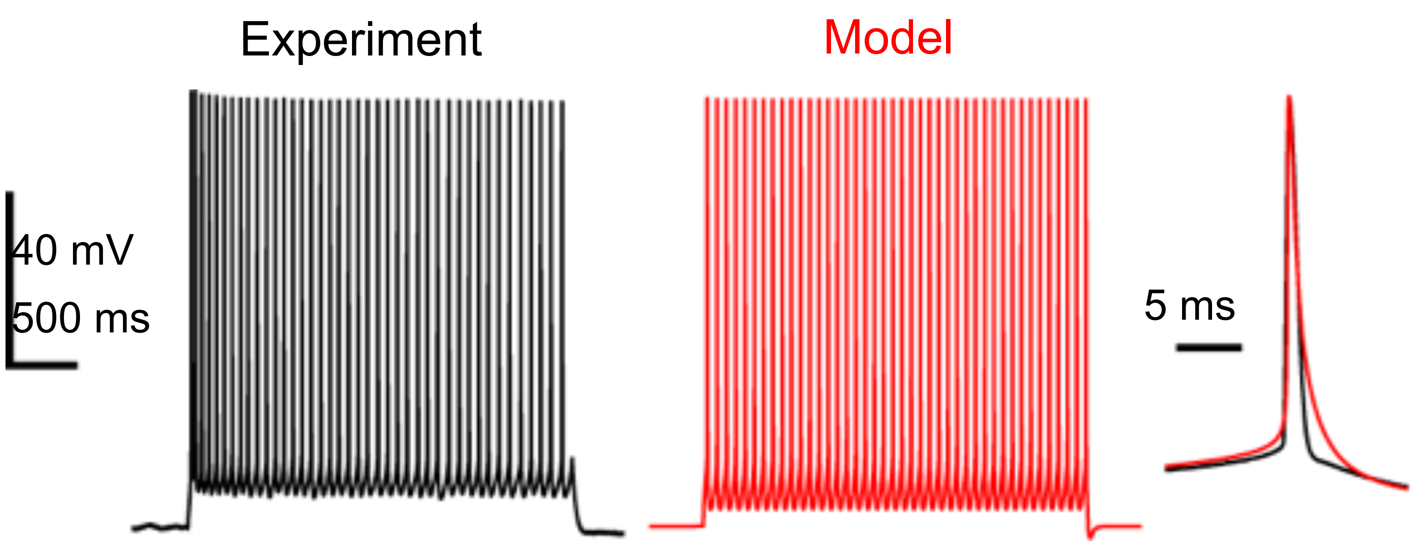


Compartmental models with passive dendrites

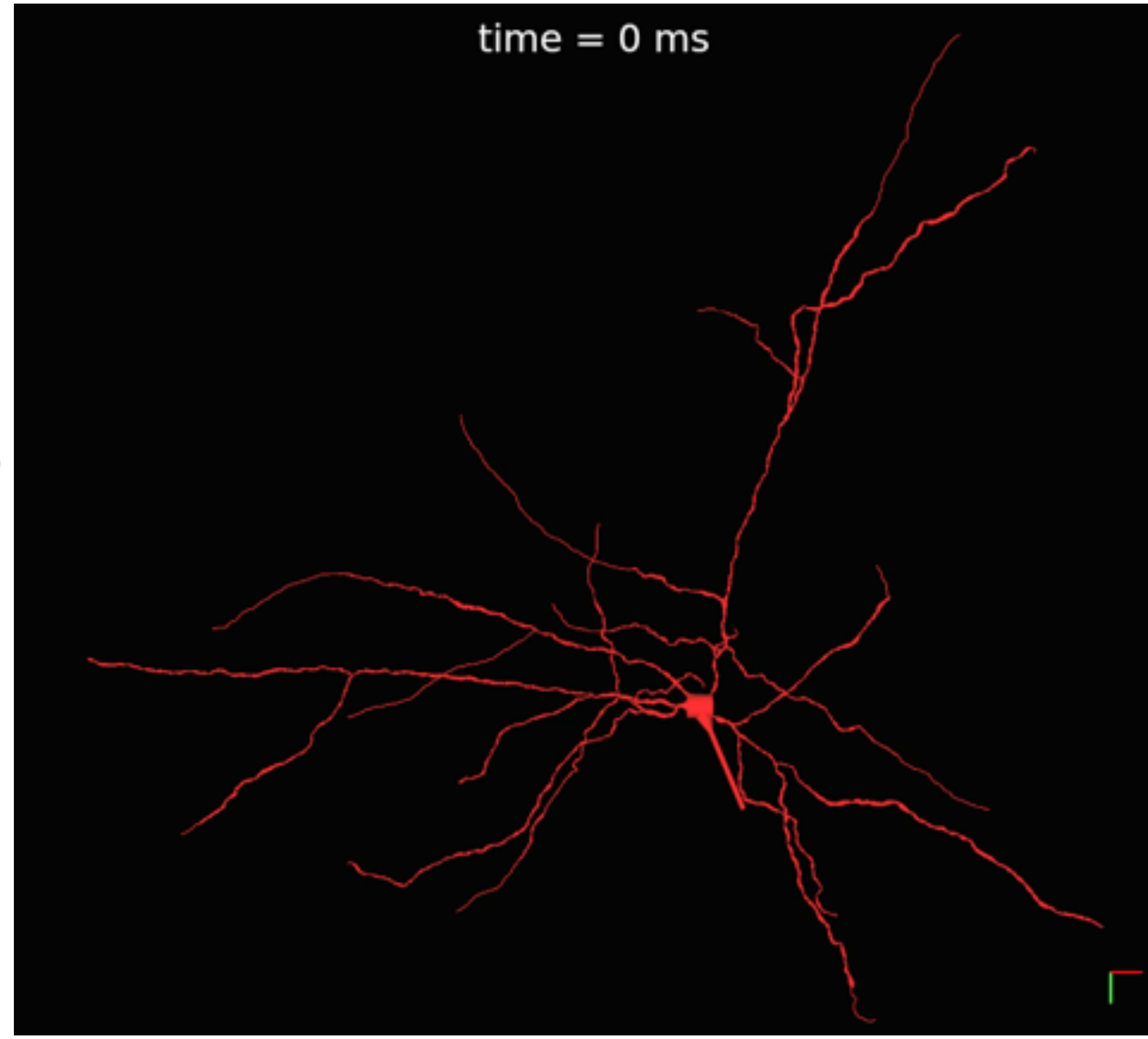
Database Statistics

Cre Line	Excitatory / Inhibitory (Expected)	Dominant Layers	Ephys Recordings	Morphology Reconstruction	GLIF Models	Biophysical Models
Rorb-IRES2-Cre	*Excitatory*	*4, 5*	*31*	*5*	*19*	*5*
Scnn1a-Tg2-Cre	*Excitatory*	*4*	*17*	*6*	*8*	*5*
Scnn1a-Tg3-Cre	*Excitatory*	*4, 5*	*36*	*8*	*17*	*7*
Nr5a1-Cre	*Excitatory*	*4*	*30*	*12*	*19*	*9*
Rbp4-Cre_KL100	*Excitatory*	*5*	*12*	*4*	*7*	*2*
Ntsr1-Cre	*Excitatory*	*6, 6b*	*8*	*3*	*7*	*1*
Sst-IRES-Cre	*Inhibitory*	*2/3, 4, 5, 6*	*36*	*11*	*16*	*7*
Pvalb-IRES-Cre	*Inhibitory*	*2/3, 4, 5, 6*	*51*	*18*	*9*	*9*
Htr3a-Cre_NO152	*Inhibitory*	*1, 2/3, 4, 5, 6, 6b*	*15*	*4*	*9*	*2*
Gad2-IRES-Cre	*Inhibitory*	*1, 2/3, 4, 5, 6, 6b*	*12*	*2*	*2*	*2*

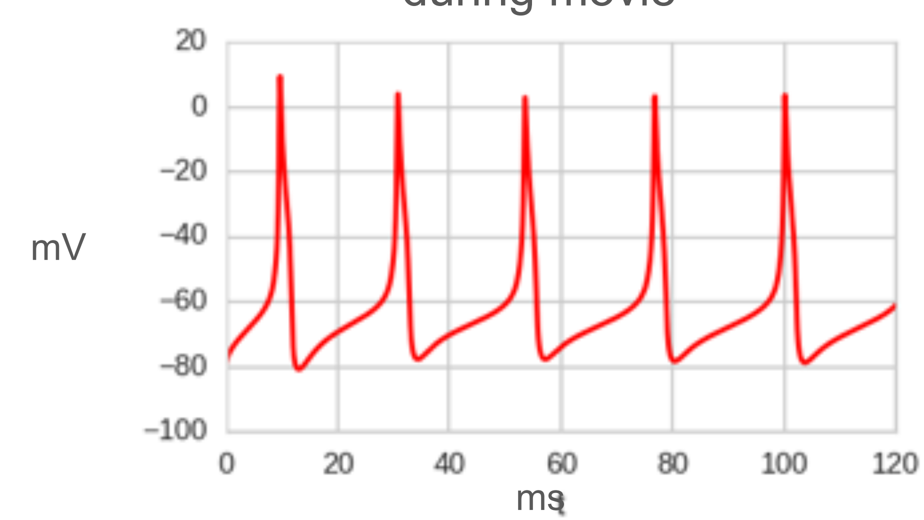
Biophysical Models of Single Cells



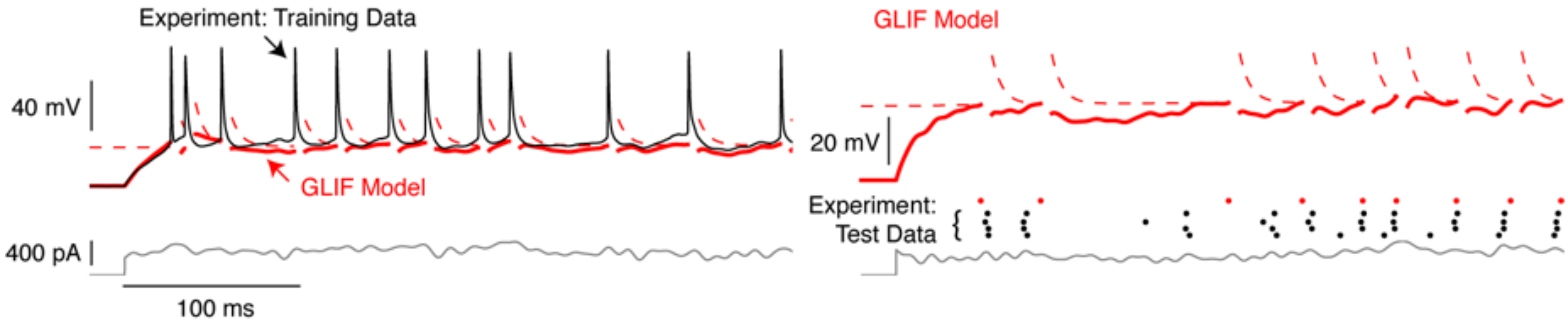
- Ephys data and morphology from the same cell recorded in slices
- ~10 active conductances placed at soma
- Optimization via a genetic algorithm (Druckmann et al., 2007; Hay et al. 2011)
- Fitness assessed by comparing electro-physiological features of responses to current steps
- Good performance on global features (firing frequency, AP height, etc.), less so with AP shape



Membrane potential at soma during movie



GLIF Models of Single Cells



- Point neuron model (no morphology)
- Responses defined by abstracted mathematical expressions that represent membrane voltage, action potential threshold, etc.
- Optimized to match spike times in training data consisting of firing in response to noisy current injection
- Quality of fit assessed by how well model explains the variance in spike times from responses to another noisy current stimulus
- Five types of GLIF models are present in the database with varying levels of complexity
  - LIF
  - LIF with decaying threshold and reset rule
  - LIF with after-spike currents
  - LIF, decaying threshold *and* ASC's
  - LIF, adapting threhold, reset, and ASC's

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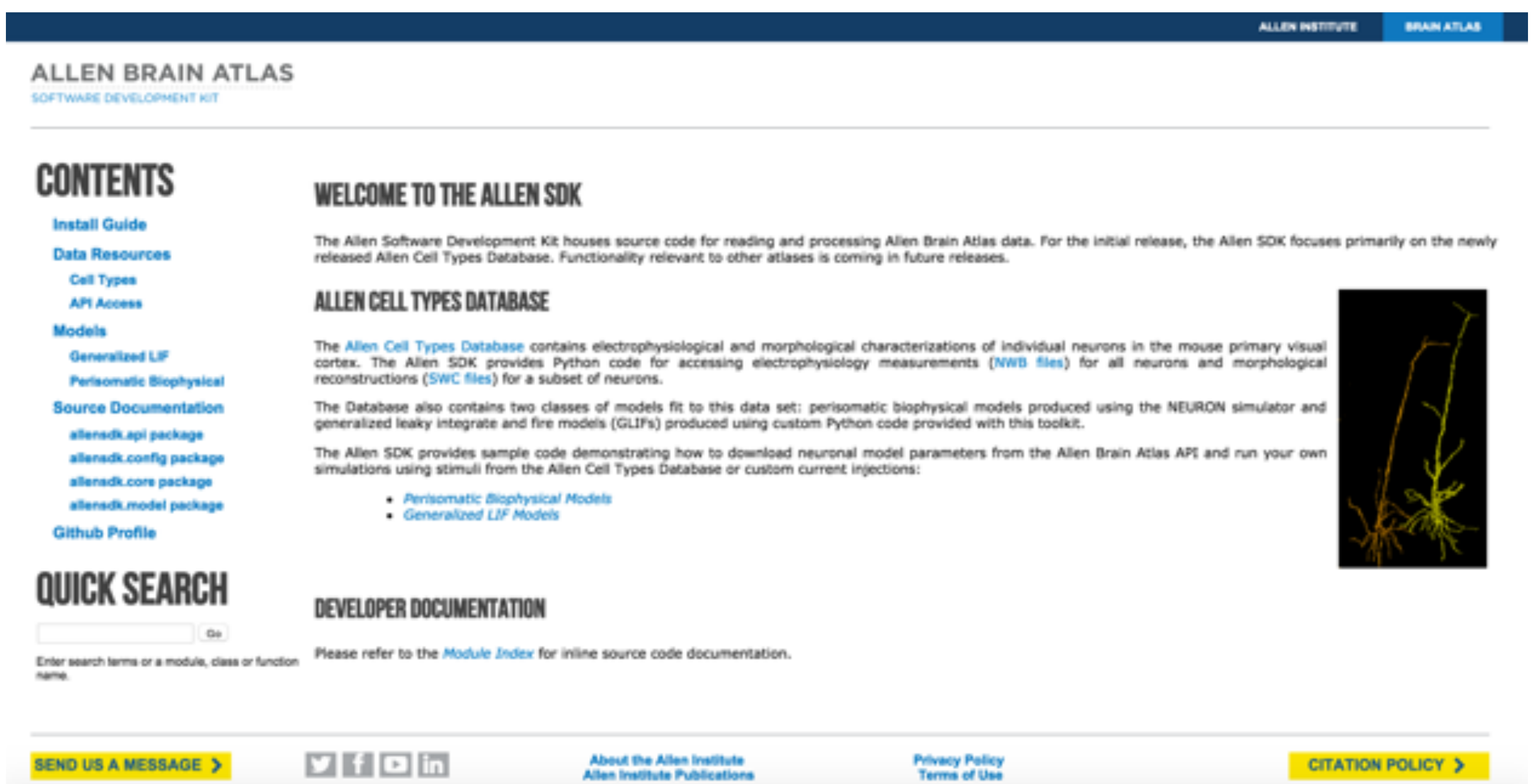
- **Allen SDK** (http://alleninstitute.github.io/AllenSDK/)
- DiPDE (http://alleninstitute.github.io/dipde/)

Allen SDK: (http://alleninstitute.github.io/AllenSDK/)

Goal: Python code for reading and processing AIBS data:

- Cell Types database API
  - Morphology (SWC files)
  - Ephys data (Neurodata without borders, i.e. HDF5)
  - Code to run GLIF and biophysically detailed models
- Allen Brain Atlas API



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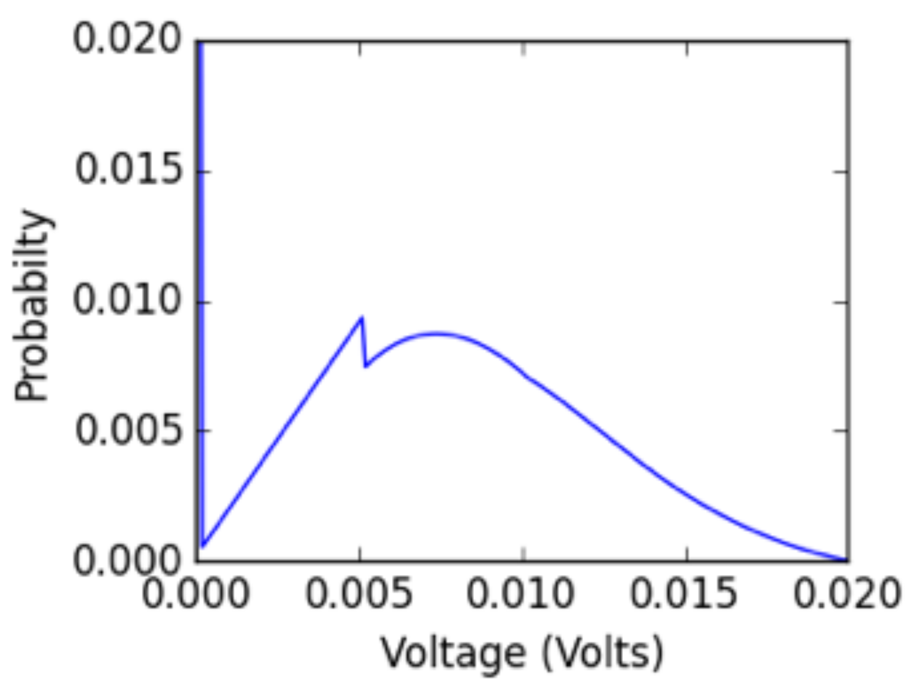
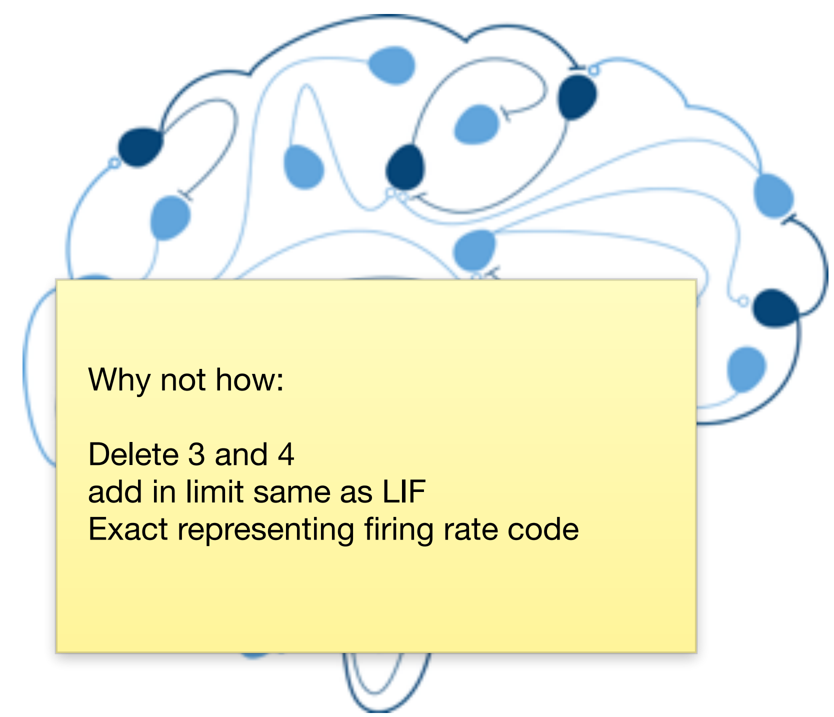
DiPDE: (http://alleninstitute.github.io/dipde/)

Goal: Provide a fast, flexible, python-based population statistic simulator for coarse-scale modeling

- Solve coupled population density equations
- Absorbing boundary condition at threshold
- Same mean firing rate as LIF population as N increases
- Exact when representing, ex., firing rate code





Why not how:

Delete 3 and 4
add in limit same as LIF
Exact representing firing rate code

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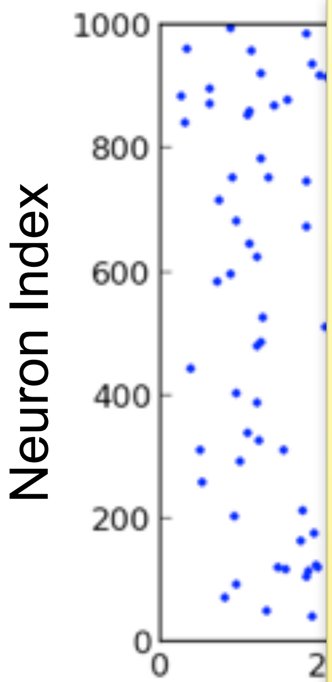
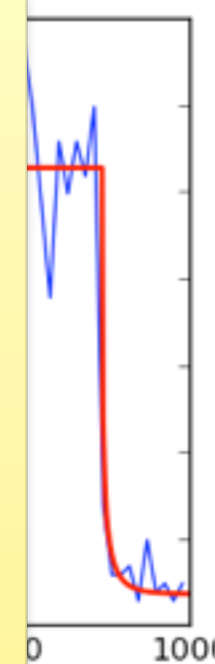
DiPDE: (http://alleninstitute.github.io/dipde/)

N = 1000 LIF neurons



The first term on the RHS in equation (3) incorporates the drift due to non-synaptic currents. The second term removes the probability for neurons which previously were at potential v and received a synaptic input. The third term adds the probability that a neuron w away in potential receives a synaptic input such that its potential is changed to v. The last term j(v,t) represents a probability current injection of the neuron which previously spiked. j(v,t) includes the effect of any excess synaptic input above the threshold at which spiking occurs, due to large super-threshold synaptic events. To account for the effect of the excess input with instantaneous synapses, the probability current is injected between the resting potential and vz, where vz represents the membrane potential that would be reached due to the excess input. This serves the purpose of 'remembering' the excess input, whose effect would have been held by the synaptic variables in the case of slow synapses, without losing it on resetting the membrane potential after spiking.



$$\partial_t p(v,t) = \partial_v \left(L(v)p(v,t)\right) - f(t)p(v,t) + f(t)\int_{w_1}^{w_2} p(v-w,t)q(w)H(\theta - v + w)dw + j(v,t)$$

$$j(v,t) = f(t)\int_{w_1}^{w_2} H(v)H(w-v)p(v+\theta-w,t)q(w)dw$$

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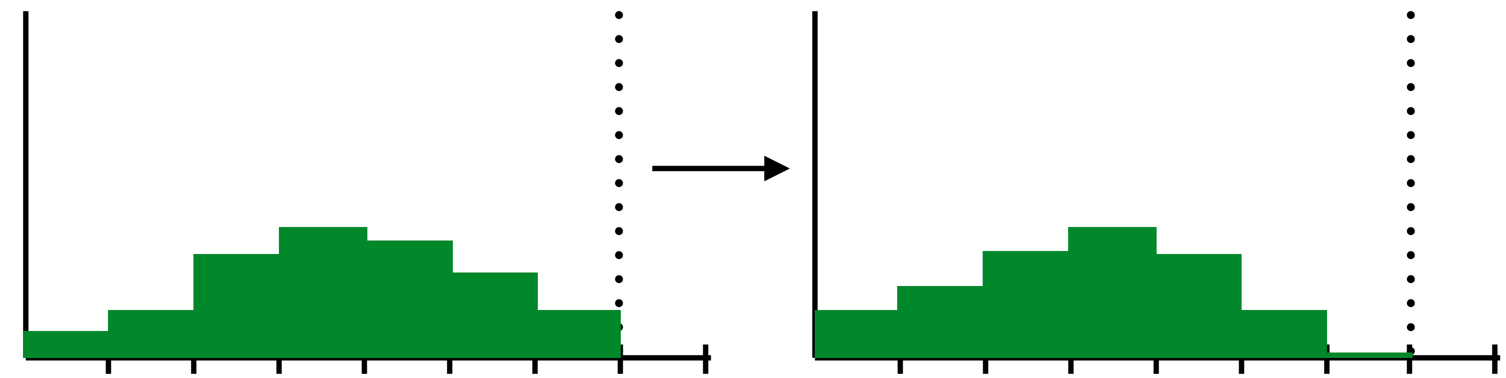
DiPDE: (http://alleninstitute.github.io/dipde/)

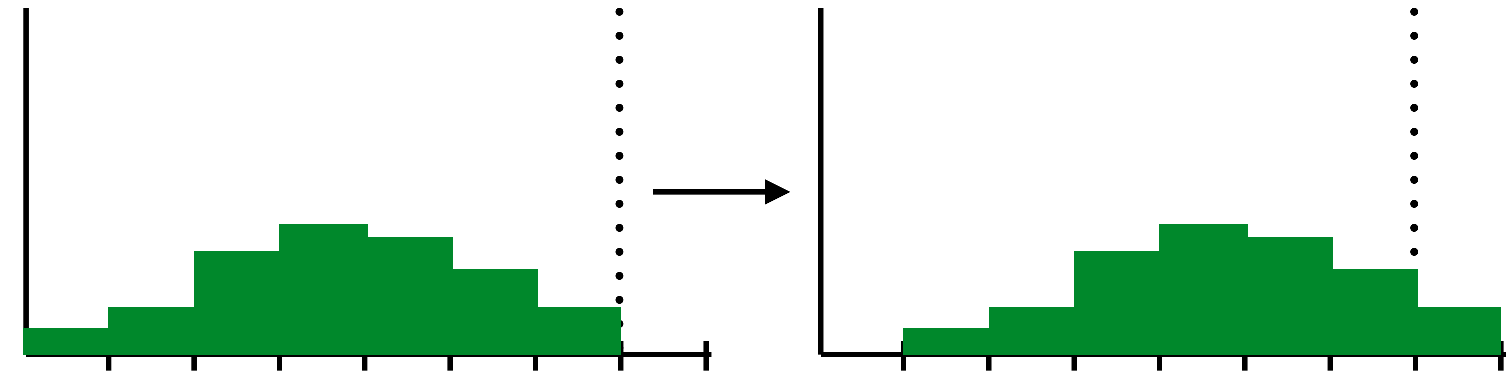
$$\partial_t p(v,t) = \boxed{\partial_v \left(L(v) p(v,t) \right)} - f(t) p(v,t) + f(t) \int_{w_1}^{w_2} p(v-w,t) q(w) H(\theta - v + w) dw + j(v,t)$$

$$j(v,t) = f(t) \int_{w_1}^{w_2} H(v) H(w-v) p(v+\theta-w,t) q(w) dw$$

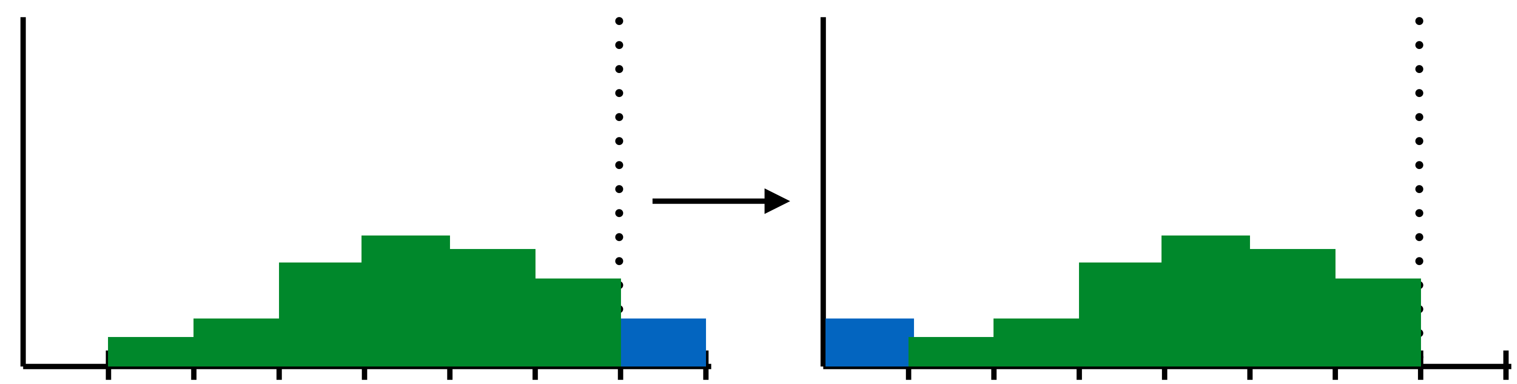
Leak:



Synaptic Activation:



Thresholding:



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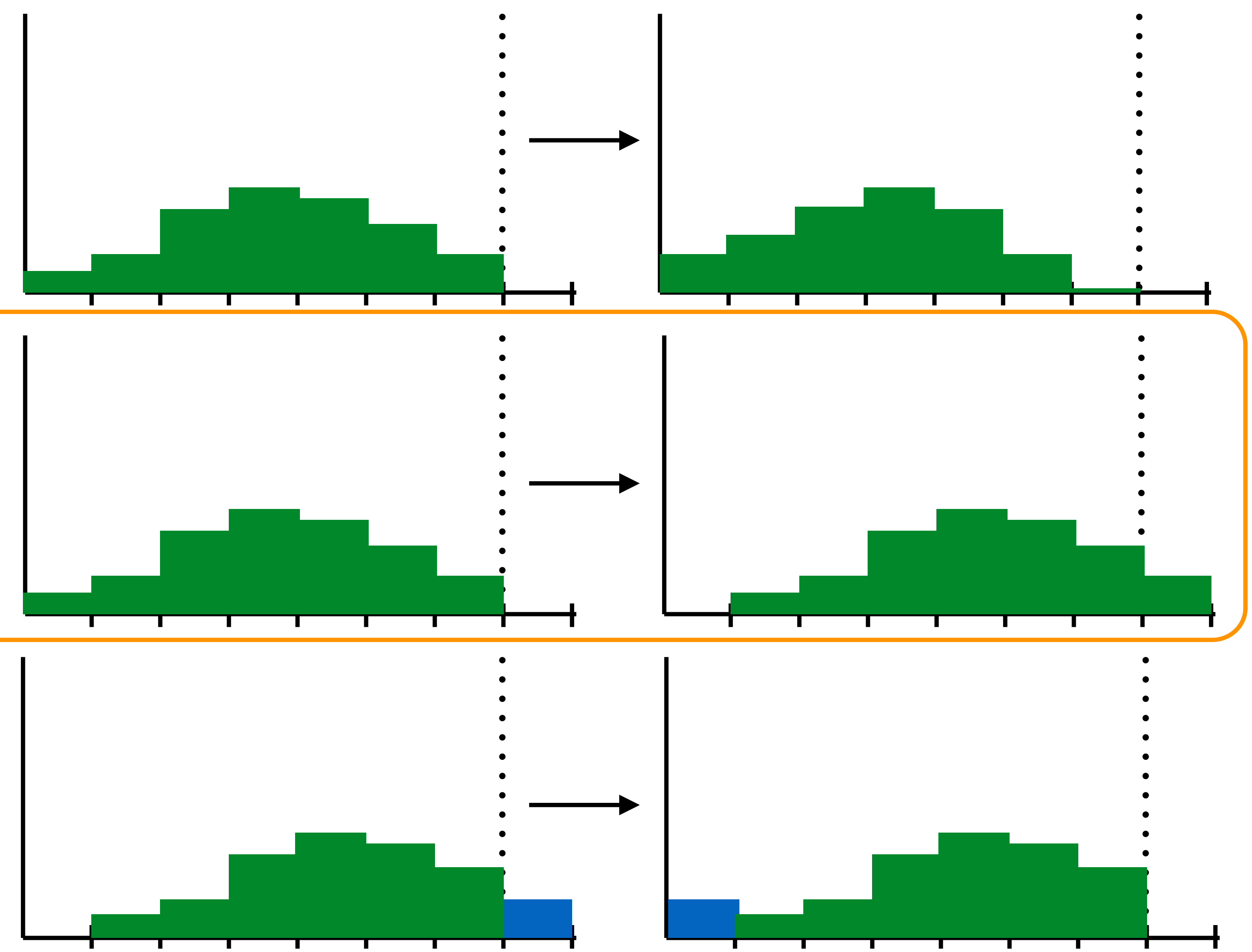
$$j(v,t) = f(t)\int_{w_1}^{w_2} H(v)H(w-v)p(v+\theta-w,t)q(w)dw$$

Leak:

Synaptic Activation:

Thresholding:



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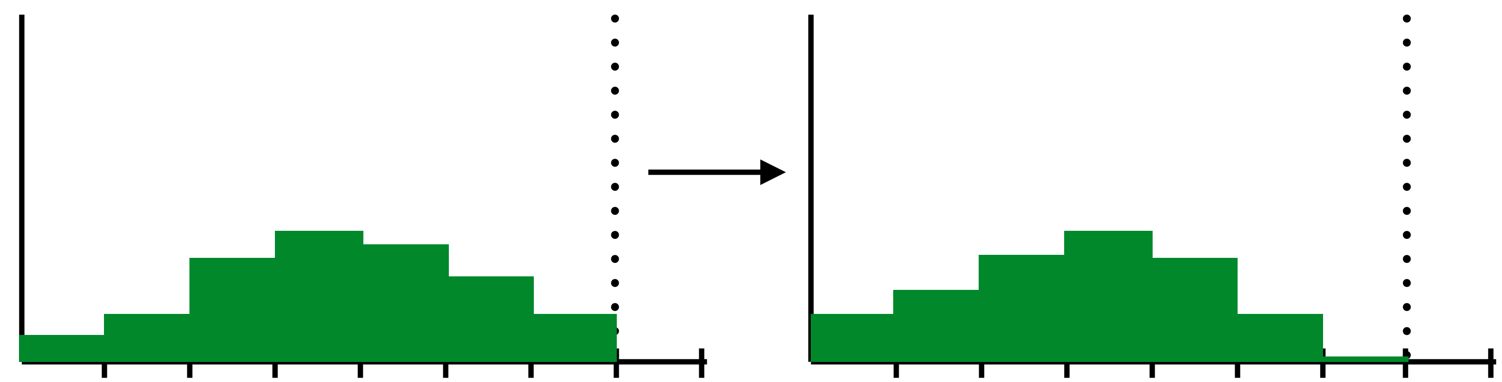
$$j(v,t) = \boxed{f(t)\int_{w_1}^{w_2} H(v)H(w-v)p(v+\theta-w,t)q(w)dw}$$

Leak:



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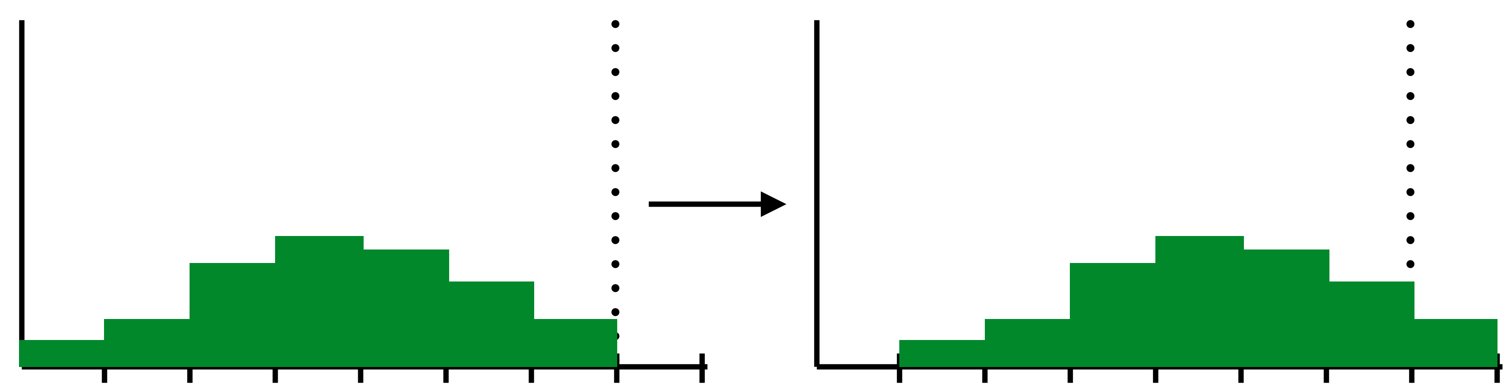
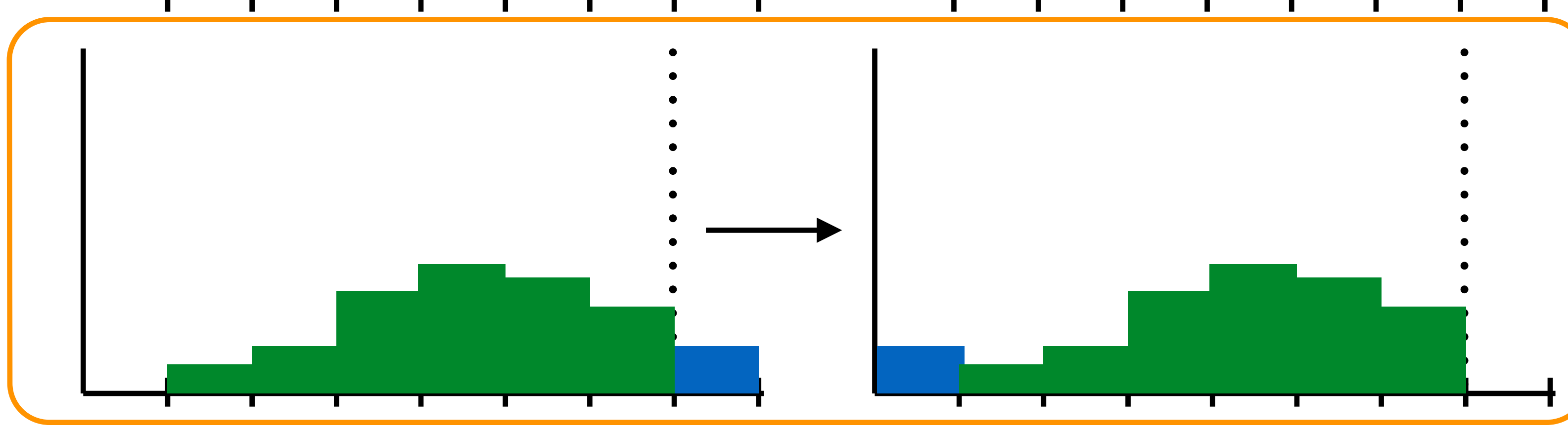


Thresholding:



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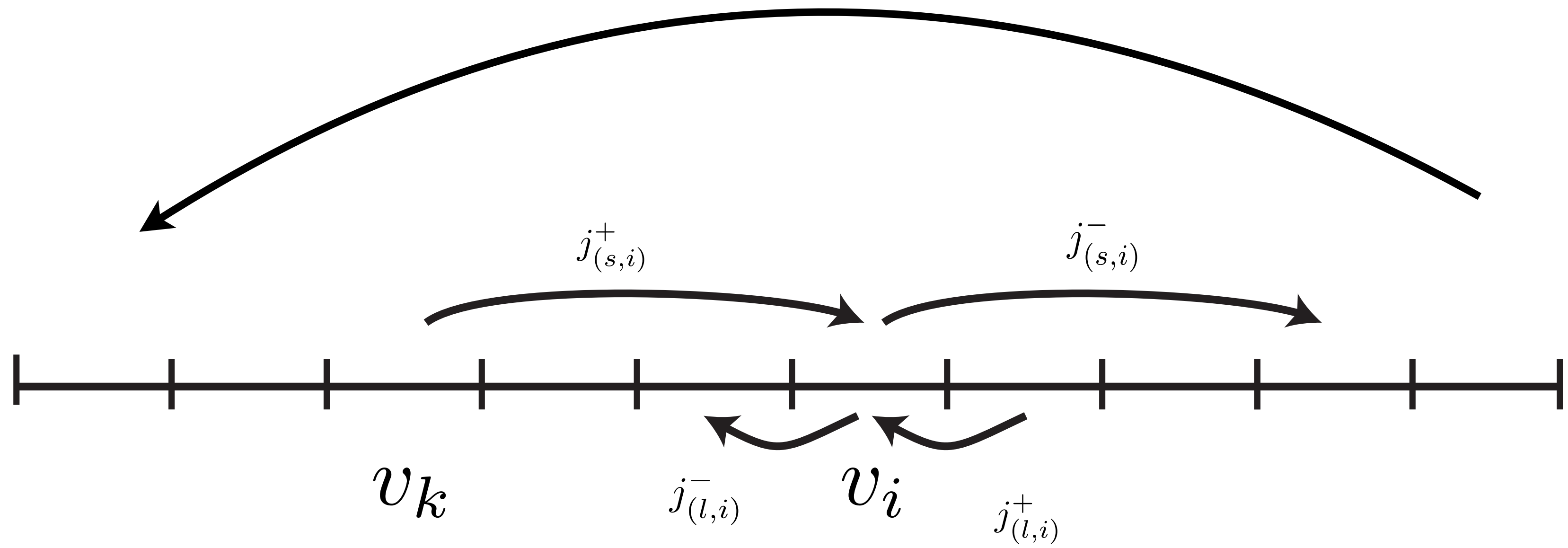
$$\frac{\partial p}{\partial t} = -\frac{\partial J}{\partial v}$$



$$\frac{\partial p_i}{\partial t} = -\frac{\Delta J_i}{\Delta v_i}$$

$$\begin{aligned}\Delta J_i &= f_{i+\frac{1}{2}} - f_{i-\frac{1}{2}} \\ &= (j^{-}_{(s,i)} - j^{+}_{(l,i)}) - (j^{+}_{(s,i)} - j^{-}_{(l,i)}).\end{aligned}$$

$$\begin{aligned} j^{+}_{(s,i)} &= p_k \Delta v_k \lambda_{in}(t) \\ j^{-}_{(s,i)} &= p_i \Delta v_i \lambda_{in}(t) \\ j^{+}_{(l,i)} &= \frac{p_{i+1} v_{i+\frac{1}{2}}}{\tau} \\ j^{-}_{(l,i)} &= \frac{p_i v_{i-\frac{1}{2}}}{\tau} \end{aligned}$$

$$\frac{d\mathbf{p}}{dt} = (L+S)\mathbf{p}$$

$$\mathbf{p}(t+\Delta t) = \exp\left(\Delta t \left(L + \sum_{s=0}^{m} S_s\right)\right)\mathbf{p}(t)$$

$$\lambda_{out}(t) = \frac{\sum_{s=0}^{m} j^{+}_{(s,0)}}{\Delta t}$$

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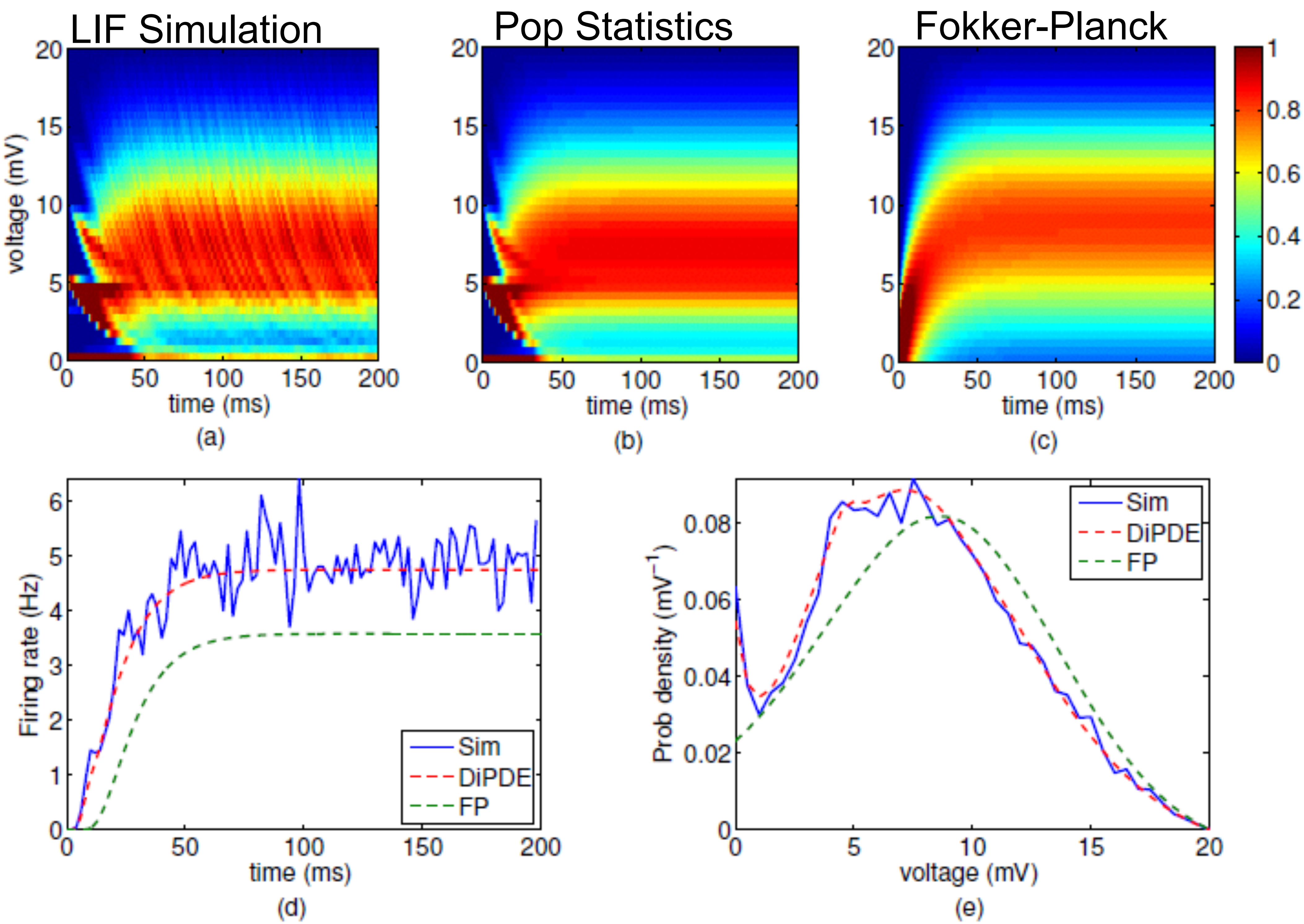

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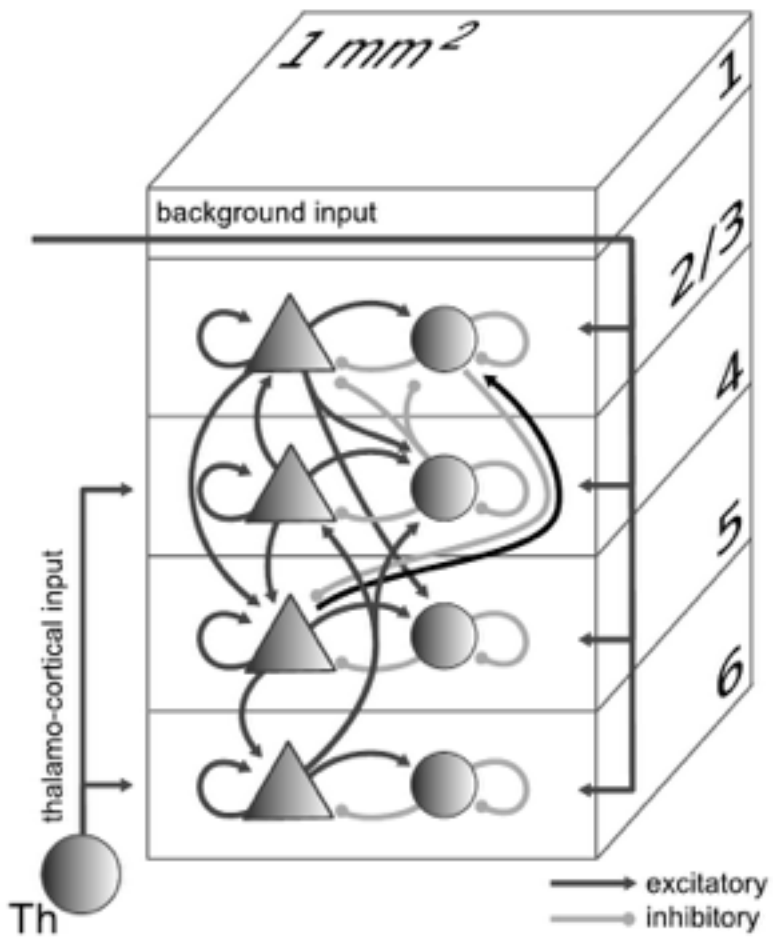
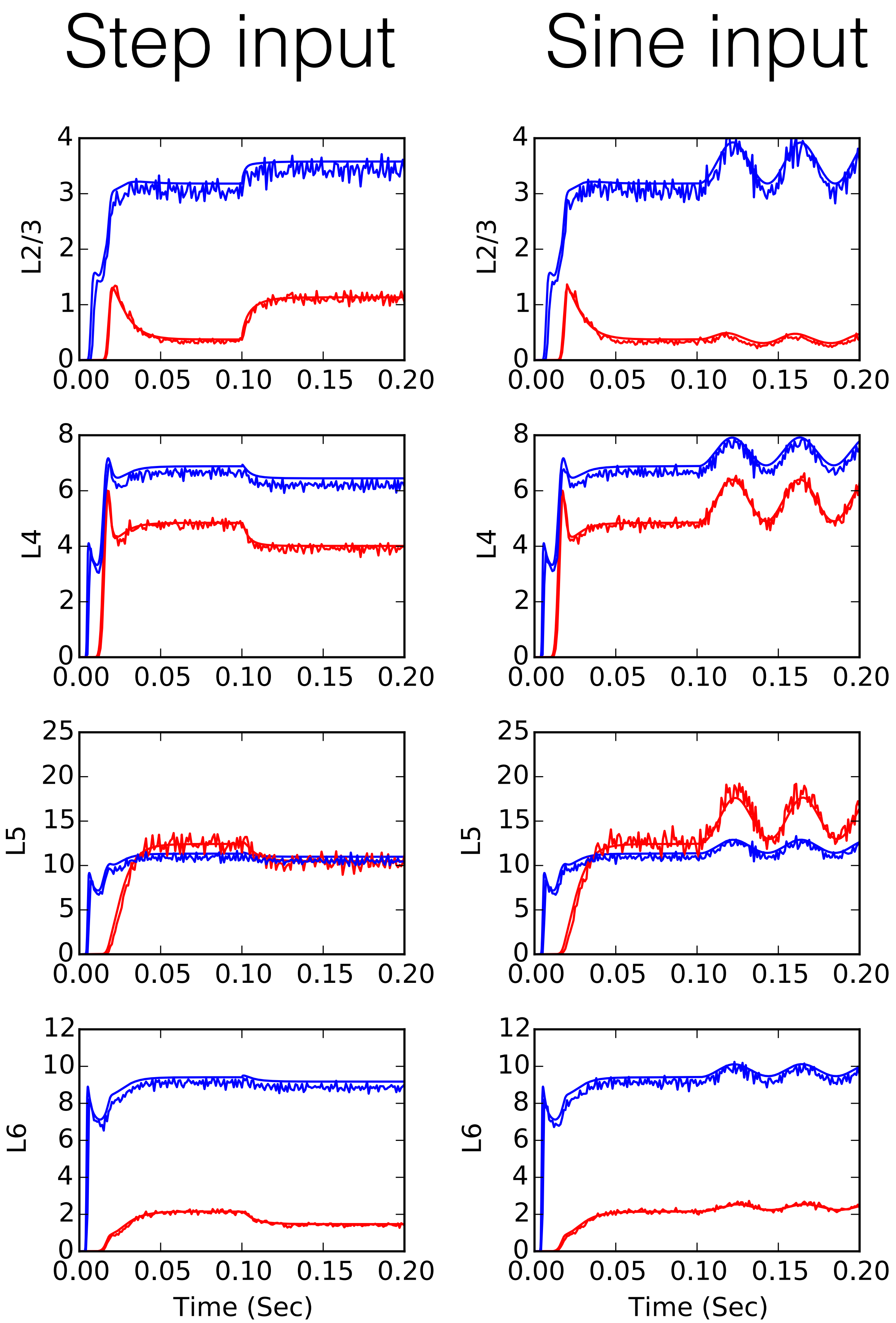
Iyer et al. PLoS Comp. Biol. 2013

DiPDE: (http://alleninstitute.github.io/dipde/)

- DiPDE well-approximates a simplified cortical column



Potjans and Diesmann
(Cerebral Cortex, 2014)



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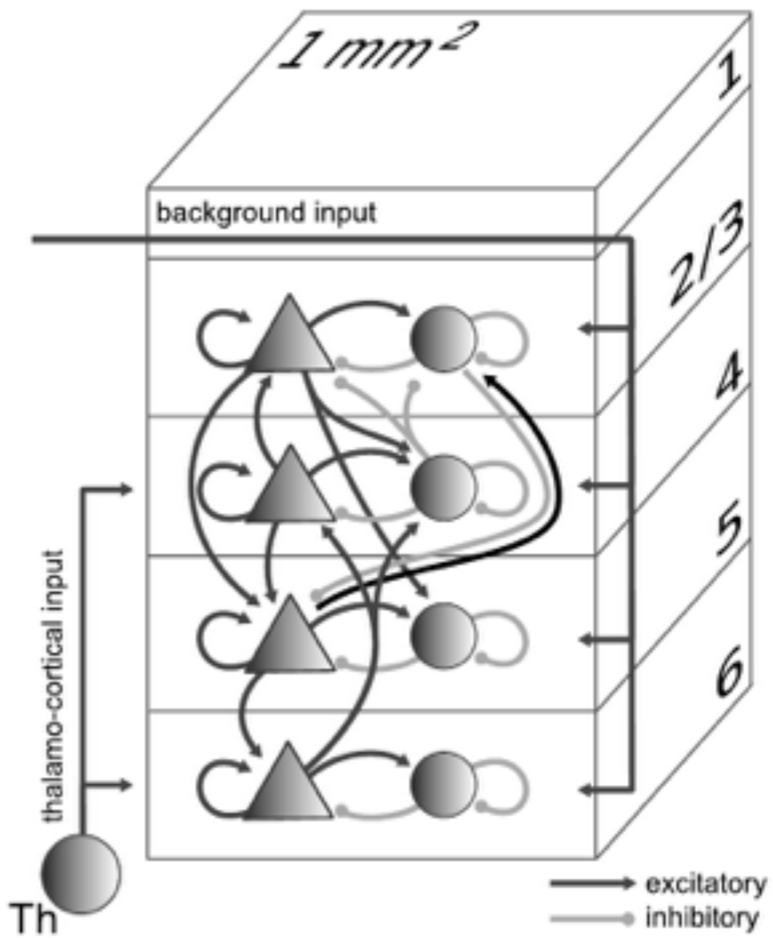
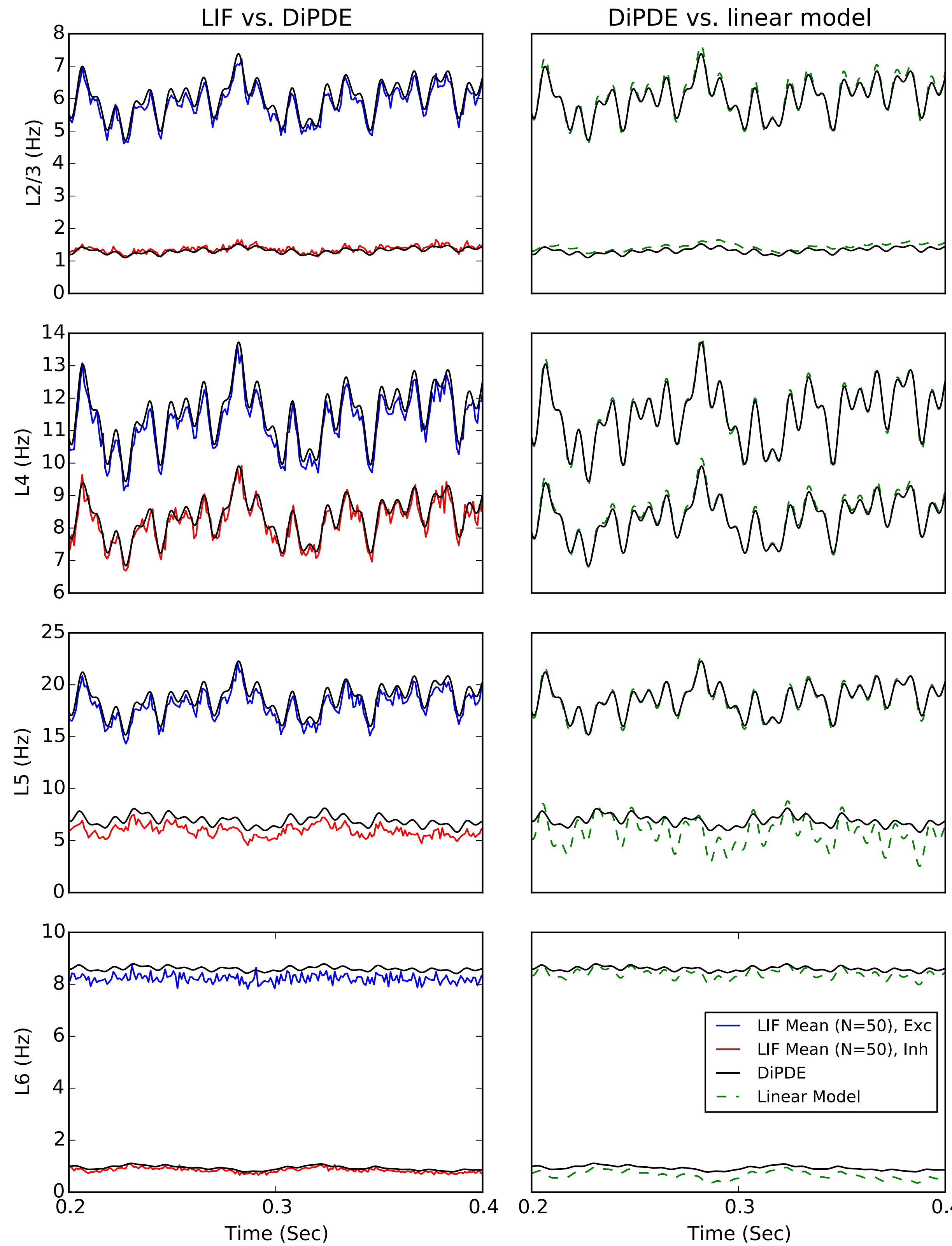
- Model responds linearly to perturbations





Potjans and Diesmann
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Conclusion

- Allen Cell Types Database:
  - http://celltypes.brain-map.org/
  - Open collection of whole cell patch recordings
  - Biophysically detailed and point-neuron model fits
- Allen SDK
  - http://alleninstitute.github.io/AllenSDK/
  - Source code for reading + processing ABA data
- DiPDE
  - http://alleninstitute.github.io/dipde/
  - Coupled population density equation solver
  - Coarse-grained model of firing rate simulations

SUMMER WORKSHOP ON THE DYNAMIC BRAIN

CO-HOSTED BY UNIVERSITY of WASHINGTON COMPUTATIONAL NEUROSCIENCE TRAINING PROGRAM ALLEN INSTITUTE for BRAIN SCIENCE

Partial funding is provided by The Simons Foundation

Friday Harbor Laboratories, Friday Harbor, WA
http://alleninstitute.org/news-events/events-training/event/summer-workshop-dynamic-brain-2015

- 2 Week project-based summer course:
- This year: August 23 – September 6, 2015 (Applications closed)
- Open resources introduction to:
  - Cell Types Database
  - Mouse Connectivity Map
  - Cortical Activity Map (2P)

This talk at: https://goo.gl/Xpxce3

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BRAIN-MAP.ORG

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