

Generalized Leaky Integrate-and-Fire Model

Building blocks of models
for cortical computation

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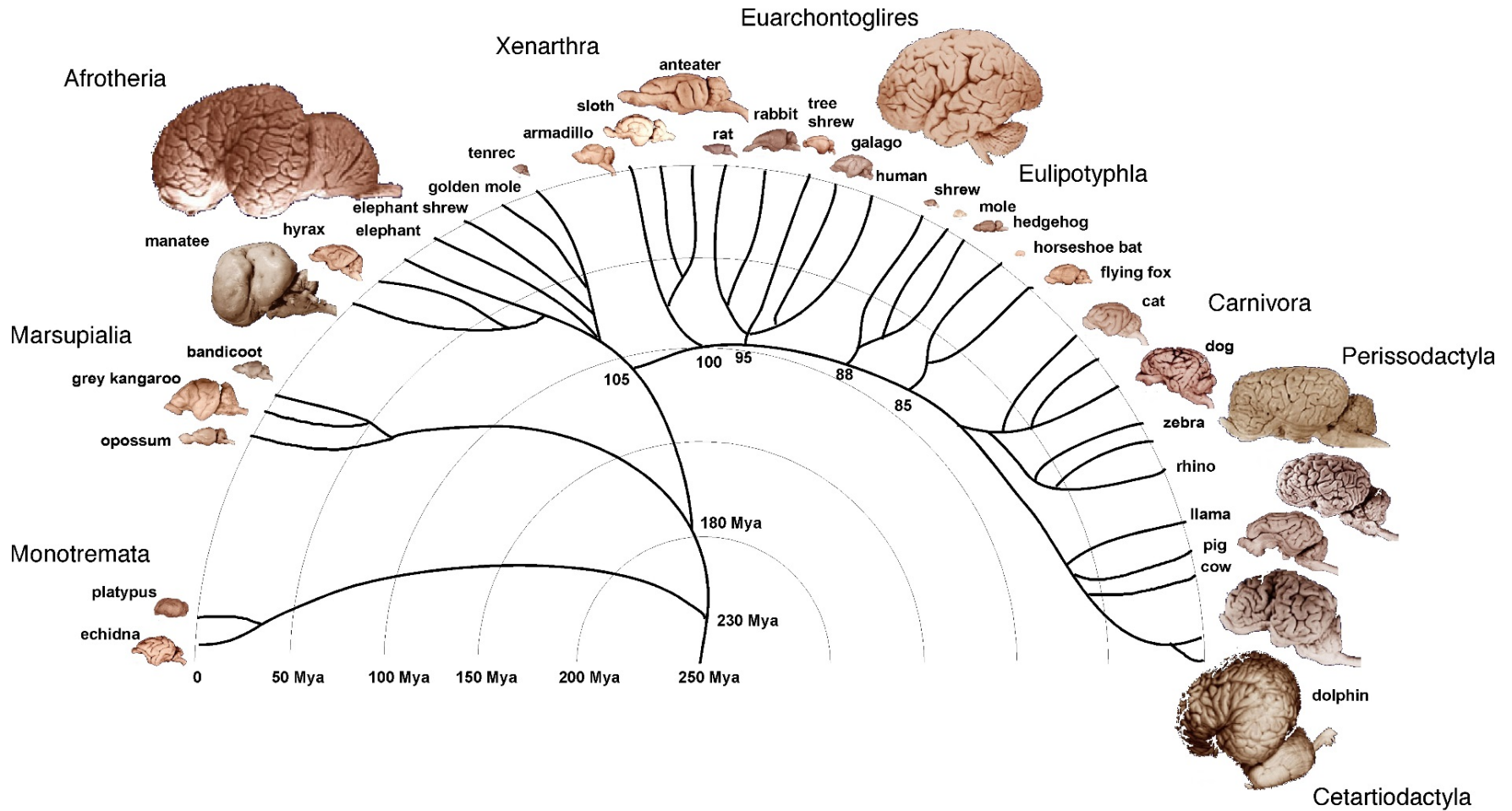
ALLEN INSTITUTE
for BRAIN SCIENCE
Fueling Discovery

Lecture plan

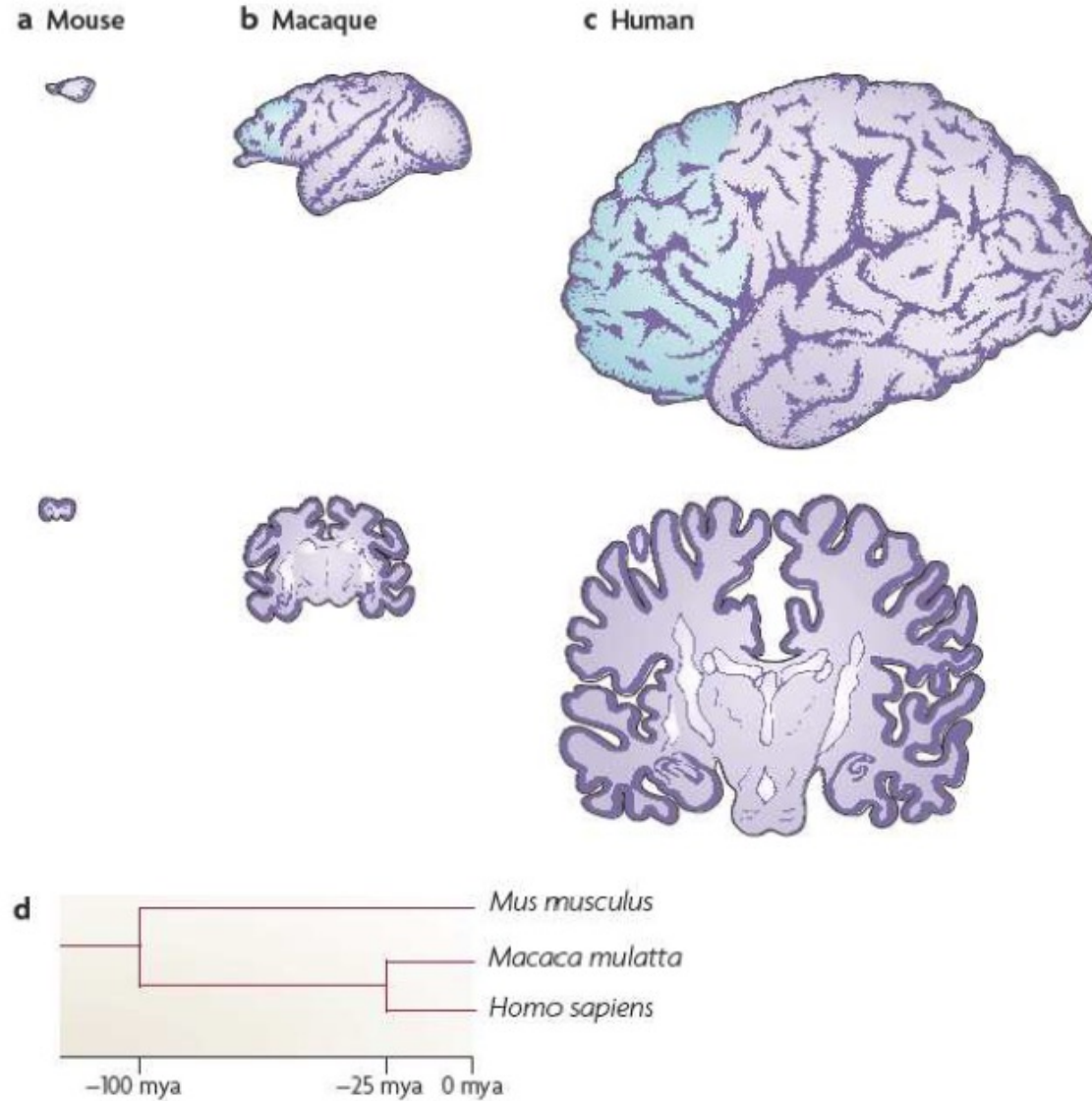
1. Motivation: why we study mouse cortex
2. Single neuron models: From dynamical systems to hybrid systems
3. Generalized leaky integrate-and-fire model
4. Fitting GLIF models
5. Cell classification using GLIF models

1. Why study cortex?

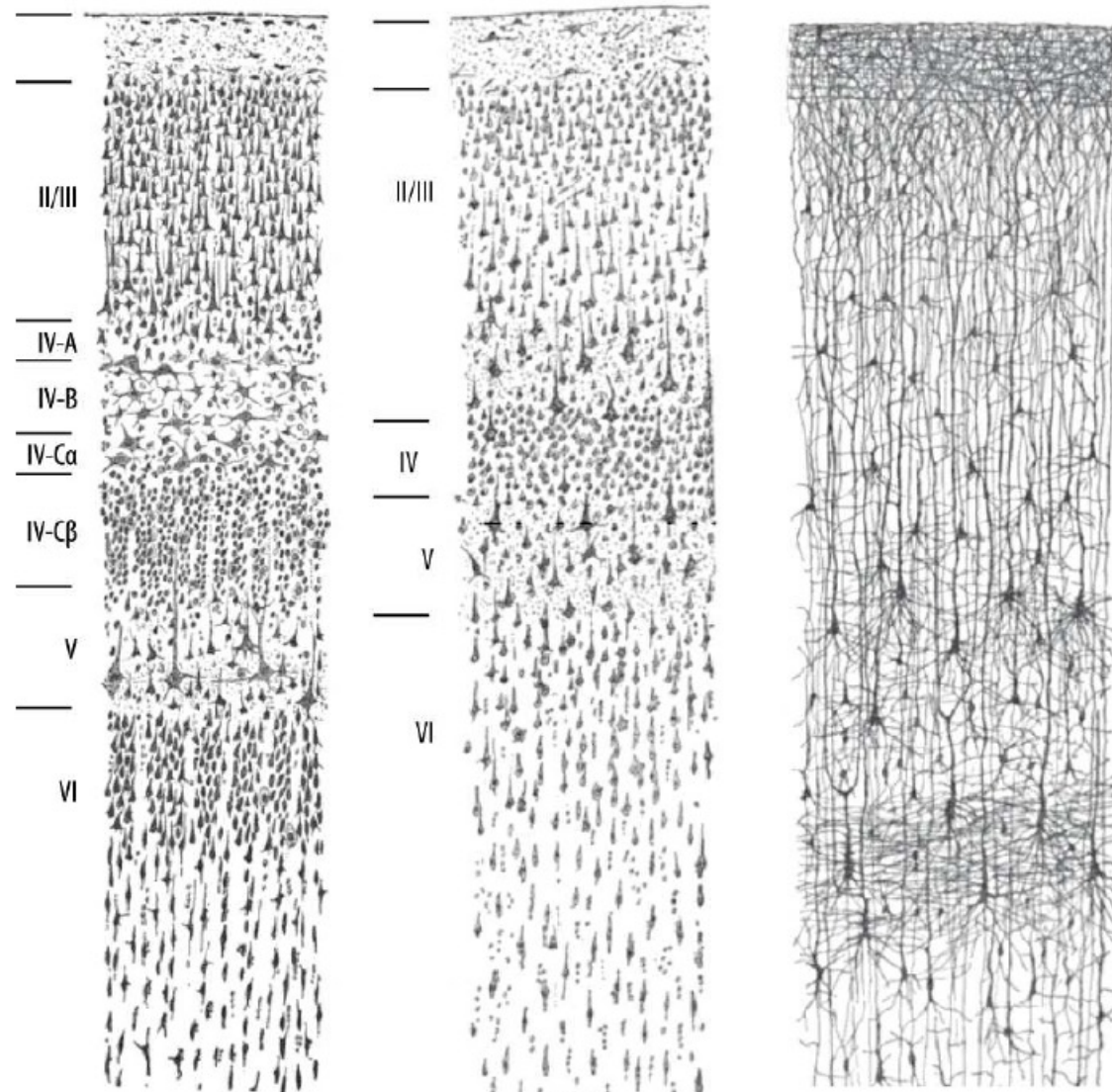
Cerebral cortex can vary in size



Cerebral cortex can vary in size



But the basic microstructure is very similar across areas

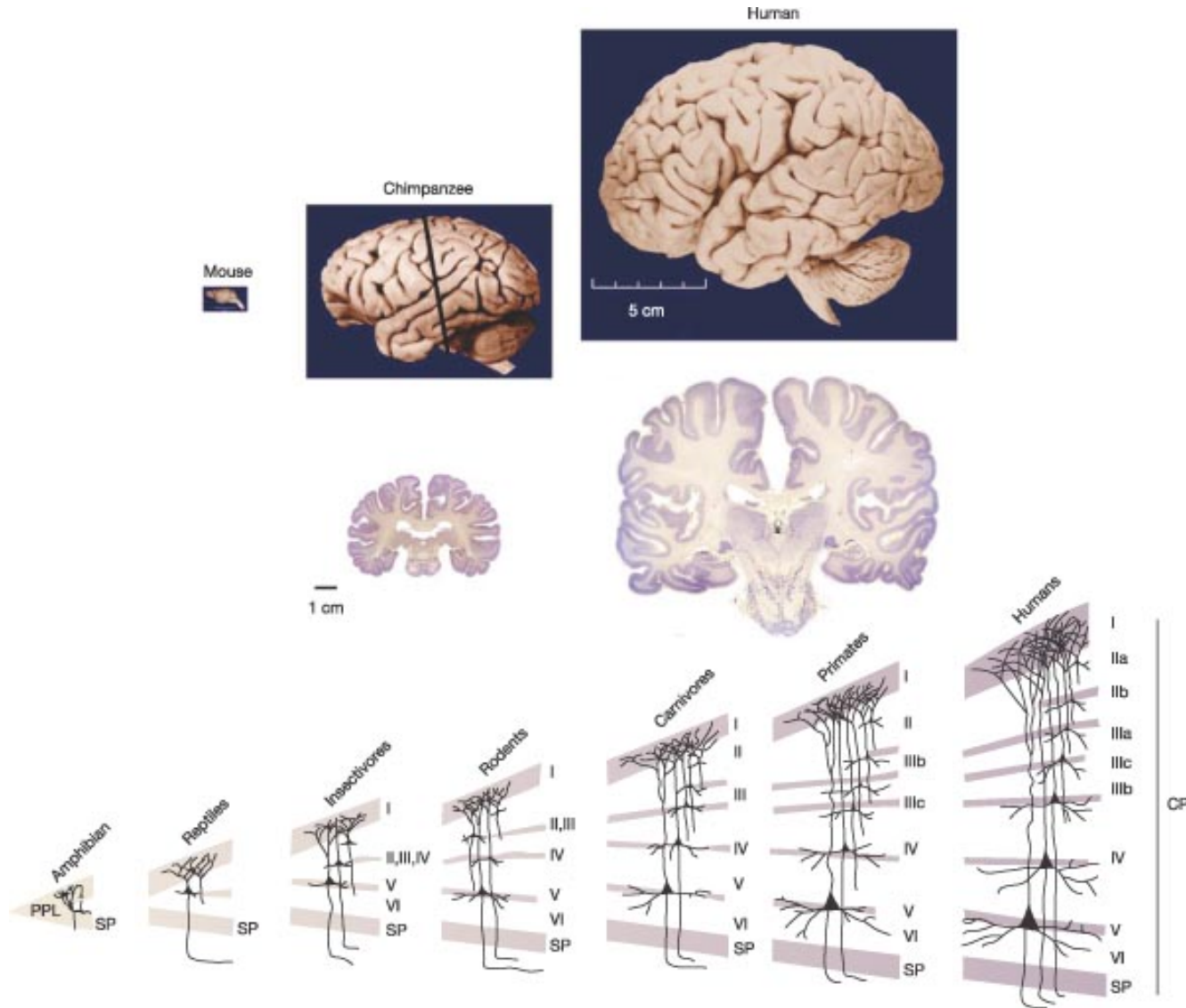


Adult V1

Adult M1

Infant

And across species

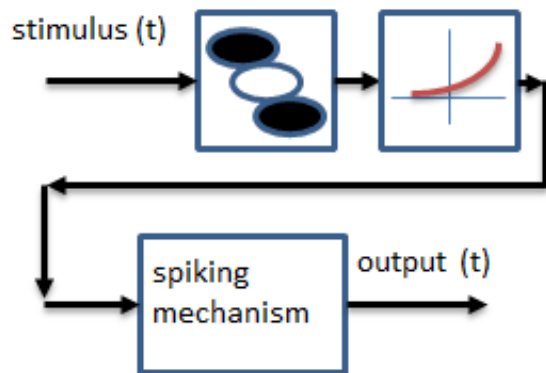
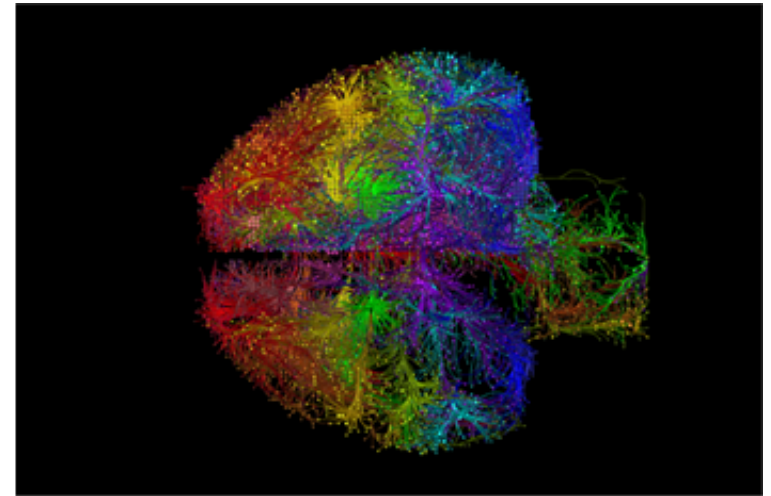
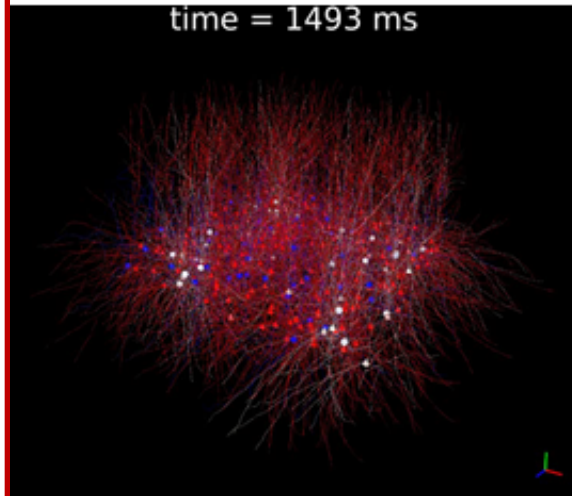
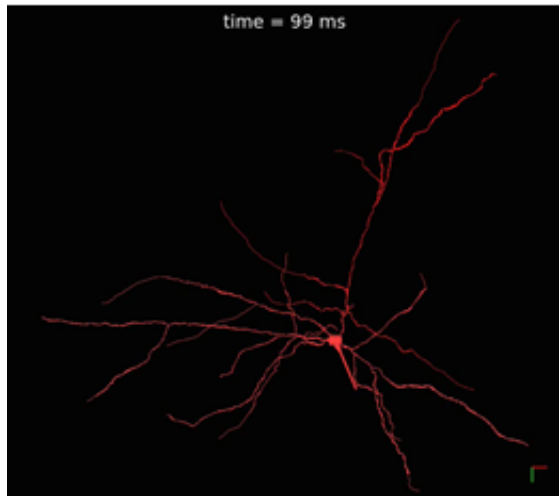


Cortical column computations

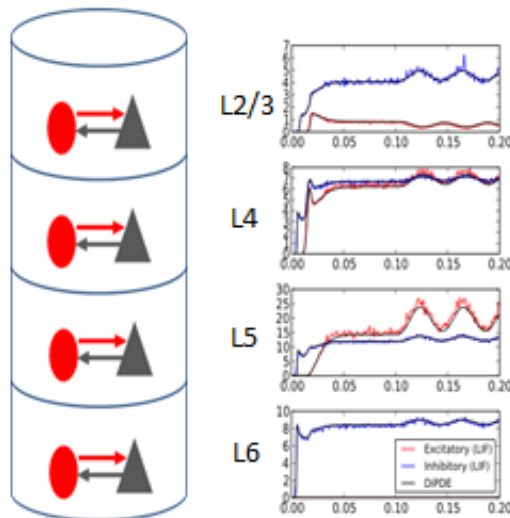
Hope:

- Cortical columns implement canonical computations
- The function of the cortex arises from a hierarchical organization of such computations

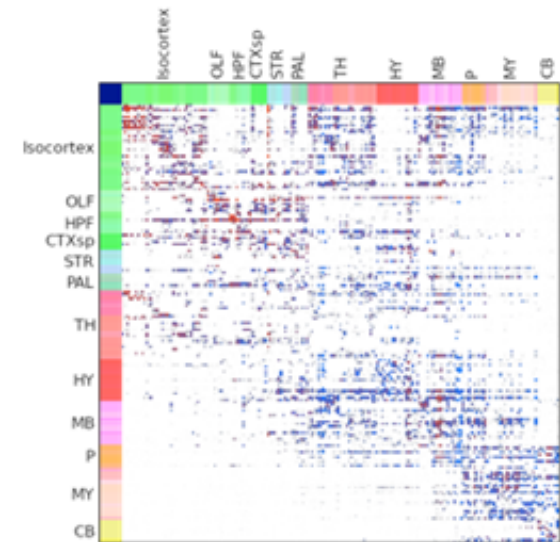
Constructing minimalistic models which reproduce a desired function



Single neuron activity

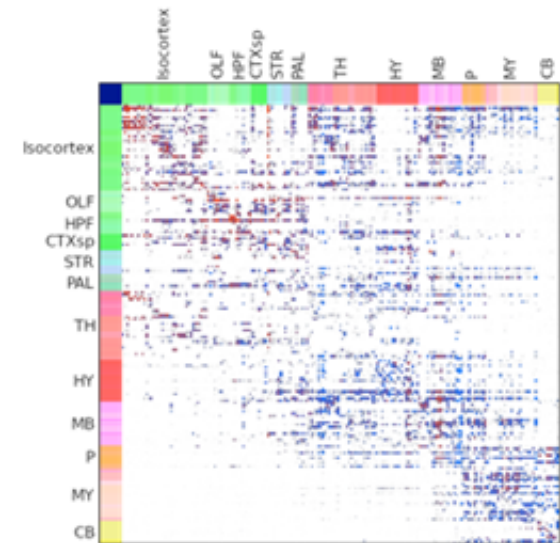
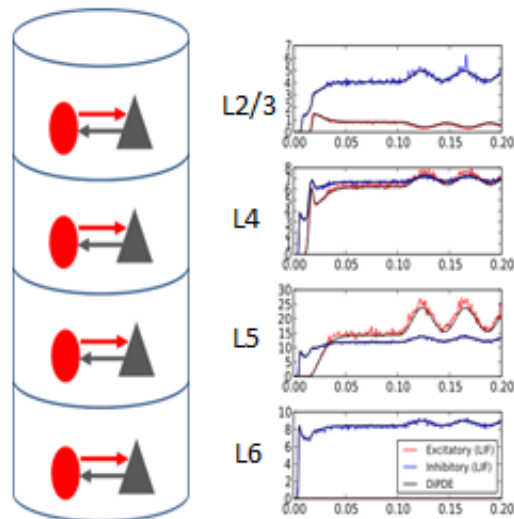
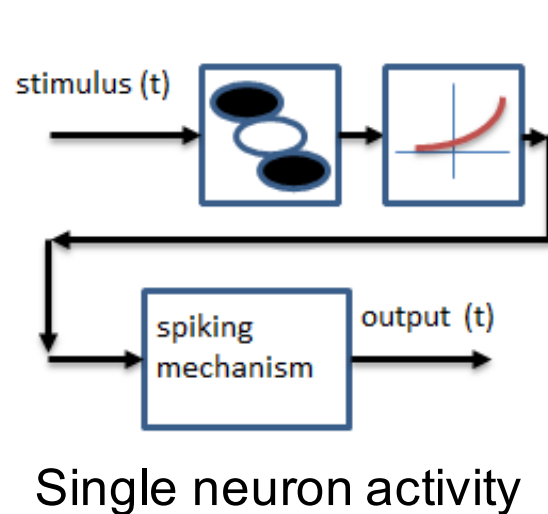


Activity in local circuits

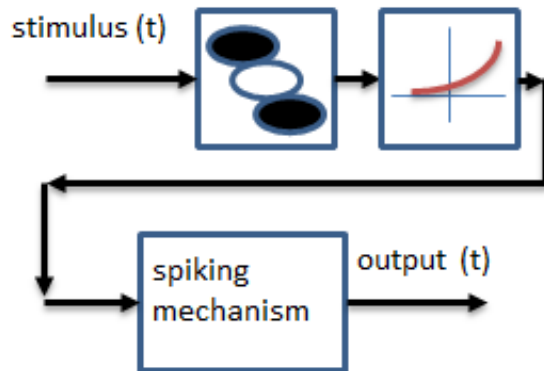
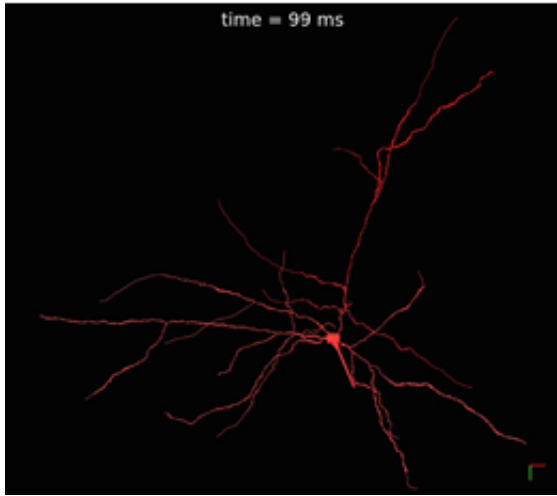


Mesoscopic models

Long term goal: Integrate models across scales into a model of cortical computation in the mouse visual system



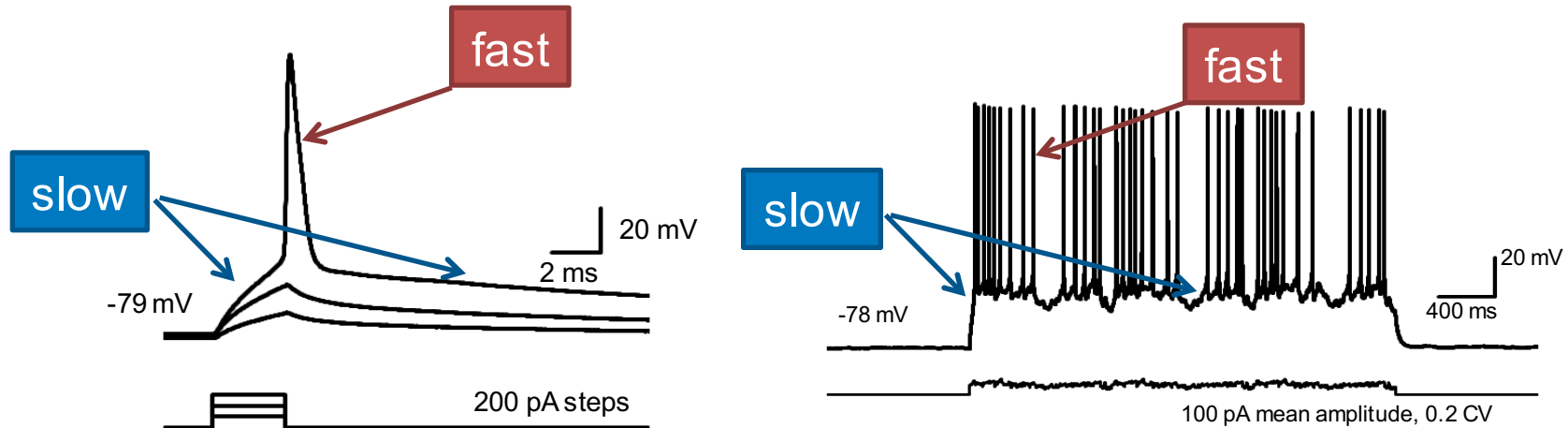
In Vitro single neuron models



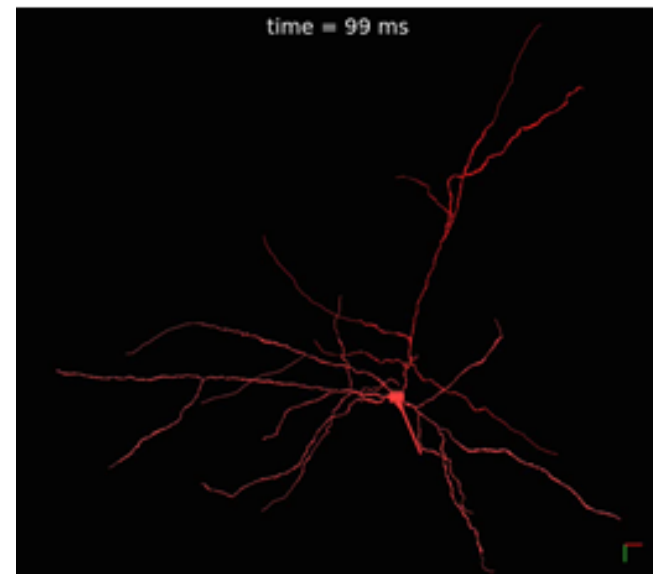
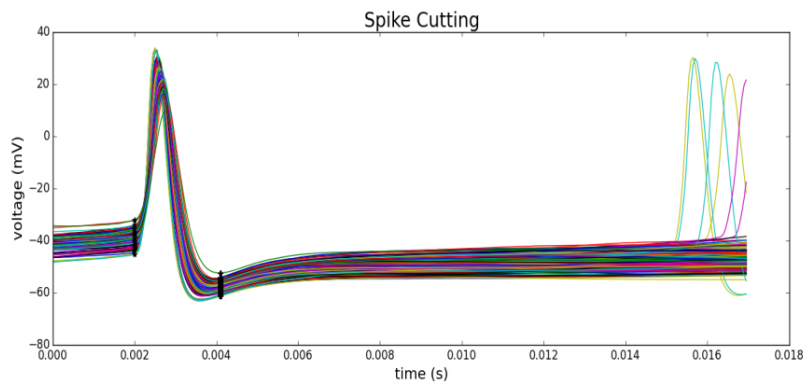
Single neuron activity

2. Why spiking models?

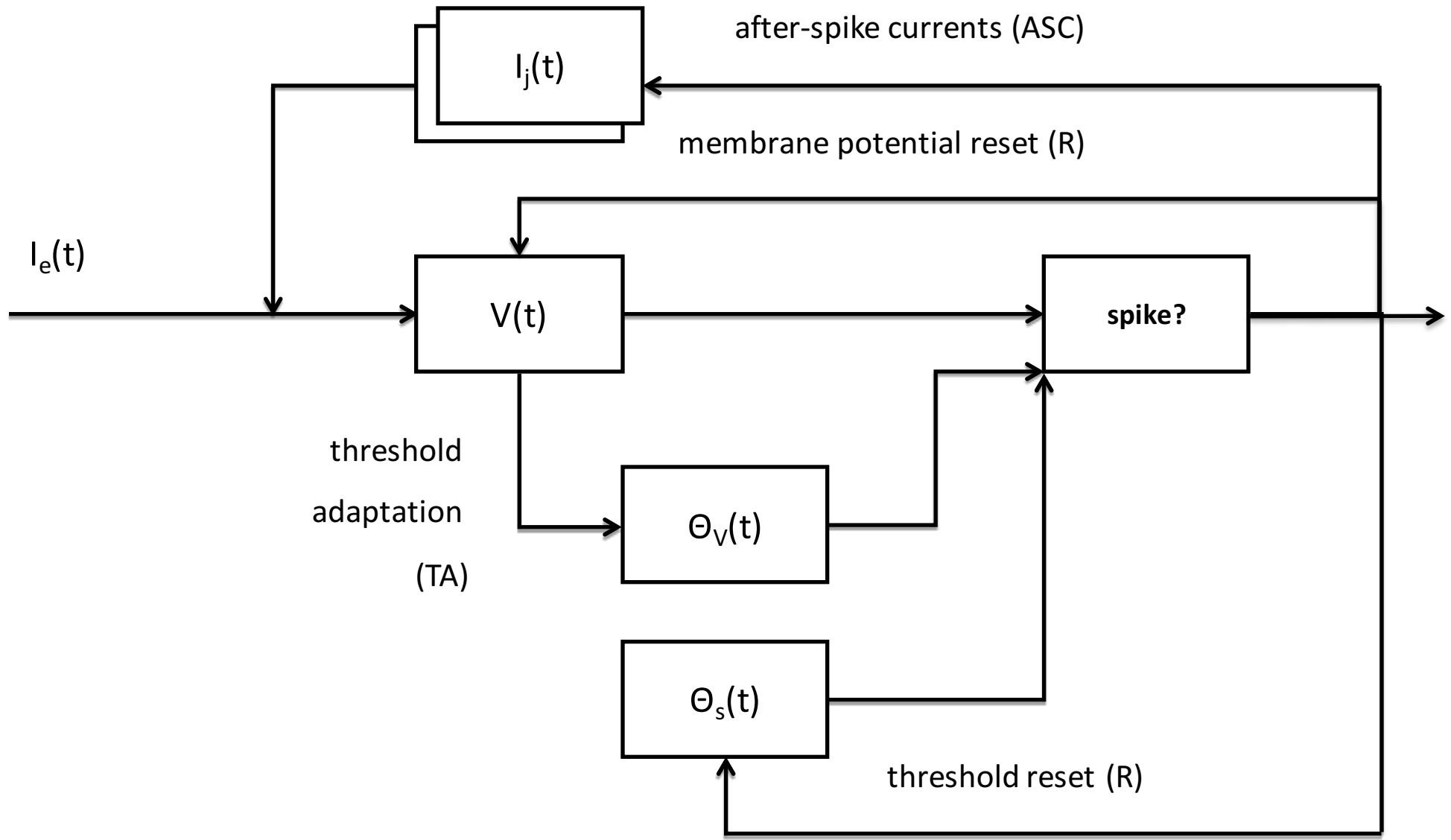
- Time scale separation of the subthreshold vs spiking dynamics



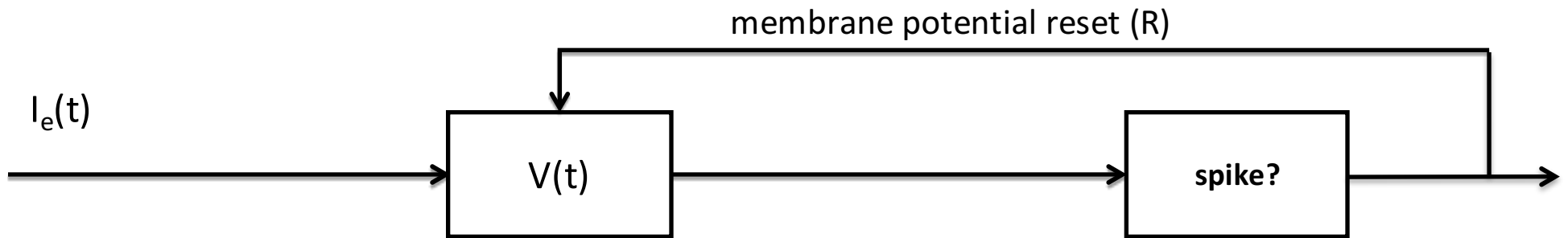
- Spikes are stereotyped



3. Generalized Leaky Integrate and Fire Models



Leaky Integrate and Fire Models

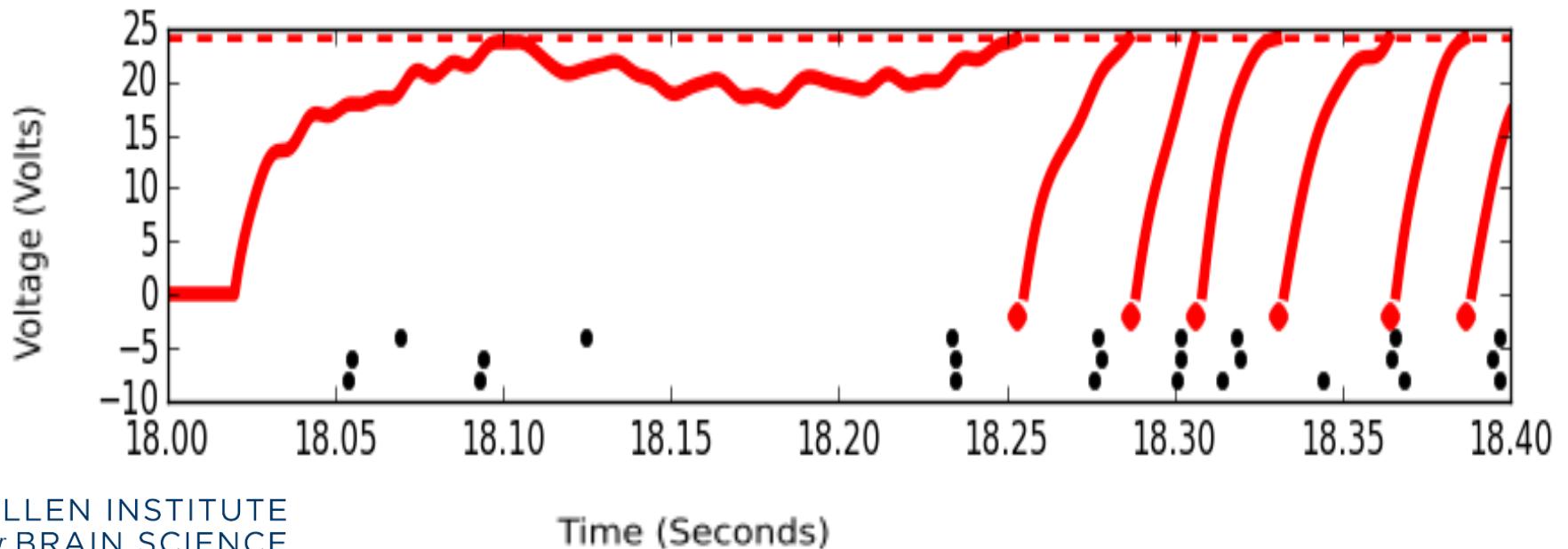


Dynamics: between spikes

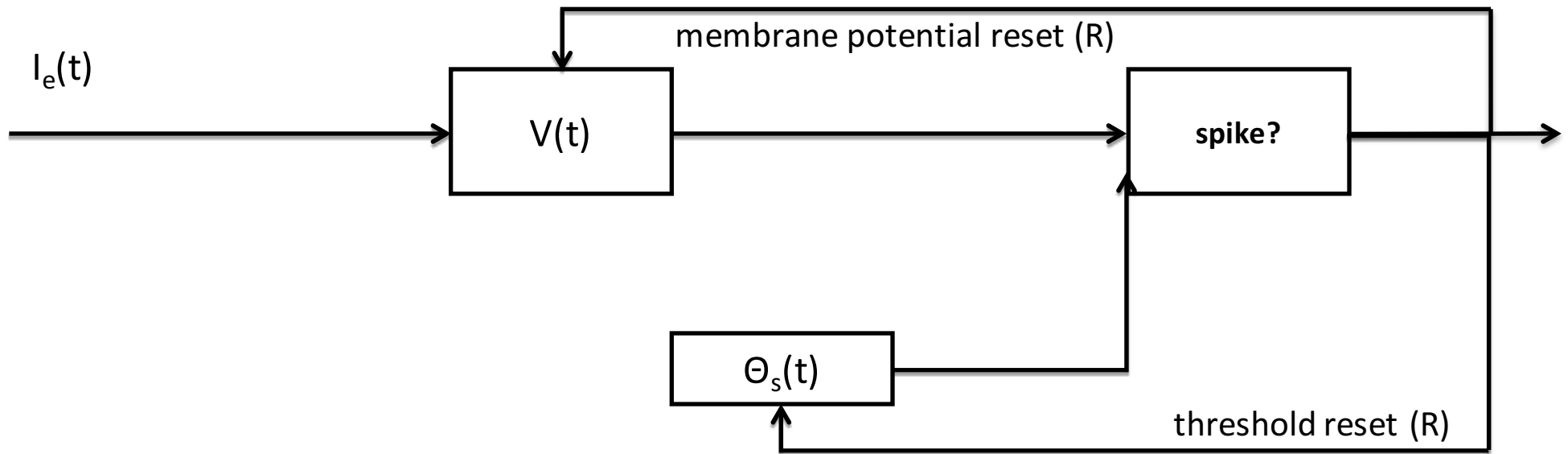
$$V'(t) = \frac{1}{C} (I_e(t) - G(V(t) - E_L))$$

Reset: if $V(t) > \Theta_\infty$

$$V(t) \leftarrow V_r$$



LIF with reset rules



Dynamics: between spikes

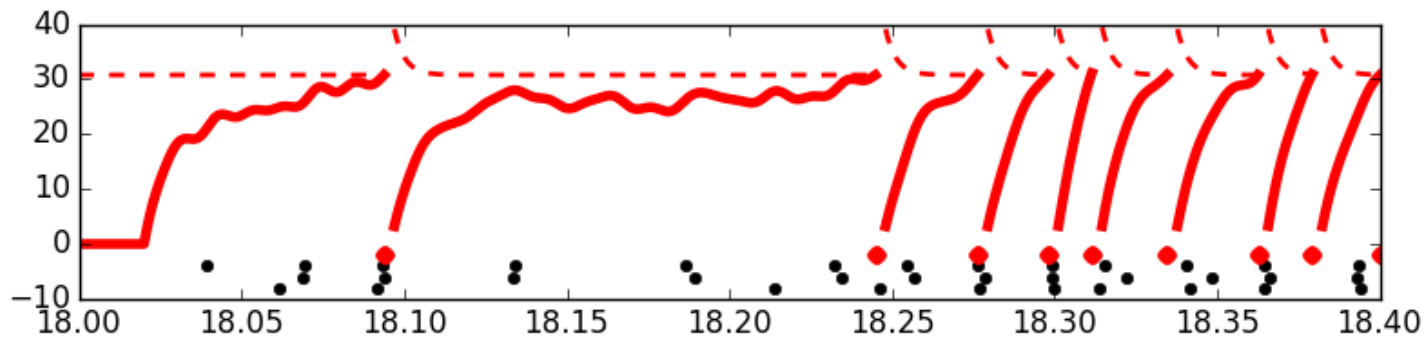
$$V'(t) = \frac{1}{C} \left(I_e + \sum_j I_j(t) - G(V(t) - E_L) \right)$$

$$\Theta_s'(t) = -b_s \Theta_s(t)$$

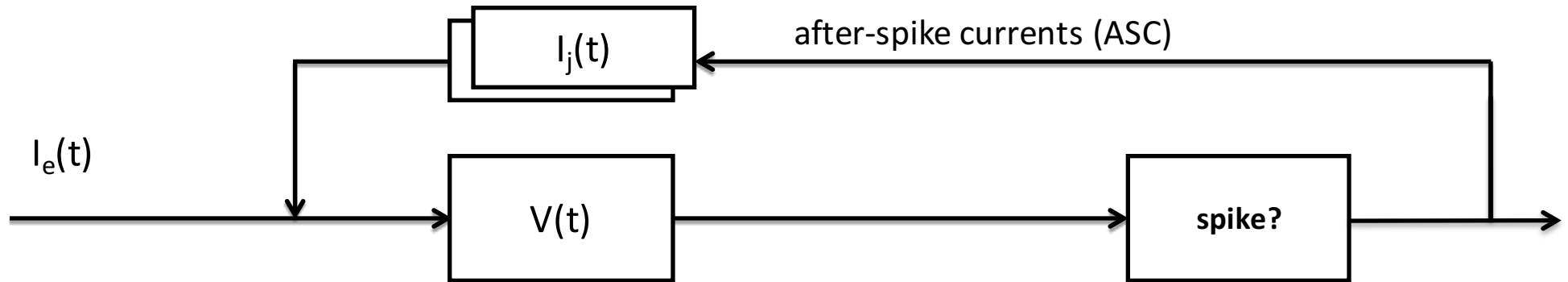
Reset: if $V(t) > \Theta_\infty + \Theta_s(t)$

$$V(t_+) \leftarrow E_L + f_v \times (V(t_-) - E_L) - \delta V$$

$$\Theta_s(t_+) \leftarrow \Theta_s(t_+) + \delta \Theta_s$$



LIF with after-spike currents - optimization



Dynamics: between spikes

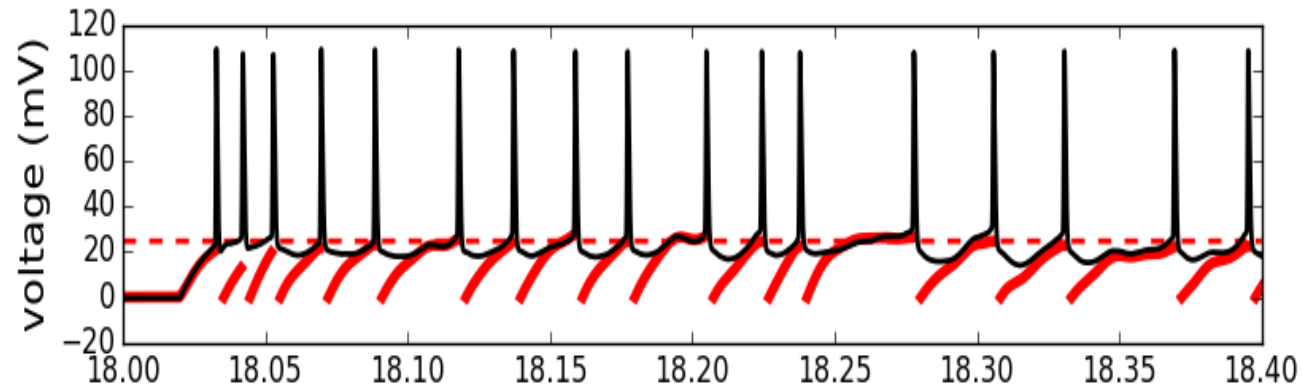
$$I'_j(t) = -k_j I_j(t); \quad j = 1, \dots, N$$

$$V'(t) = \frac{1}{C} \left(I_e(t) + \sum_j I_j(t) - G(V(t) - E_L) \right)$$

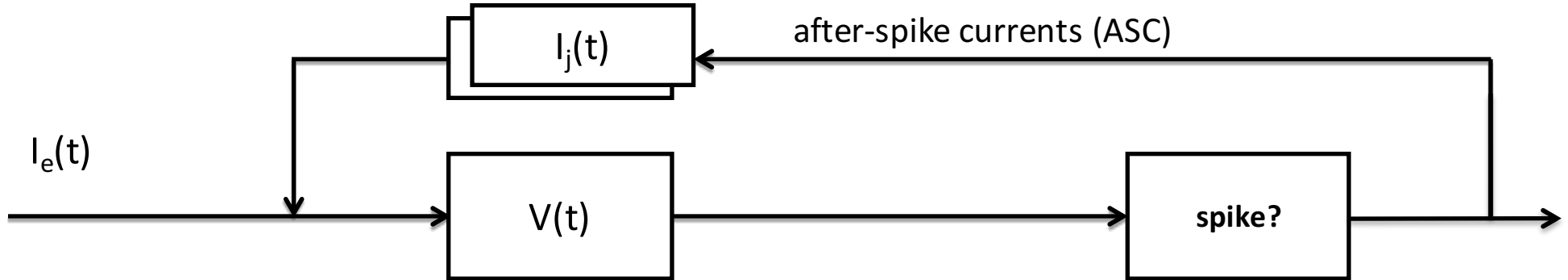
Reset: if $V(t) > \Theta_\infty$

$$I_j(t_+) \leftarrow R_j \times I_j(t_-) + A_j$$

$$V(t_+) \leftarrow V_r$$



LIF with after-spike currents



Dynamics: between spikes

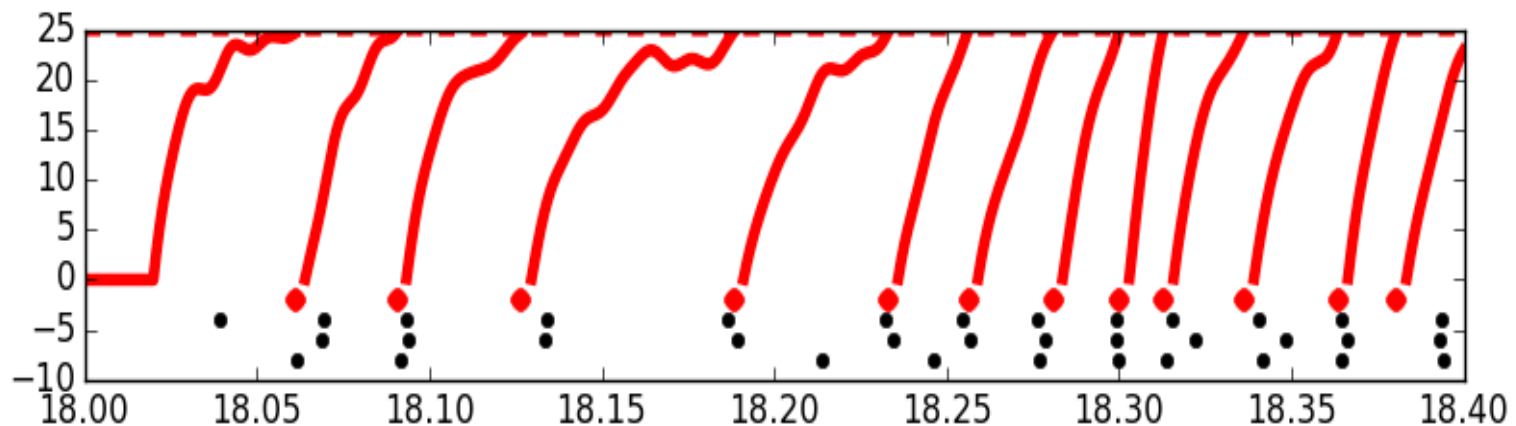
$$I'_j(t) = -k_j I_j(t); \quad j = 1, \dots, N$$

$$V'(t) = \frac{1}{C} \left(I_e(t) + \sum_j I_j(t) - G(V(t) - E_L) \right)$$

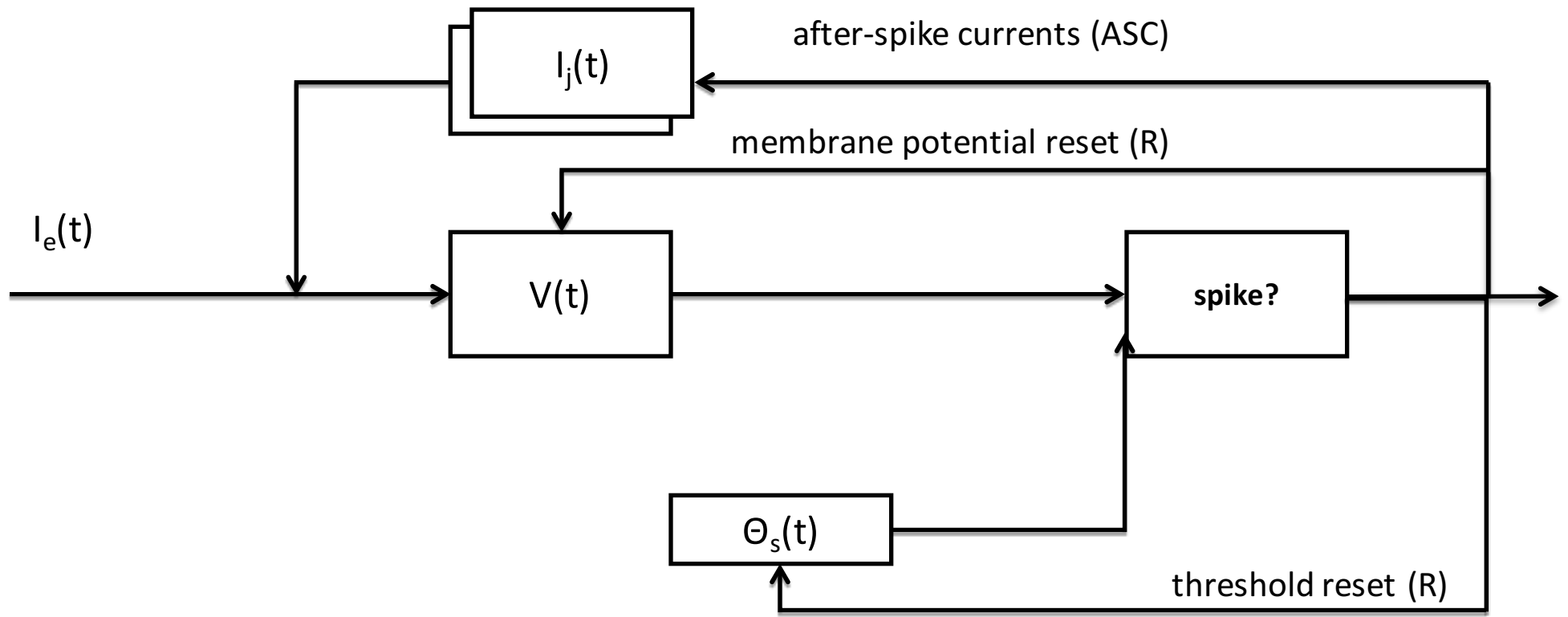
Reset: if $V(t) > \Theta_\infty$

$$I_j(t_+) \leftarrow R_j \times I_j(t_-) + A_j$$

$$V(t_+) \leftarrow V_r$$



LIF with after-spike currents and voltage dependent threshold



Dynamics: between spikes

$$I_j'(t) = -k_j I_j(t); \quad j = 1, \dots, N$$

$$V'(t) = \frac{1}{C} \left(I_e(t) + \sum_j I_j(t) - G(V(t) - E_L) \right)$$

$$\Theta_s'(t) = -b_s \Theta_s(t)$$

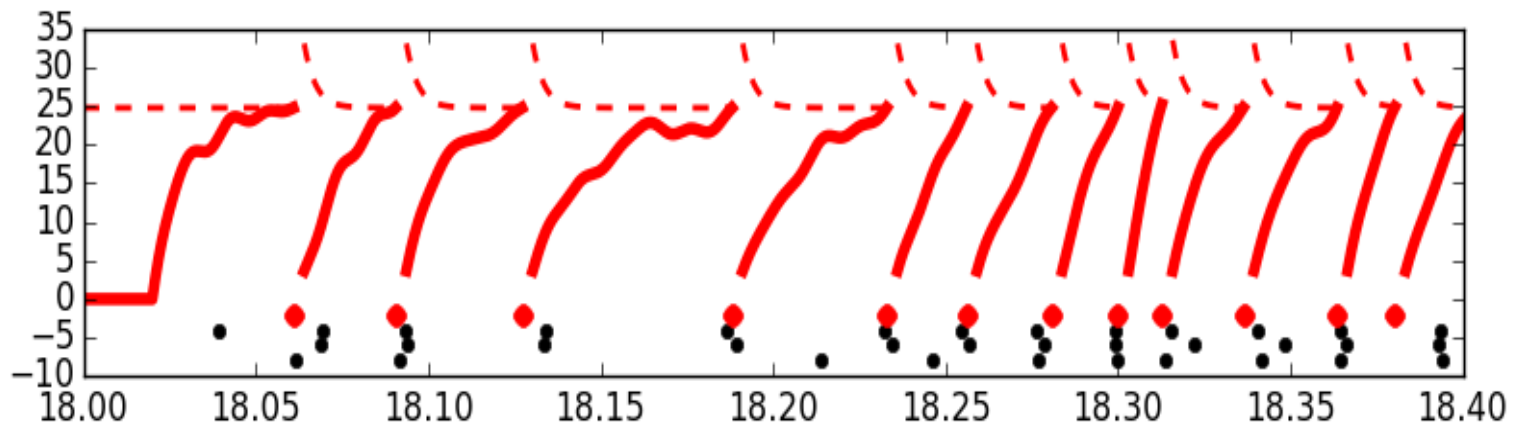
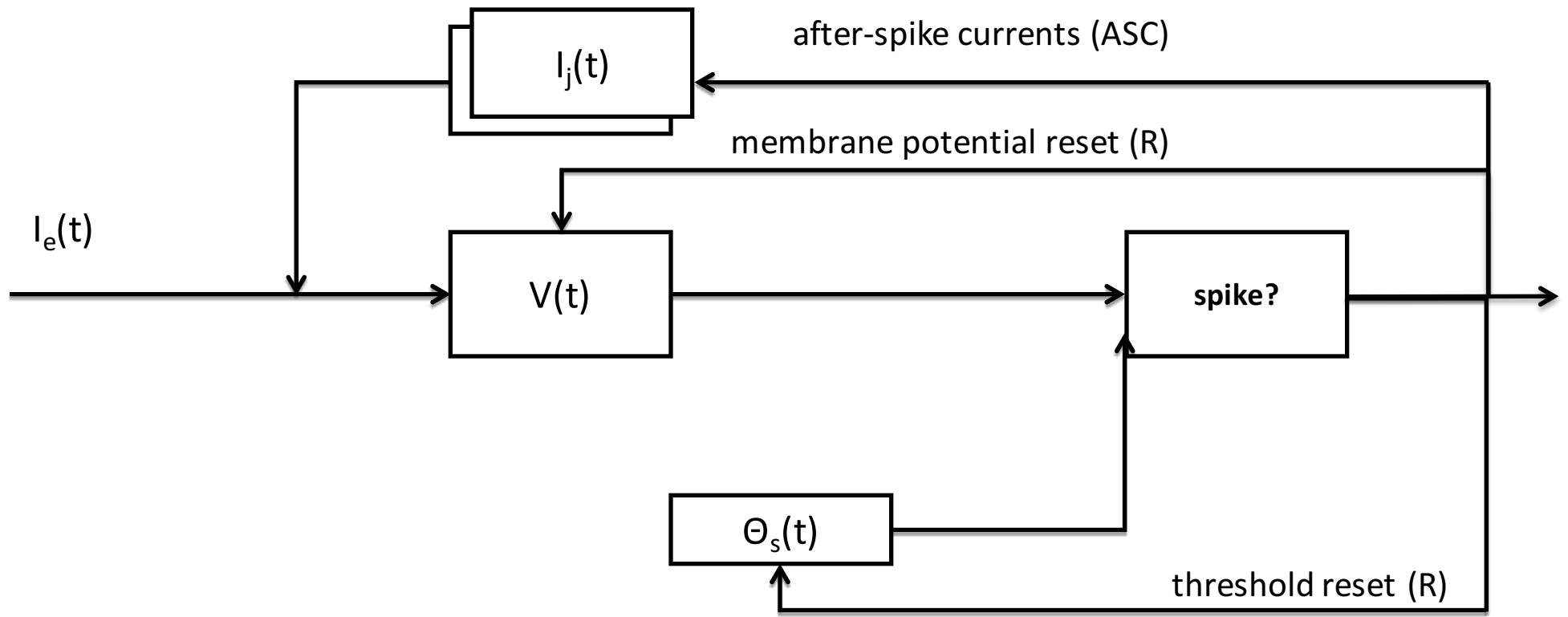
Reset: if $V(t) > \Theta_\infty + \Theta_s(t)$

$$I_j(t_+) \leftarrow f_j \times I_j(t_-) + \delta I_j$$

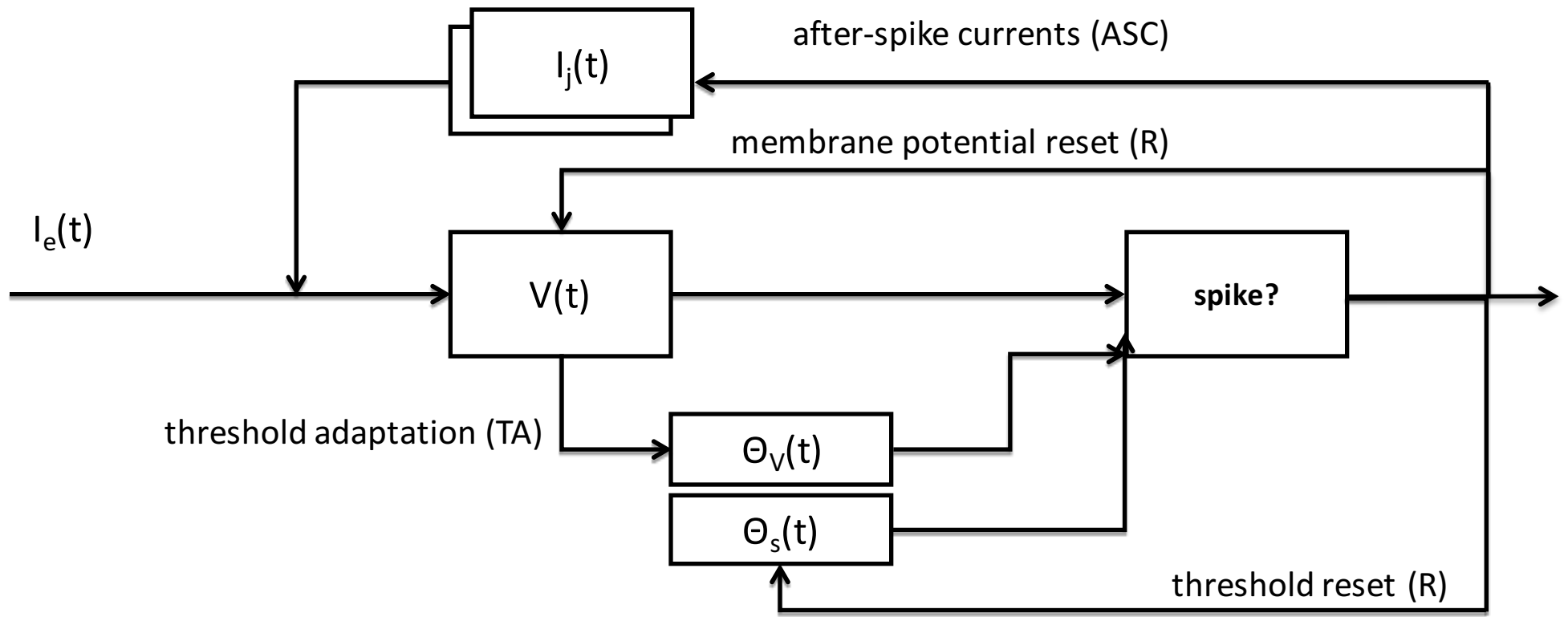
$$V(t_+) \leftarrow E_L + f_v \times (V(t_-) - E_L) - \delta V$$

$$\Theta_s(t_+) \leftarrow \Theta_s(t_-) + \delta \Theta_s$$

LIF with after-spike currents and voltage dependent threshold



LIF with after-spike currents spiking and voltage dependent threshold



Dynamics: between spikes

$$I_j'(t) = -k_j I_j(t); \quad j = 1, \dots, N$$

$$V'(t) = \frac{1}{C} \left(I_e(t) + \sum_j I_j(t) - G(V(t) - E_L) \right)$$

$$\Theta_s'(t) = -b_s \Theta_s(t)$$

$$\Theta_v'(t) = a(V(t) - E_L) - b_v(\Theta_v(t) - \Theta_\infty)$$

Reset: if $V(t) > \Theta_v(t) + \Theta_s(t)$

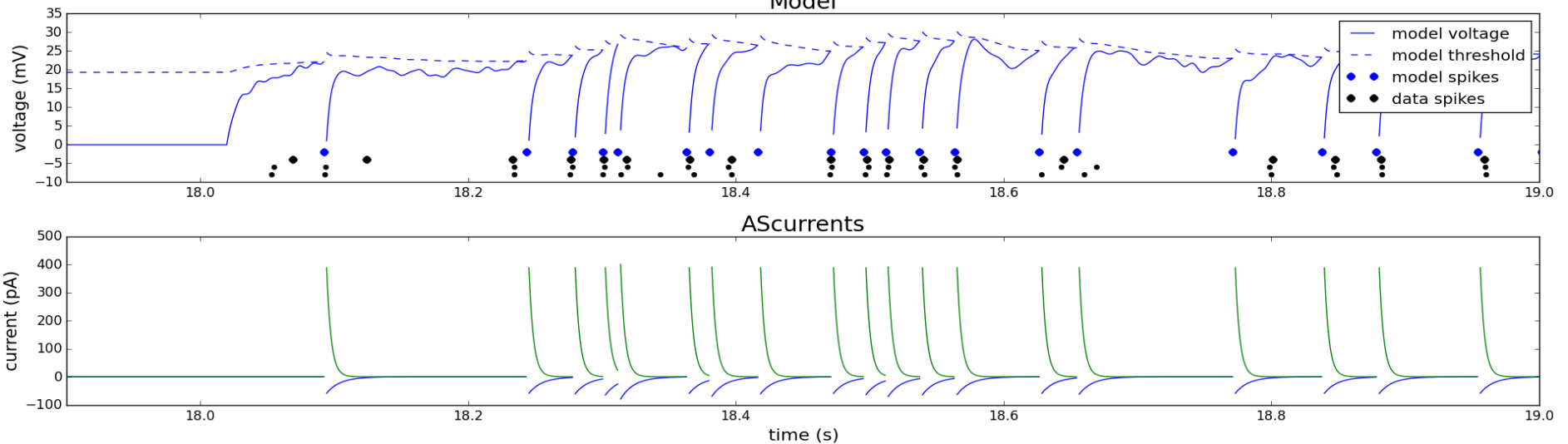
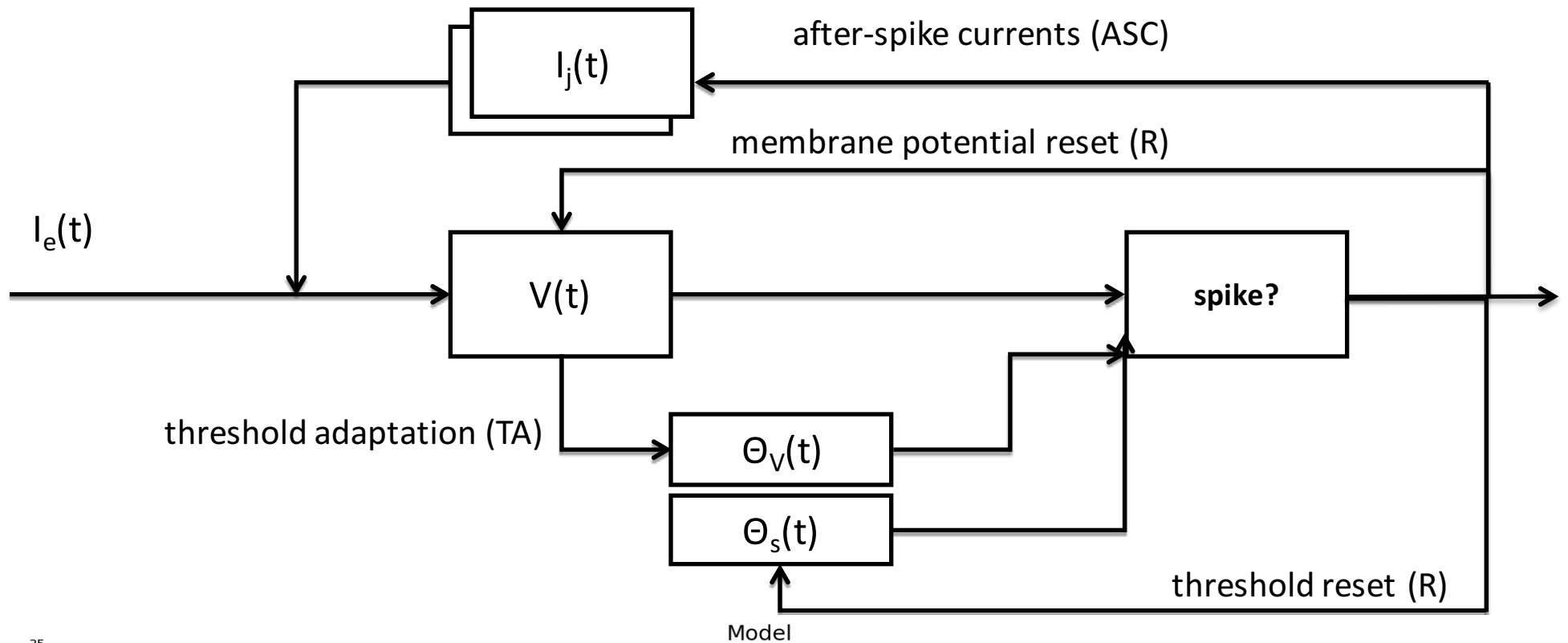
$$I_j(t_+) \leftarrow f_j \times I_j(t_-) + \delta I_j$$

$$V(t_+) \leftarrow E_L + f_v \times (V(t_-) - E_L) - \delta V$$

$$\Theta_s(t_+) \leftarrow \Theta_s(t_+) + \delta \Theta_s$$

$$\Theta_v(t_+) \leftarrow \Theta_v(t_-)$$

LIF with after-spike currents spiking and voltage dependent threshold



4. Allen Cell Types Database

ALLEN BRAIN ATLAS
DATA PORTAL

HOME GET STARTED HELP **CELL TYPES** ▾

SEARCH... 🔍

DATA DOWNLOAD DOCUMENTATION HELP

Filters ?

Mouse Line
[All Lines]

Layer
[All Layers] ▾

Hemisphere
Left Right Either

Sort By
Upstroke:Downstroke ▾

More Options +

Reset Filters

View Mode
 Electrophysiology
 Electrophysiology + Morphology

Showing 49 of 248 cells

Cell Location

Sonn1a-Tg2-Cre
VISp
Layer 4

1mm

Pia

White Matter

Cell Summaries Permalink

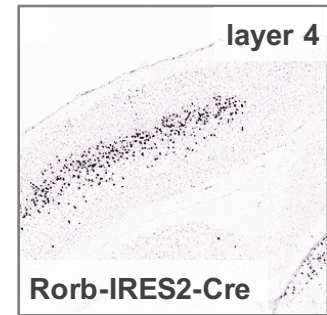
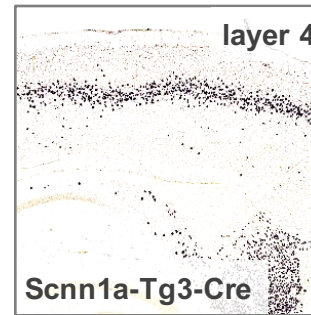
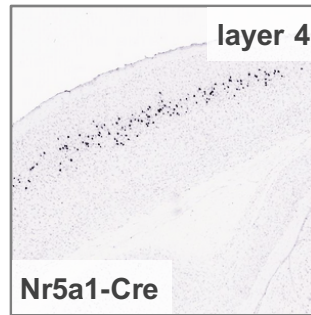
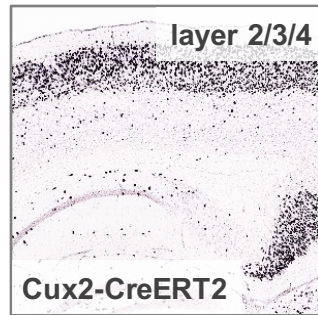
<input type="checkbox"/>	Cre Line: Scnn1a-Tg2-Cre	Upstroke:Downstroke: 5.95		
	Area: VISp	Fast AP Trough (mV): -49.28		
	Layer: 4	FI Curve Slope: 0.15		
	Hemisphere: right	Rheobase (pA): 190.00		
	Dendrite Type: spiny	Ramp AP Time (s): 2.55		
	Apical Dendrite: intact	Resting Vm (mv): -63.57		
<input type="checkbox"/>	Cre Line: Scnn1a-Tg2-Cre	Upstroke:Downstroke: 4.43		
	Area: VISp	Fast AP Trough (mV): -49.72		
	Layer: 4	FI Curve Slope: 0.22		
	Hemisphere: right	Rheobase (pA): 70.00		
	Dendrite Type: spiny	Ramp AP Time (s): 3.11		
	Apical Dendrite: intact	Resting Vm (mv): -79.30		
<input type="checkbox"/>	Cre Line: Rbp4-Cre_KL100	Upstroke:Downstroke: 4.43		
	Area: VISp	Fast AP Trough (mV): -41.56		
	Layer: 6a	FI Curve Slope: 0.09		
	Hemisphere: left	Rheobase (pA): 130.00		
	Dendrite Type: spiny	Ramp AP Time (s): 4.47		
	Apical Dendrite: intact	Resting Vm (mv): -72.24		
<input type="checkbox"/>	Cre Line: Nr5a1-Cre	Upstroke:Downstroke: 4.18		
	Area: VISpm	Fast AP Trough (mV): -47.66		
	Layer: 4	FI Curve Slope: 0.05		
	Hemisphere: right	Rheobase (pA): 150.00		
	Dendrite Type: spiny	Ramp AP Time (s): 6.48		

Search and Filter Options

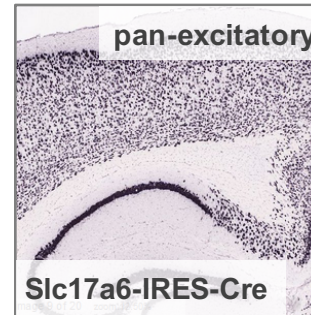
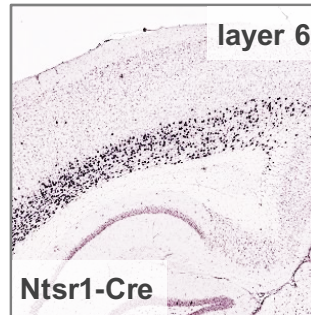
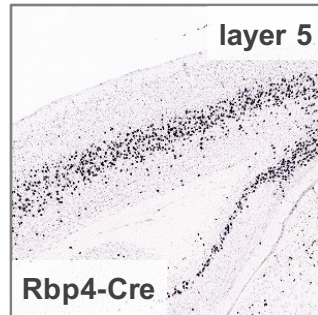
Cell Positions in Common Coordinate Framework

Summary of Cell Characteristics
(Click for additional details)

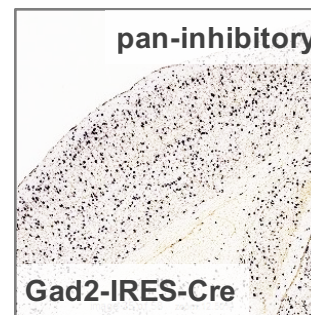
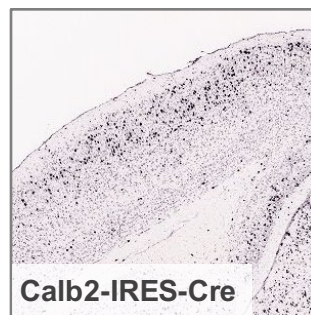
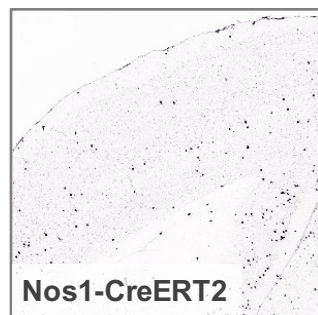
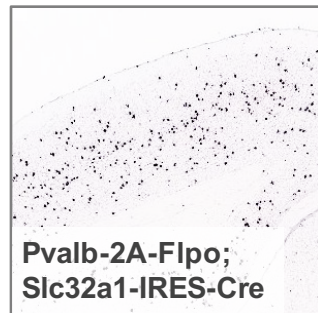
Excitatory neurons



Genetic Markers via Cre Lines



Inhibitory neurons



Electrophysiology Protocol

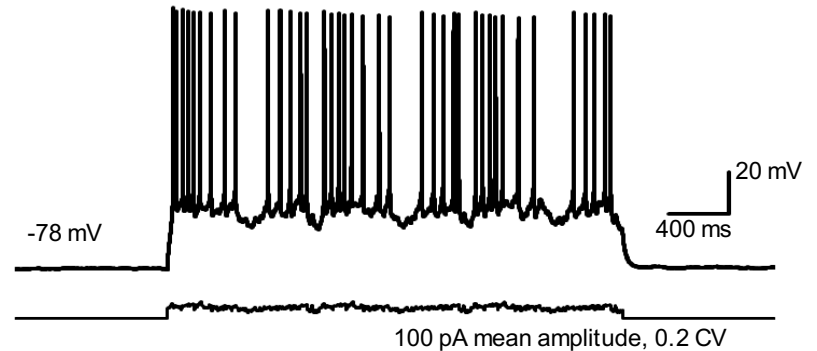
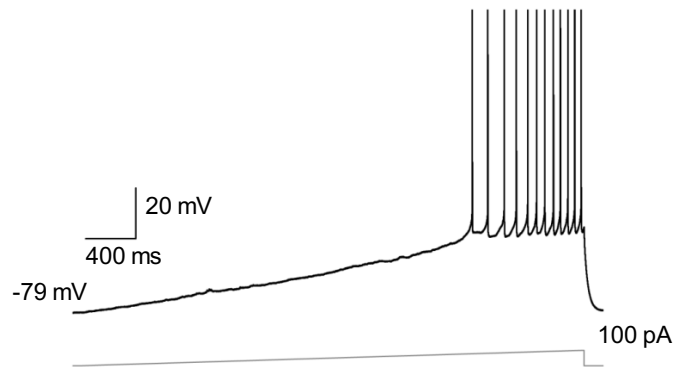
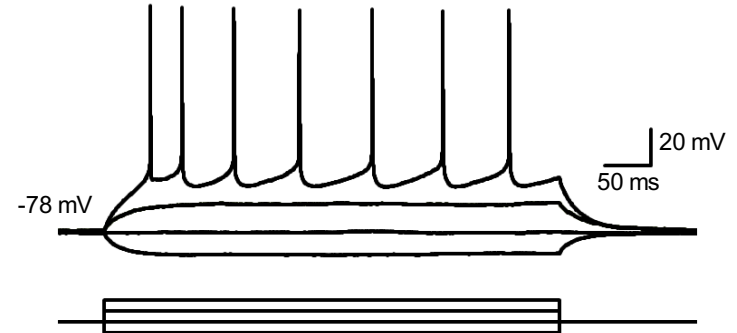
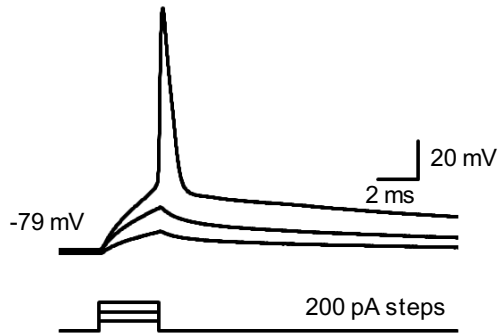


Instantaneous threshold

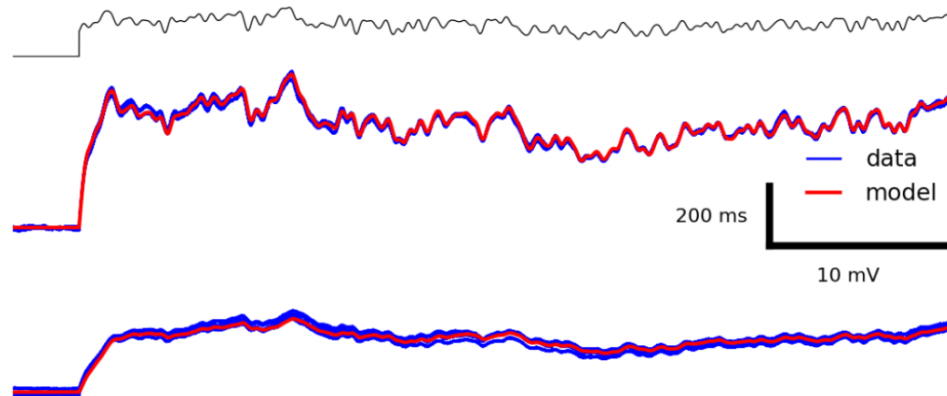
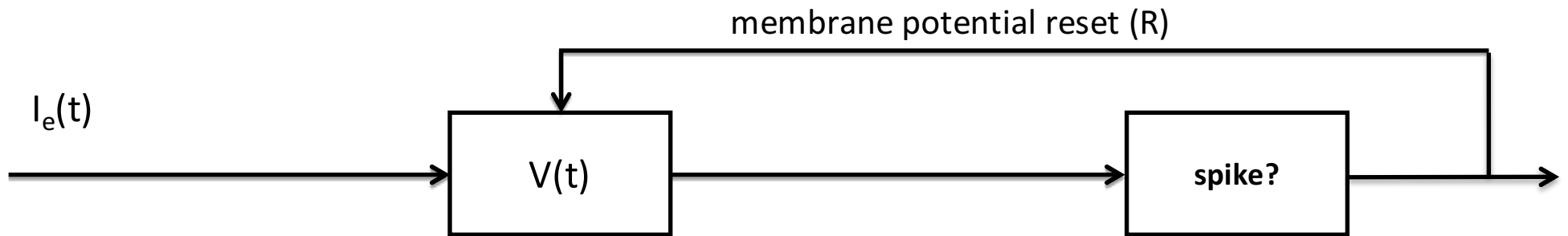
Adaptive threshold

Subthreshold, Rheobase & Suprathreshold

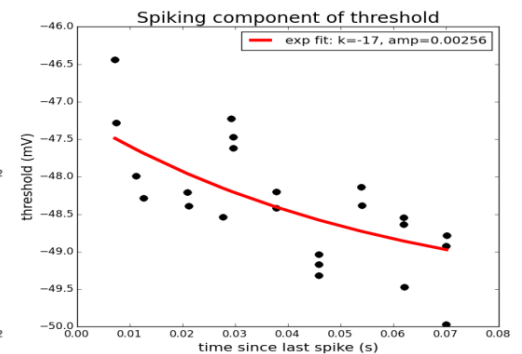
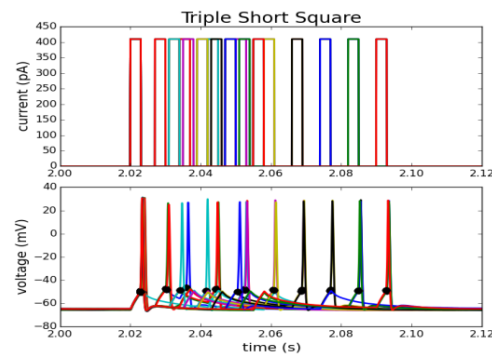
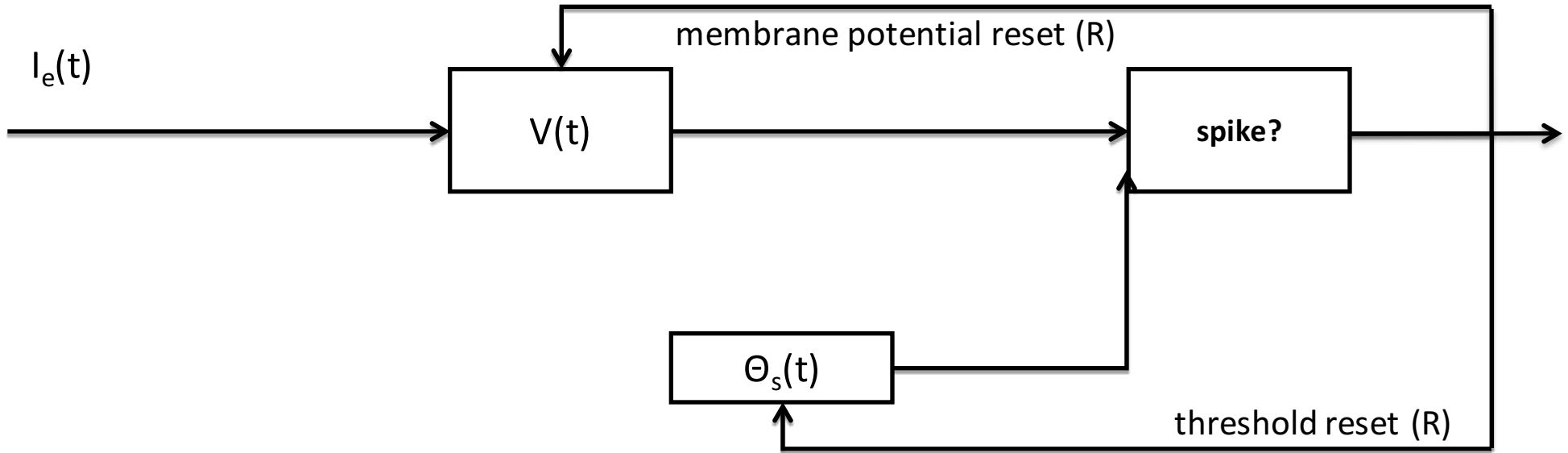
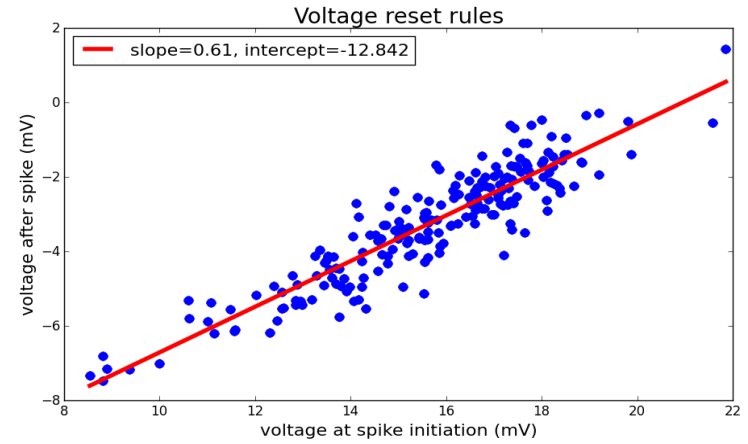
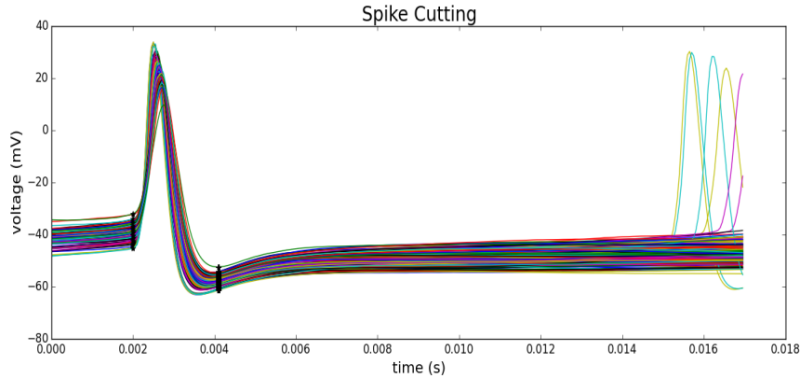
Naturalistic response



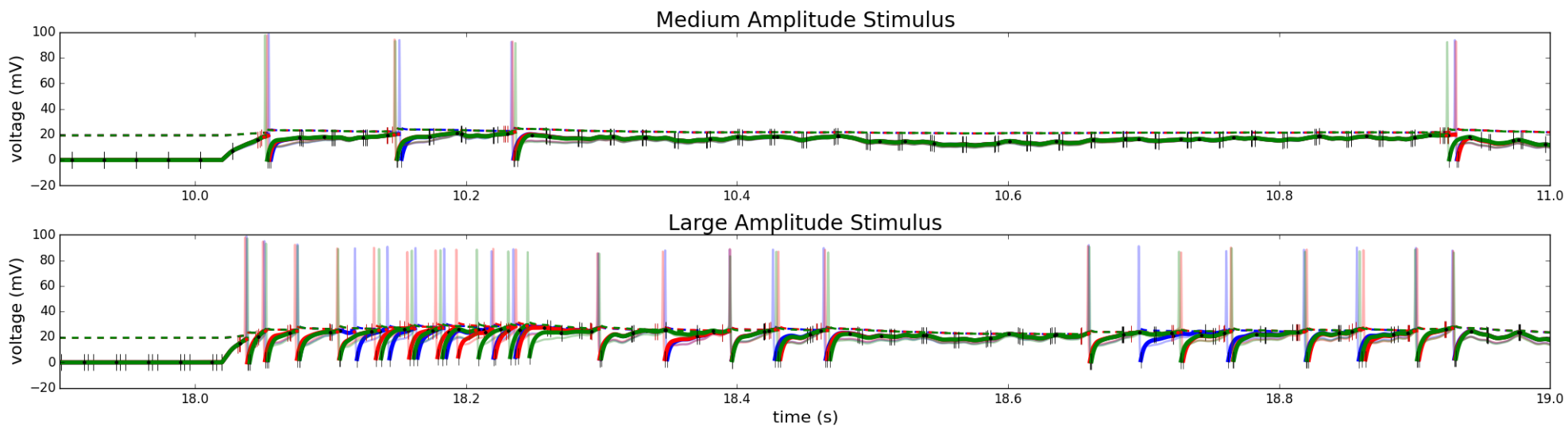
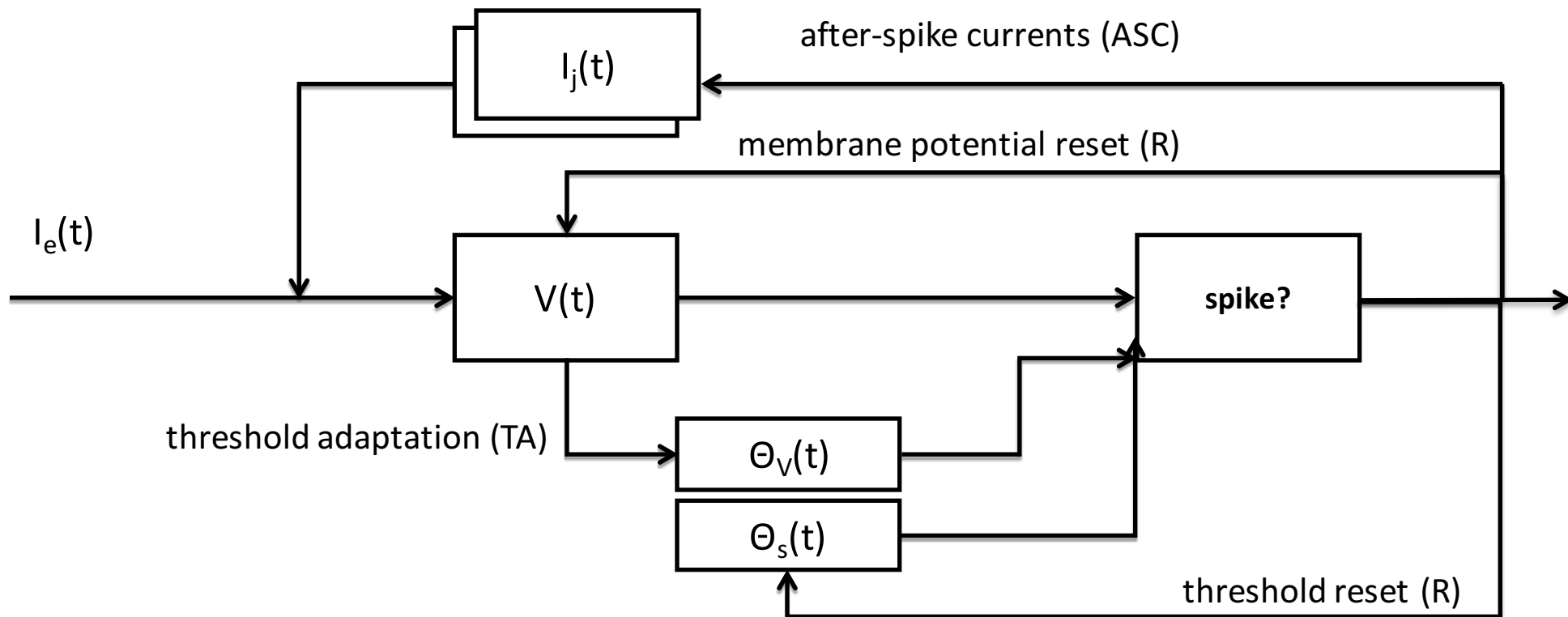
Leaky Integrate and Fire Models - optimization



LIF with reset rules - optimization

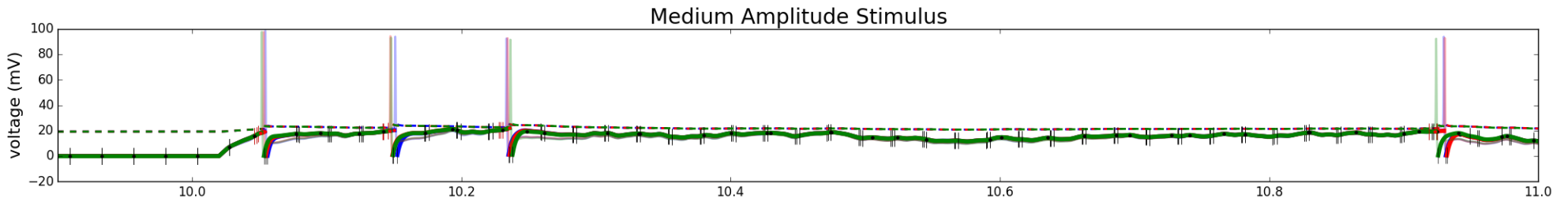


LIF R ASC AT - optimization



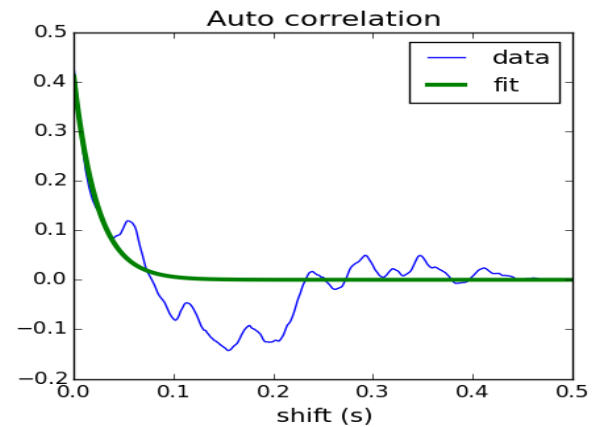
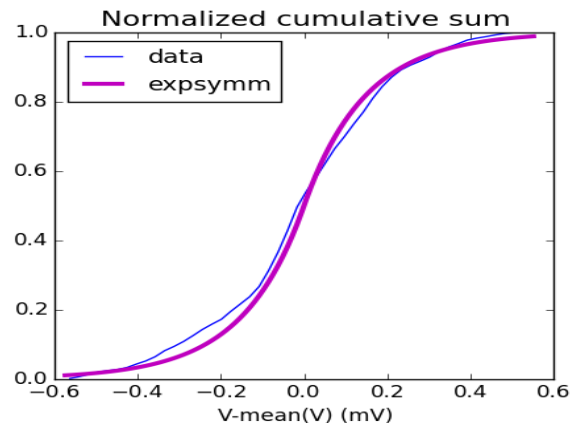
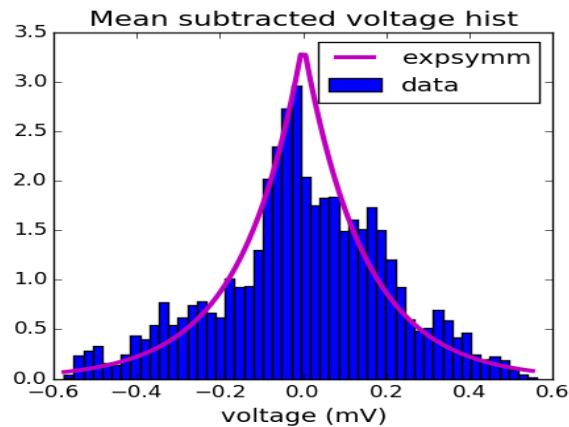
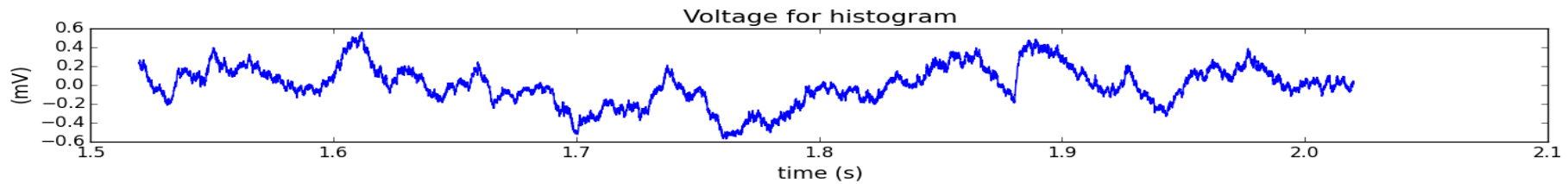
LIF R ASC AT – optimization

Maximum likelihood based on internal noise (MLIN)

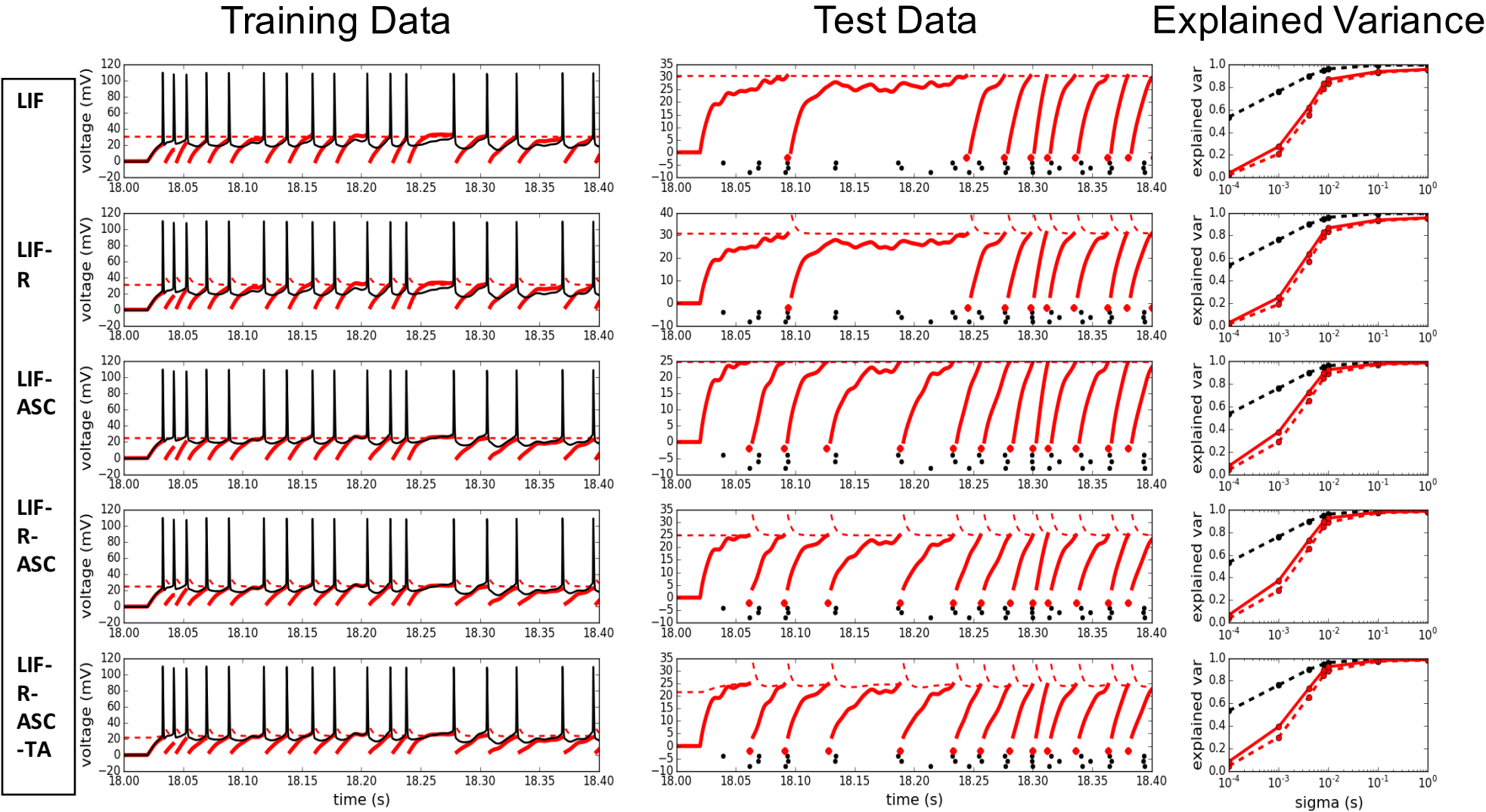


$$p_{spike}(t) = \int_{\Delta V(t)}^{\infty} p(v)dv = \int_{\Delta V(t)}^{\infty} \frac{1}{2\delta v} \exp\left(-\frac{|v|}{\delta v}\right) dv = 1 - c(\Delta V(t)) \quad p_{spikes} = \prod_{t \in t_s} p_{spike}(t)$$

$$LLIN = \text{Log}(p_{spikes} p_{nospike}) = \sum_{t \in t_s} (1 - c(\Delta V(t))) + \sum_{t \in t_{grid}} c(\Delta V_{grid})$$



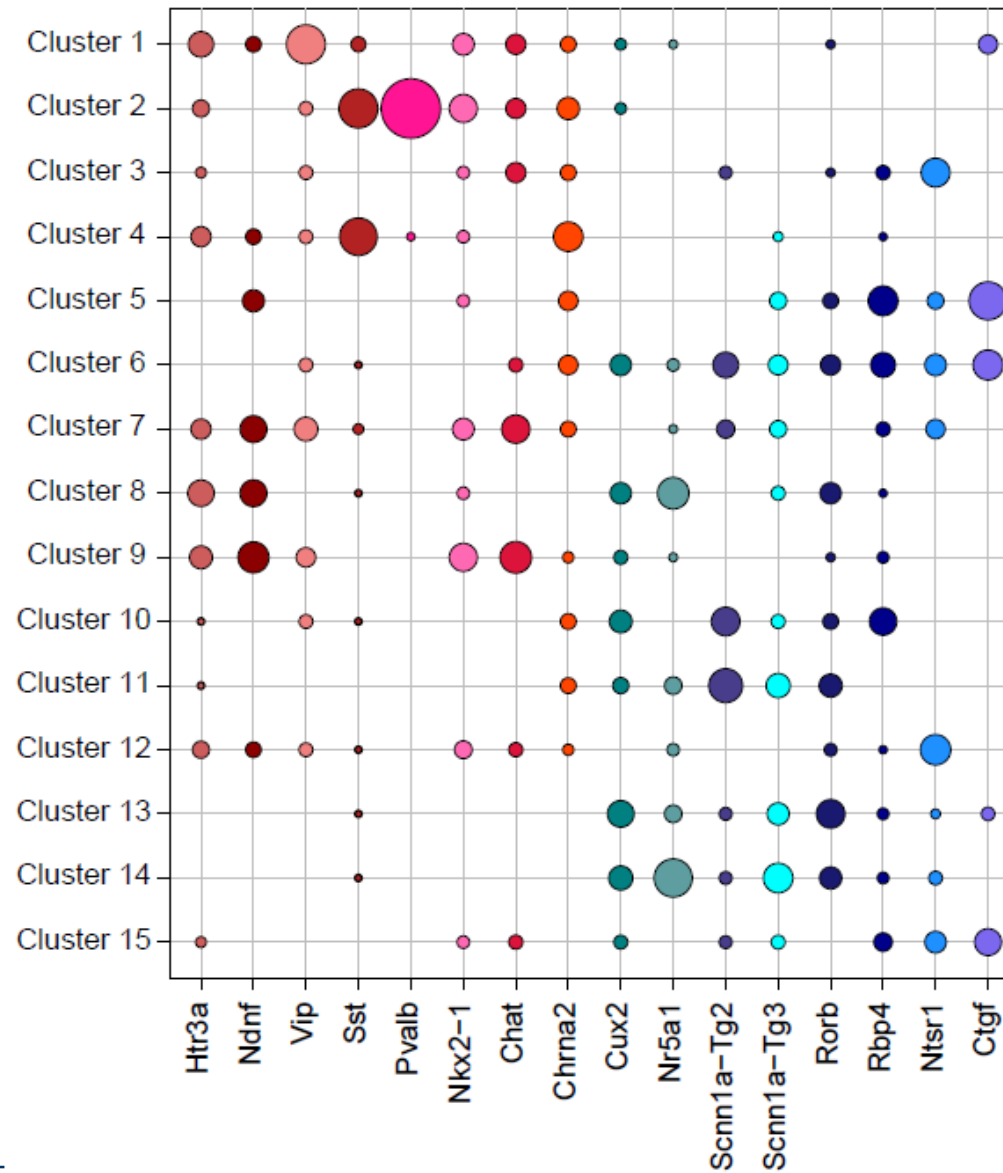
Generalized Leaky Integrate and Fire Models



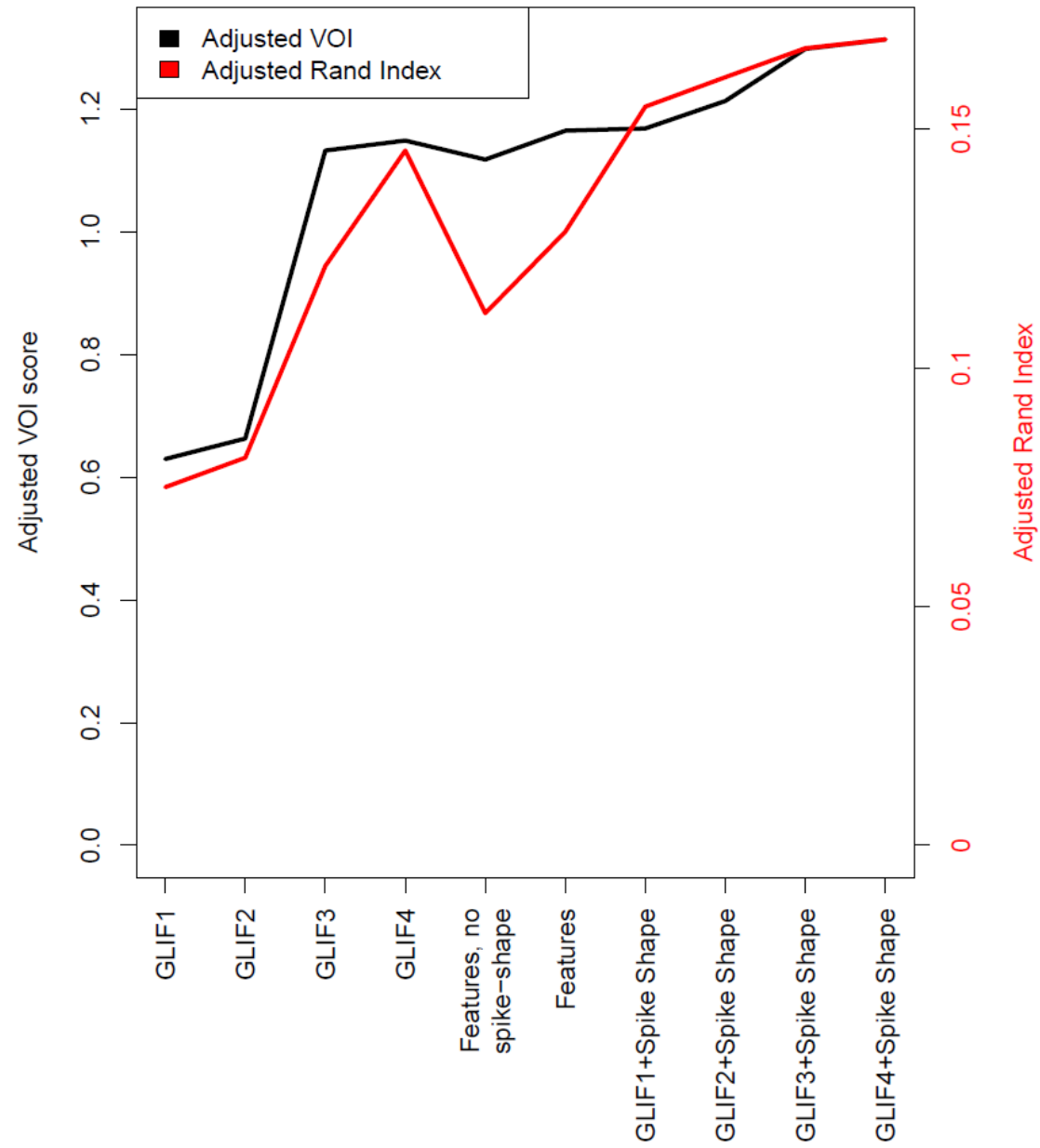
Average explained variance

- Glif 5: 75% - excitatory 84% for inhibitory
- Biophysical perisomatic – 65%
- Biophysical all-active – 69%

Defining cell types based on models



Comparison between model/feature clusters and Cre line partitioning



Single Cell Type Models Conclusion

- A large diversity of neurons can be characterized and modeled
- GLIF models still outperform detailed biophysical ones due to individual recording length limitation
- Parameters in GLIF models can be used to classify cell types
- visit our website: <http://www.brain-map.org/>