A CORTICAL MICROCIRCUIT MODEL FOR STUDYING THE ROLES OF INTERNEURON SUBTYPES

September 21, 2022 | Han-Jia Jiang, Sacha J. van Albada | Jülich Research Centre

OUTLINE

Introduction

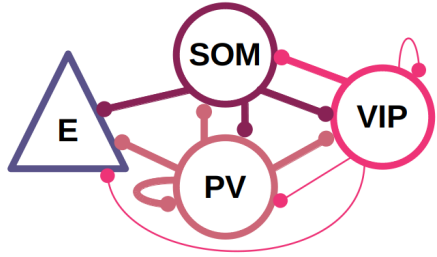
Model parameters

Simulation Results

Discussion

INTRODUCTION

- Major subtypes of inhibitory interneurons in the neocortex, PV, SOM, and VIP cells, have distinct properties in
  - Cell electrophysiology
  - Connectivity
  - Synaptic short-term plasticity (STP)
- We established a microcircuit model for the computational study of their roles in network dynamics and sensory signal processing



Interneurons and their projections in L2/3 of neocortex
PV: parvalbumin-expressing cell
SOM: somatostatin-expressing cell
VIP: vasoactive intestinal peptide-expressing cell

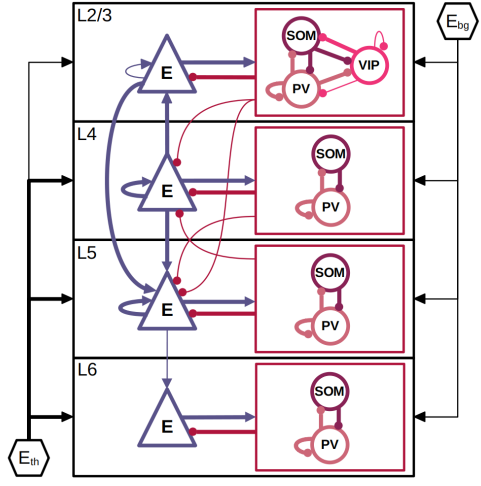
OUTLINE

MODEL OVERVIEW

- Adapted from Potjans & Diesmann (2014)
- Uses LIF neurons (N=6448) with current-based synapses
- Simulates a mouse barrel column ($200 \times 300 \times 1026$ μm)

	E	PV	SOM	VIP
L2/3	1691	90	74	85
L4	1656	85	48	-
L5	1095	109	105	-
L6	1288	56	66	-

(Lefort et al., 2009; Lee et al., 2010)



MODEL PARAMETERS

- Neuronal and synaptic parameters

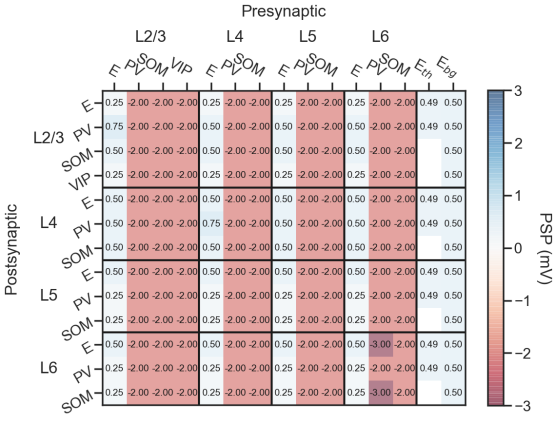
Parameter	Definition	L2/3, L4 E	L2/3, L4 PV	L2/3, L4 SOM	VIP	L5, L6 E	L5, L6 PV	L5, L6 SOM
τ_m	membrane time constant (ms)	5.16	2.95	11.22	10.37	5.94	3.8	11.13
C_m	membrane capacity (pF)	229.8	93.9	123.3	86.5	269.2	81.0	146.8
V_{rest}	resting membrane potential (mV)	-67.4	-66.4	-59.9	-65.7	-63.2	-67.1	-63.2
V_{th}	firing threshold (mV)	-41.5	-41.6	-41.8	-43.7	-45.2	-42.3	-48.1

Parameter	Definition	Value
$\tau_{syn,E}$	excitatory synaptic time constant	2.0 ms
$\tau_{syn,I}$	inhibitory synaptic time constant	4.0 ms
d_E	synaptic delays of recurrent excitatory connections	1.36±0.51 ms
d_I	synaptic delays of recurrent inhibitory connections	1.43±1.09 ms
d_{th}	synaptic delays of thalamic inputs	1.72±0.73 ms

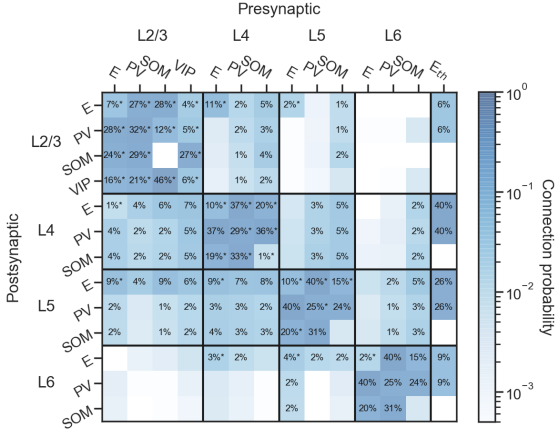
(Neske et al., 2015; Watson et al., 2008; Feldmeyer et al., 2002; Ma et al., 2012; Jouhanneau et al., 2018; Bruno & Sakmann, 2006)

MODEL PARAMETERS

- Synaptic weights (postsynaptic potentials)

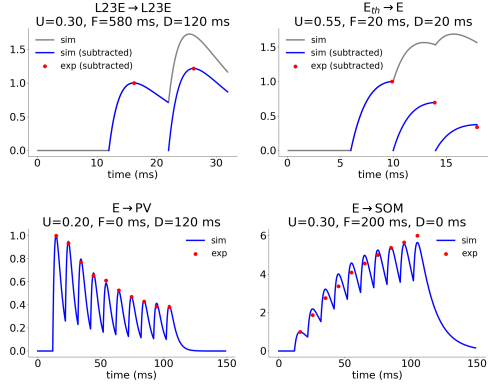


- Connection probability

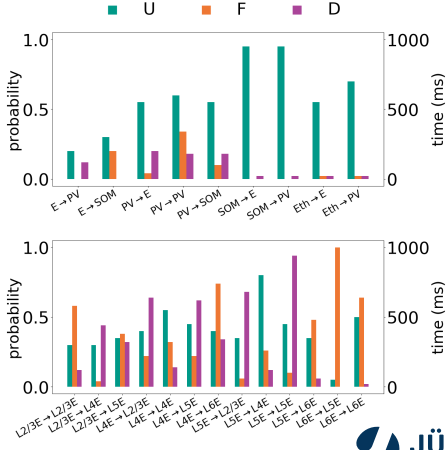


MODEL PARAMETERS

- Fitting of synaptic STP (Tsodyks et al., 2000)

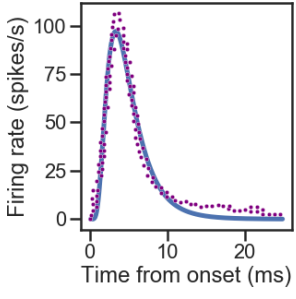


- Fitted STP parameters
  U: Release probability
  F: Facilitation time constant
  D: Depression time constant



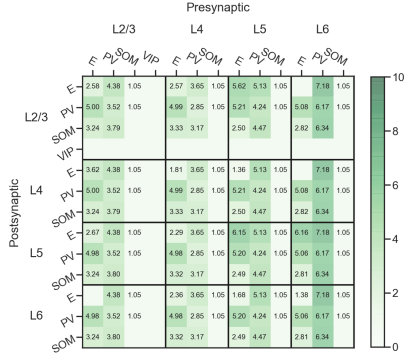
MODEL PARAMETERS

- Transient thalamic input (E_{th})
  - Excitatory cells (N=200), time courses and weights (0.49±0.13 mV) according to *in vivo* data



Fitted time course of *in vivo* thalamic firings induced by whisker touch (Yu et al., 2019)

- Background input (E_{bg}) of [E, PV, SOM, VIP] = [5000, 6600, 2500(2300), 3400] spikes/s, weight = 0.5 mV, Poissonian
- Synaptic weights of STP model are scaled to optimize steady state weights



OUTLINE

Introduction

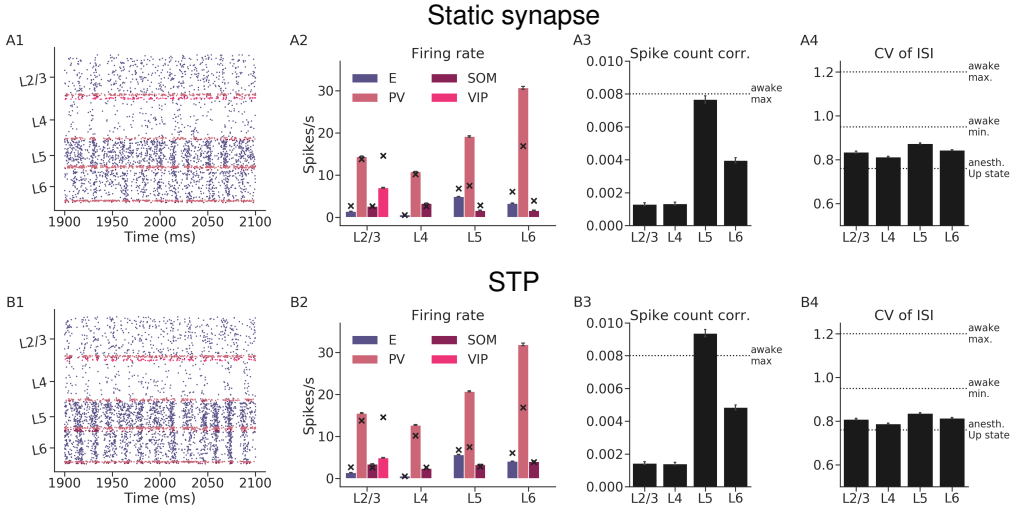
Model parameters

Simulation Results

Discussion

GROUND STATE

- Ground state, model vs. in vivo data (Yu et al., 2019; Maksimov et al., 2018)



CELL-TYPE-SPECIFIC STIMULATION (L2/3)

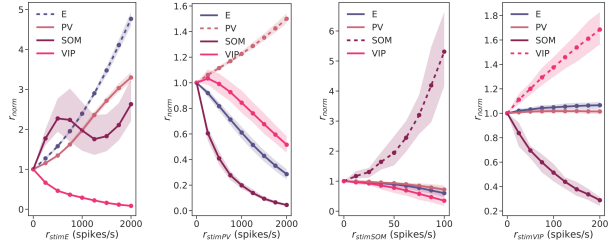
- PV, SOM: inhibitory
- VIP: disinhibitory

r_{norm}: normalized population firing rate
r_{stim}: firing rate of stimulation

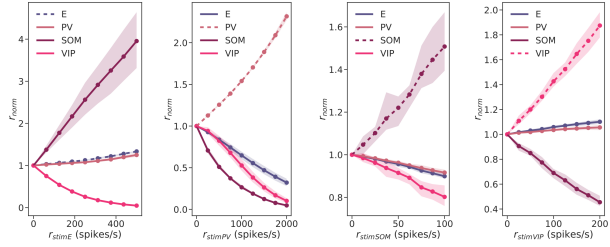
Shaded: r_{bg} of [E, PV] = [4900∼5100, 6500∼6700]

n of instantiation = 10
n of repeat = 10

Static synapse



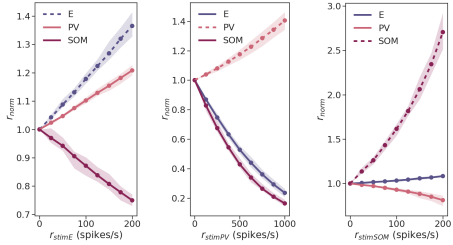
STP



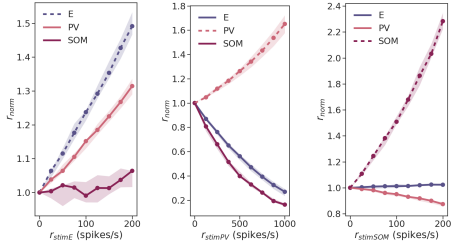
CELL-TYPE-SPECIFIC STIMULATION (L4)

- PV: inhibitory
- SOM: disinhibitory

Static synapse

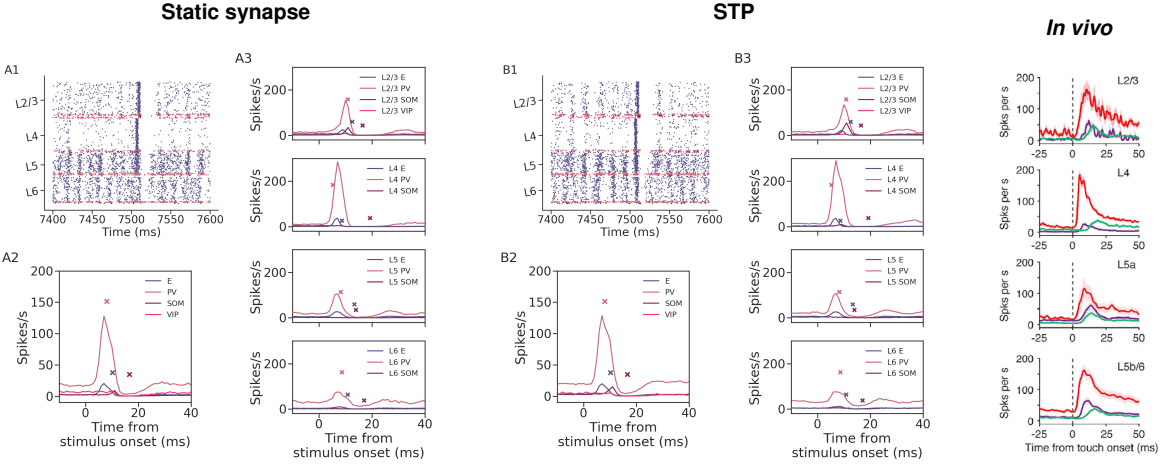


STP



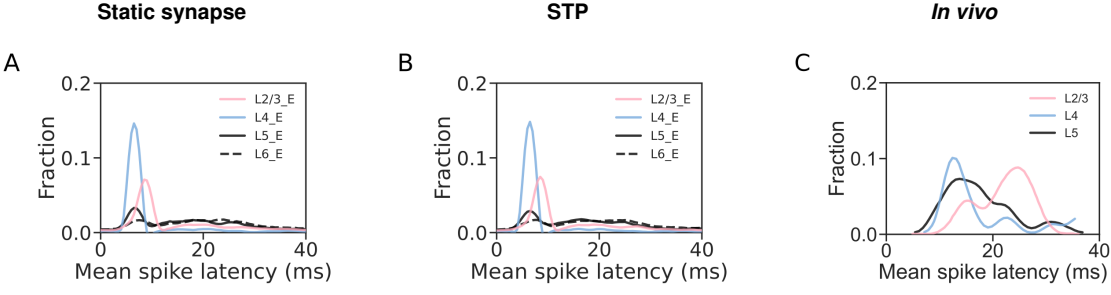
RESPONSES TO THALAMIC INPUT

- Grand average and layer-specific PSTH, model vs. *in vivo* data (Yu et al., 2019)



RESPONSES TO THALAMIC INPUT

- Spike latencies of **excitatory** neurons, model vs. *in vivo* data (Constantinople & Bruno, 2013)



OUTLINE

Introduction

Model parameters

Simulation Results

Discussion

DISCUSSION

- The model reproduces experimental observations of inhibitory and disinhibitory functions of interneurons, as well as sensory responses of barrel cortex
- It can be used to explore layer-specific interneuron functions regarding cell electrophysiology, connectivity, STP, and sensory signal processing
- Outlook
  - Mechanistic analysis (mean-field analysis with STP)
  - Neurotransmitter (ACh) modeling

REFERENCE

Bruno, R. M., & Sakmann, B. (2006). Cortex is driven by weak but synchronously active thalamocortical synapses. *Science 312*, 1622–1627.

Constantinople, C. M., & Bruno, R. M. (2013). Deep cortical layers are activated directly by thalamus. *Science 340*(6140), 1591–1594.

Feldmeyer, D., Lübke, J., Silver, R. A., & Sakmann, B. (2002). Synaptic connections between layer 4 spiny neurone-layer 2/3 pyramidal cell pairs in juvenile rat barrel cortex: physiology and anatomy of interlaminar signalling within a cortical column. *J. Physiol. 538*(3), 803–822.

Jouhanneau, J.-S., Kremkow, J., & Poulet, J. F. (2018). Single synaptic inputs drive high-precision action potentials in parvalbumin expressing gaba-ergic cortical neurons in vivo. *Nat. Commun. 9*(1), 1–11.

Lee, S., Hjerling-Leffler, J., Zagha, E., Fishell, G., & Rudy, B. (2010). The largest group of superficial neocortical GABAergic interneurons expresses ionotropic serotonin receptors. *J. Neurosci. 30*(50), 16796–16808.

Lefort, S., Tomm, C., Sarria, J.-C. F., & Petersen, C. C. (2009). The excitatory neuronal network of the C2 barrel column in mouse primary somatosensory cortex. *Neuron 61*(2), 301–316.

Ma, Y., Hu, H., & Agmon, A. (2012). Short-term plasticity of unitary inhibitory-to-inhibitory synapses depends on the presynaptic interneuron subtype. *J. Neurosci. 32*(3), 983–988.

Maksimov, A., Diesmann, M., & van Albada, S. J. (2018). Criteria on balance, stability, and excitability in cortical networks for constraining computational models. *Front. Comput. Neurosci. 12*, 44.

Neske, G. T., Patrick, S. L., & Connors, B. W. (2015). Contributions of diverse excitatory and inhibitory neurons to recurrent network activity in cerebral cortex. *J. Neurosci. 35*(3), 1089–1105.

Potjans, T. C., & Diesmann, M. (2014). The cell-type specific cortical microcircuit: Relating structure and activity in a full-scale spiking network model. *Cereb. Cortex 24*(3), 785–806.

Tsodyks, M., Uziel, A., & Markram, H. (2000). Synchrony generation in recurrent networks with frequency-dependent synapses. *J. Neurosci. 20*, RC1 (1–5).

Watson, B. O., MacLean, J. N., & Yuste, R. (2008). Up states protect ongoing cortical activity from thalamic inputs. *PLOSONE 3*(12), e3971.

Yu, J., Hu, H., Agmon, A., & Svoboda, K. (2019). Recruitment of gabaergic interneurons in the barrel cortex during active tactile behavior. *Neuron 104*(2), 412–427.