Data-driven model of auditory thalamocortical system rhythms

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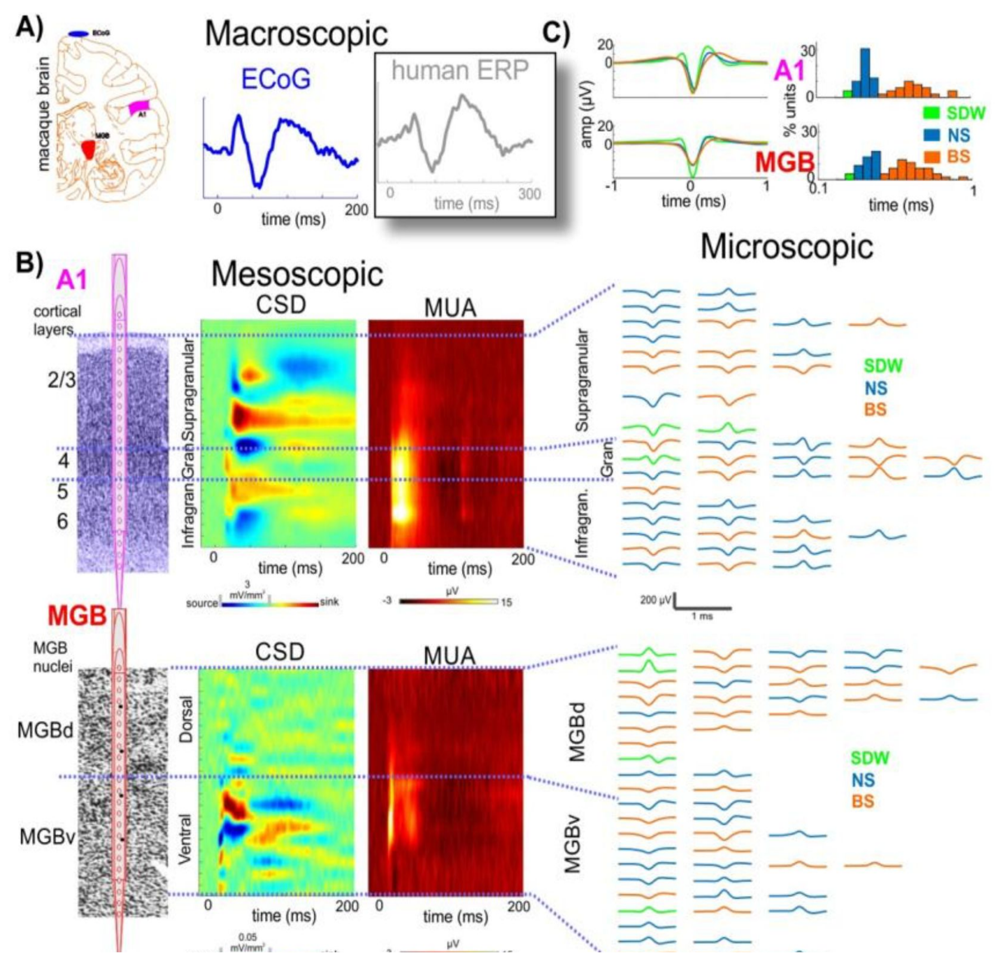
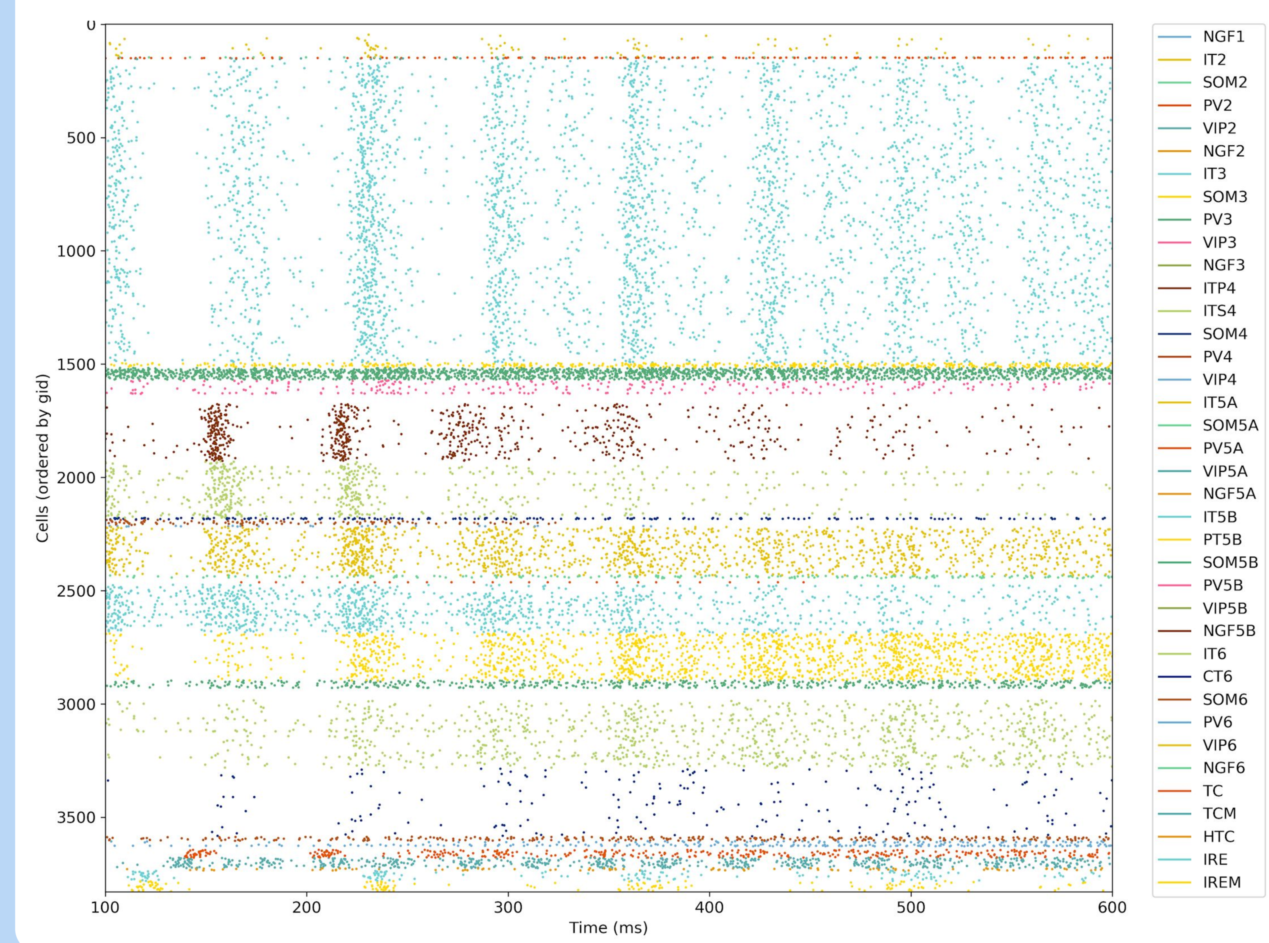
Summary

- **Detailed biophysical computer model** of the auditory thalamocortical system, using the NEURON simulator and the NetPyNE tool, with 39 neural populations consisting of multiple cell types (7 excitatory types, 5 interneuron types) distributed across the 6 A1 cortical layers and 2 thalamic regions (MGB and RTN).
- Layer **boundaries**, neuronal **densities** and cell type **distributions** per layer were based on macaque and rodent thalamocortical data.
- **Model neurons** are multicompartment, conductance-based and include multiple ion channels, with parameters optimized to reproduce physiological responses.
- **Connectivity** depended on pre- and post-synaptic cell type and layer and was derived from cortical data from macaque and rodents.
- Model will be refined using data analyses from multisite recordings, and used to **explore** the mechanistic origins of the spatiotemporal neuronal **oscillatory patterns** observed *in vivo*.
- Model will make **predictions** on the proposed roles of neuronal oscillations in auditory information processing, which will be **tested** via targeted deep brain electrical microstimulation and pharmacological manipulations.

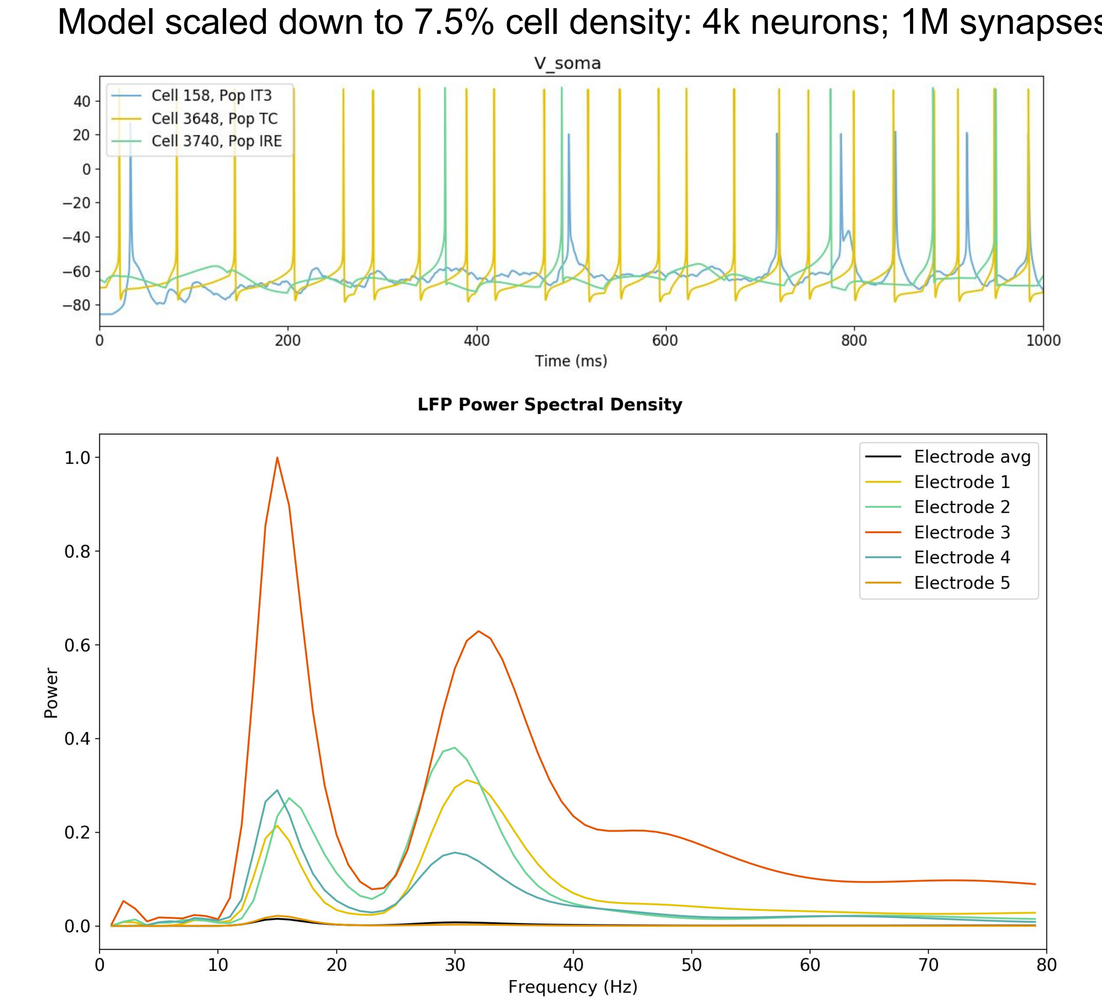


Lakatos et al 2005; 2008; 2009; Barczak et al 2018

Preliminary simulation results



Model scaled down to 7.5% cell density: 4k neurons; 1M synapses



Data-driven cell models

Cell type models developed were multi-compartment and conductance-based.

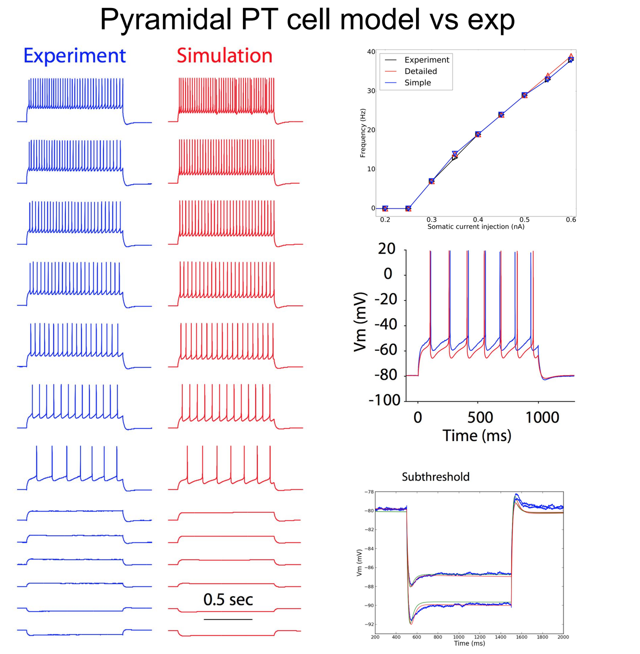
Excitatory cell types: intratelencephalic (IT), pyramidal tract (PT), spiny stellate (ITS), corticothalamic (CT) and MGB thalamocortical (TC).

Inhibitory cell types: somatostatin (SOM), parvalbumin (PV), neurogliaform (NGF), vasoactive intestinal peptide (VIP), and reticular nucleus (RT).

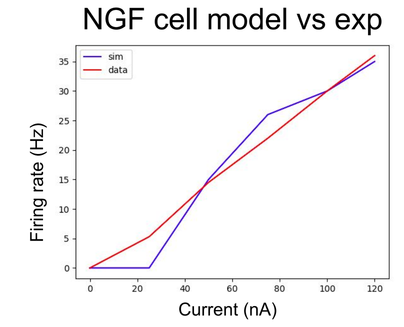
Geometry: Simplified morphologies (1 - 6 compartments). Dendritic lengths were sized to match the macaque cortex dimensions.

Parameter Fitting: Cell types in each layer were fitted to macaque (if available) or rodent electrophysiology data. This was done via either multi-objective evolutionary optimization algorithm or via hand-tuning. Passive parameters (e.g. leak channel conductance) were tuned to fit RMP and other features of subthreshold traces, including steady state voltage and sag. Active parameters (e.g. fast Na+ channel density) were then tuned to fit features like firing rate curves and adaptation.

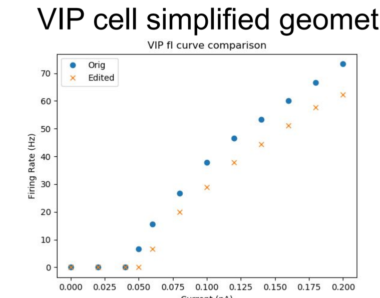
Pyramidal PT cell model vs exp



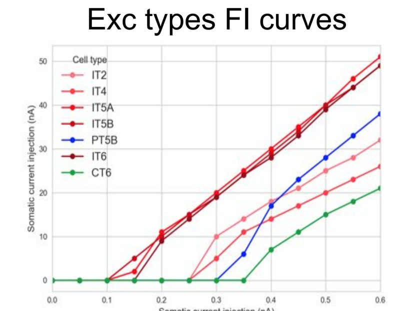
NGF cell model vs exp



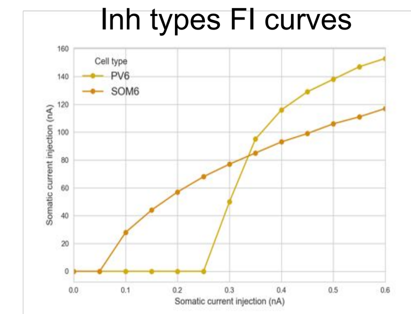
VIP cell simplified geometry



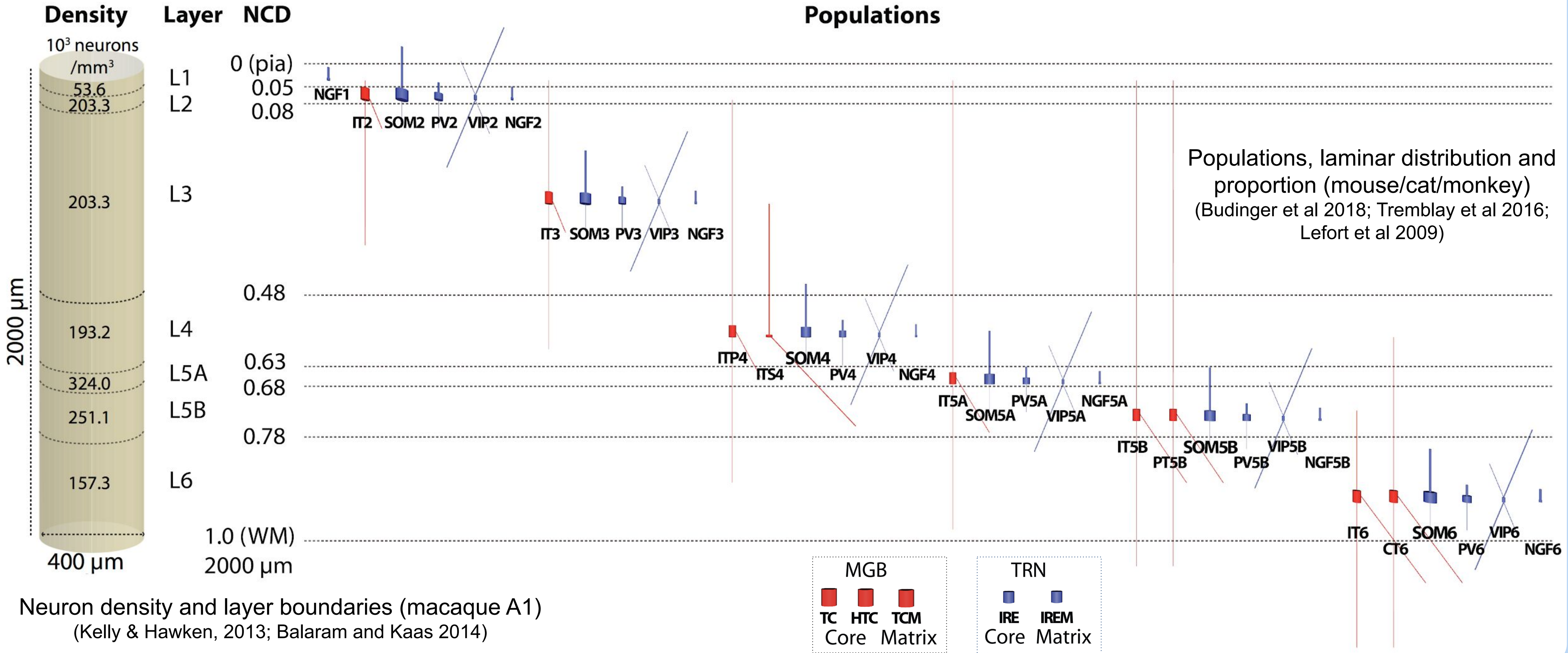
Exc types FI curves



Inh types FI curves



Data-driven network structure

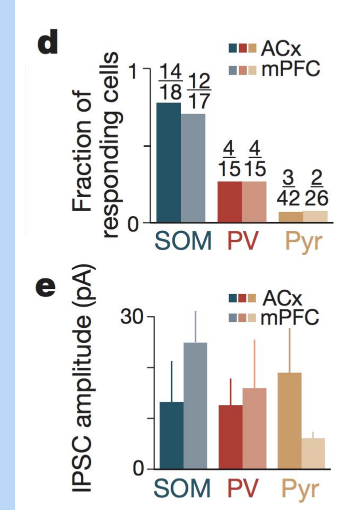


Populations, laminar distribution and proportion (mouse/cat/monkey)
(Budinger et al 2018; Tremblay et al 2016; Lefort et al 2009)

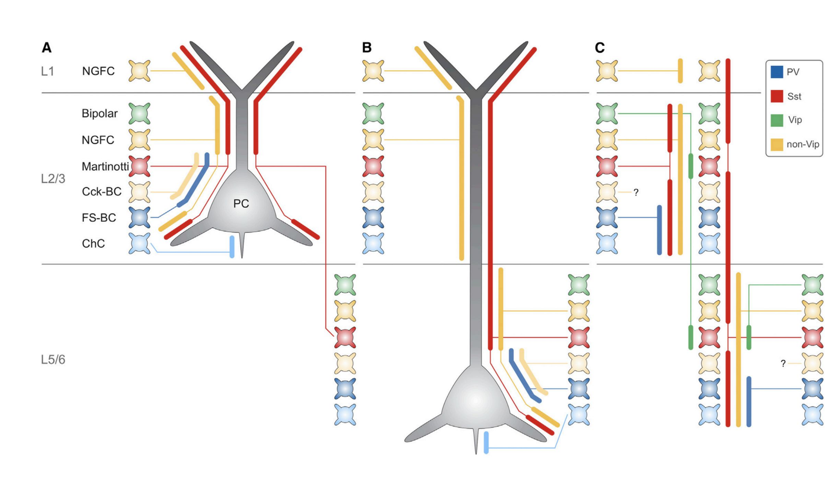
Neuron density and layer boundaries (macaque A1)
(Kelly & Hawken, 2013; Balaram and Kaas 2014)

Data-driven local microcircuit connectivity

- E -> E/I from mouse V1,S1,A1,M1 (Levy & Reyes 2012; Yoshi et al 2015; Billeh et al 2019; Lefort et al 2009; Allen Brain Institute)
- I -> E/I from mouse V1,S1,A1,M1 (Sohn et al 2016; Naka et al 2016; Tremblay et al 2016; Pi et al 2013; Pi et al 2013)

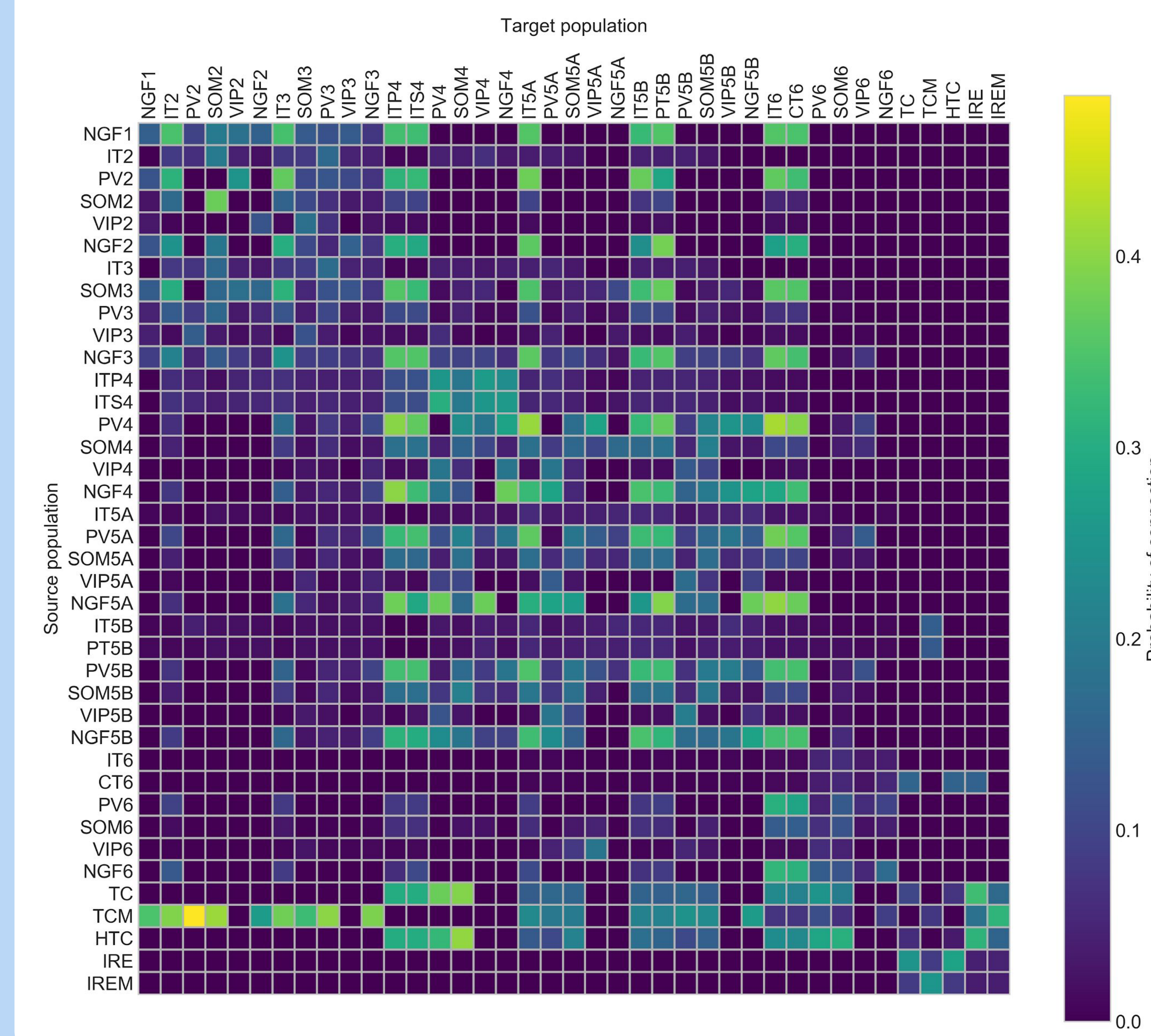


Example probabilities of connection and synaptic weights for VIP -> E/I (mouse A1) (Pi et al, 2013)

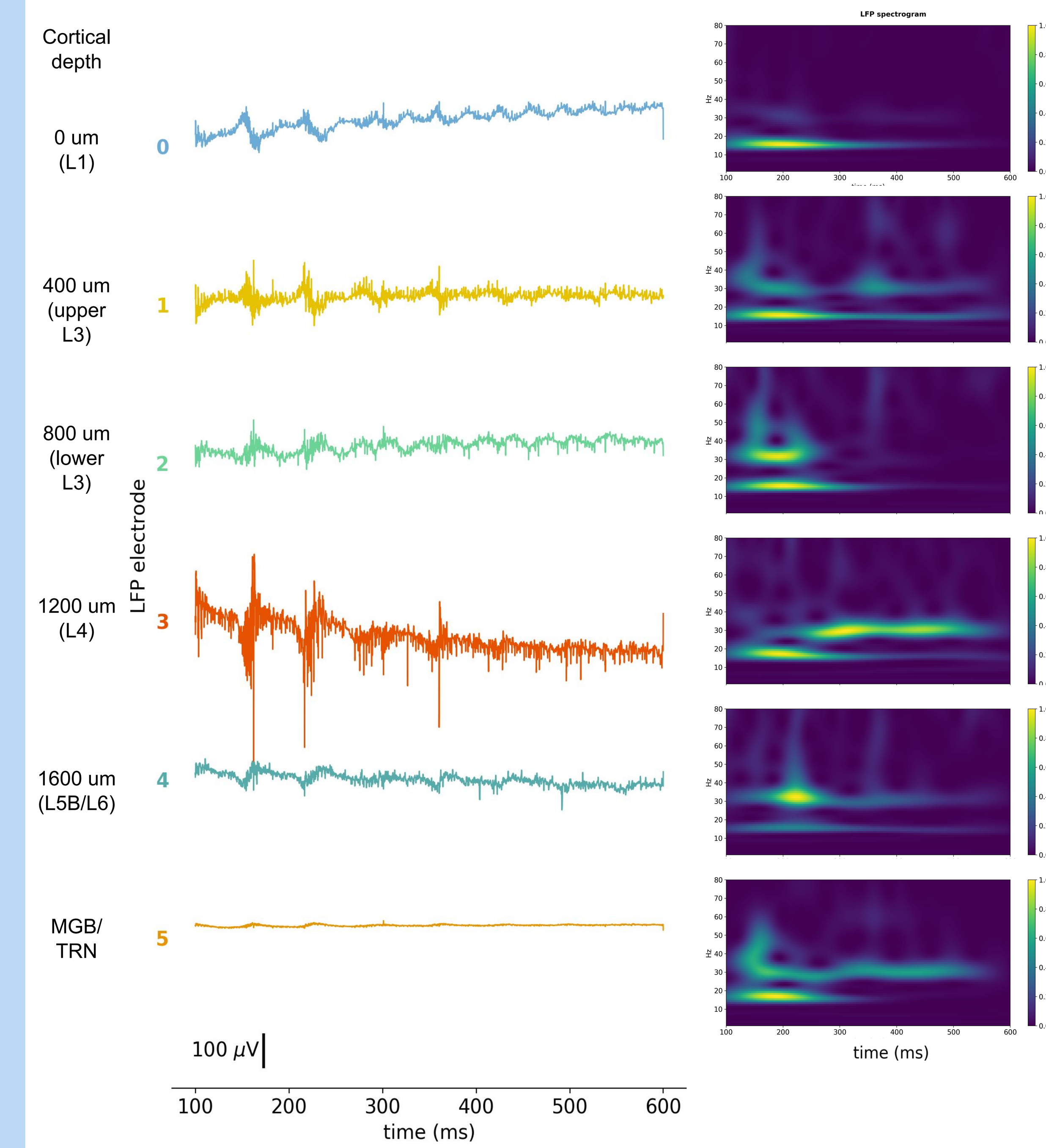


I -> E/I synaptic input distribution (Tremblay et al 2016)

Connectivity Matrix



Local Field Potential (LFP) recorded at different depths



Modeling software tool

Dura-Bernal S, Suter B, Gleeson P, Cantarelli M, … , Neymotin SA, McDougal R, Hines M, Shepherd GMG, Lytton WW. (2019)
NetPyNE: a tool for data-driven multiscale modeling of brain circuits.
eLife 2019;8:e44494 (www.netpyne.org)

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