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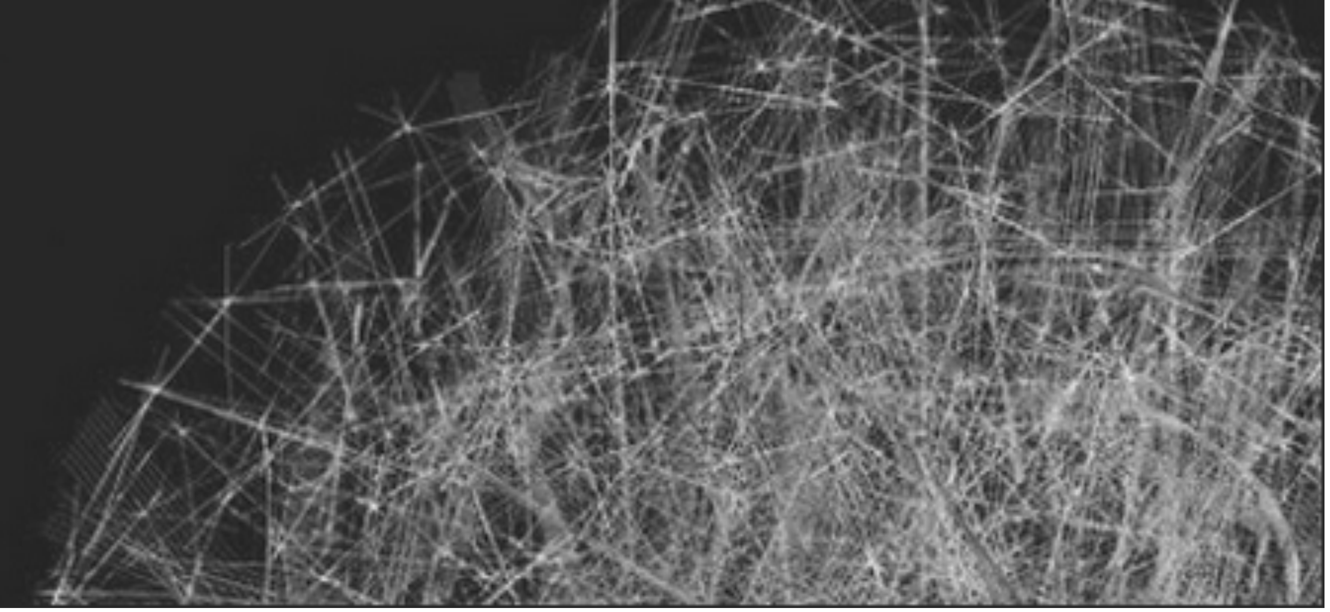
NeuroMat



# A cortical microcircuit model to study structure-activity relationships


Rodrigo Felipe de Oliveira Pena
Prof. Dr. Antônio C. Roque

University of São Paulo - USP
Ribeirão Preto

# Cortical connectivity

## Vertical view

6 layers (I - VI)

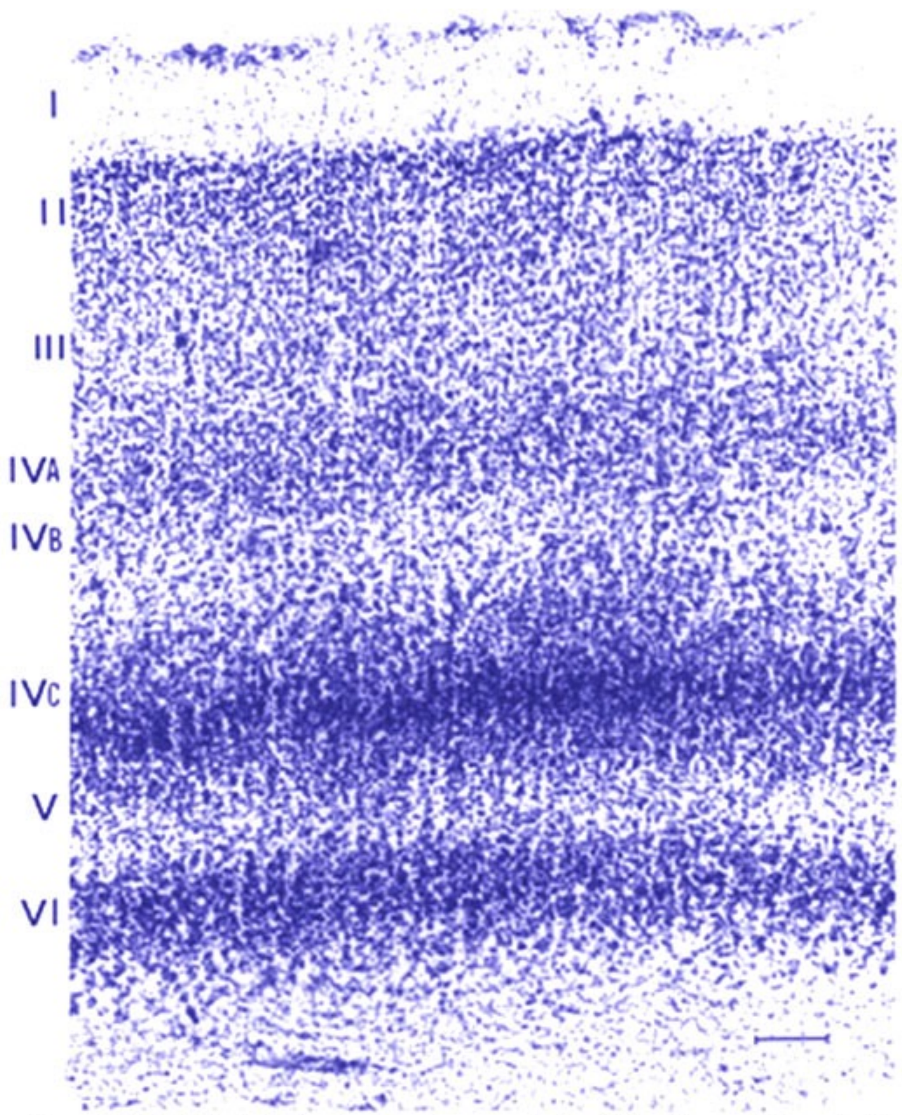
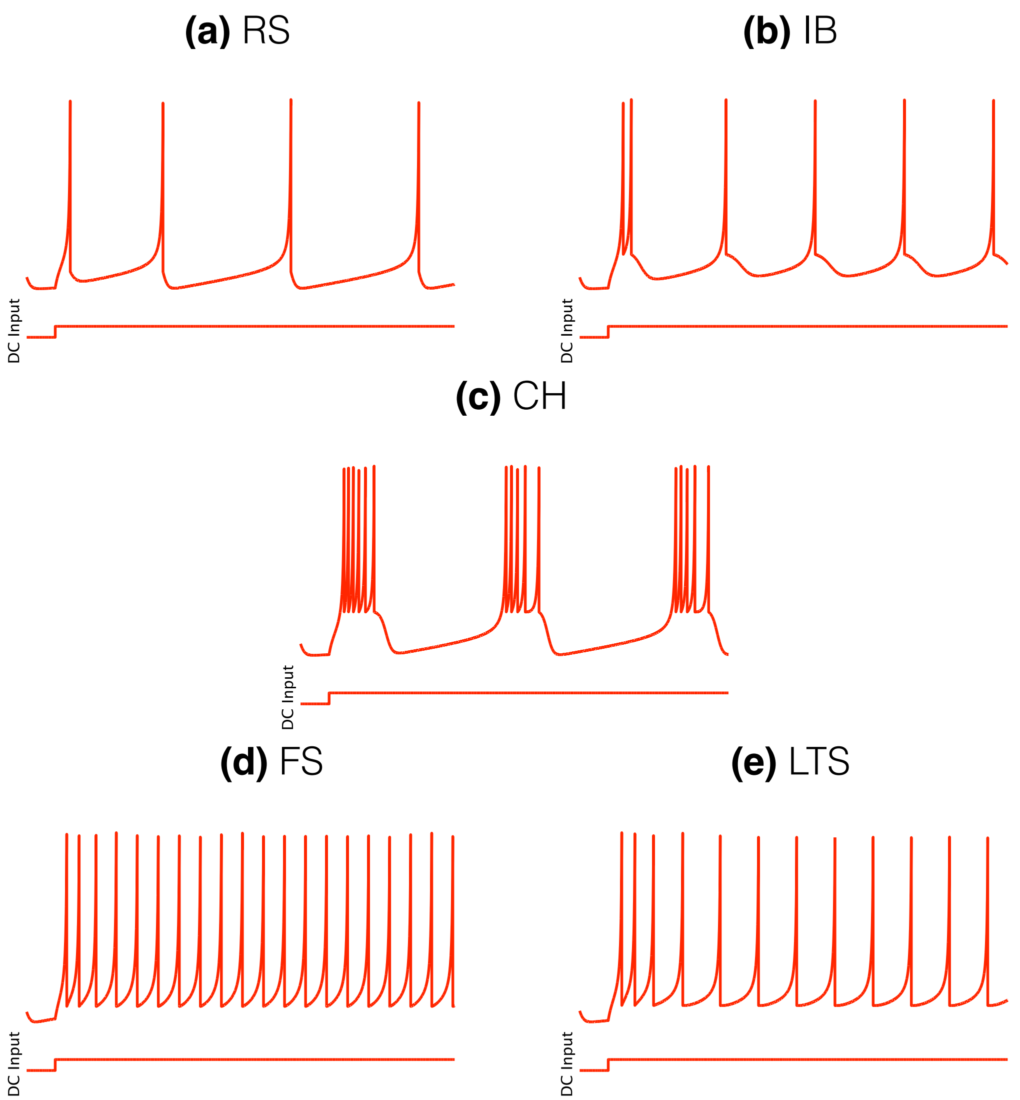



*Figure 13. Nissl stain of the visual cortex reveals the different layers I through VI quite clearly.*

## Neuronal variability

**Morphology**:
pyramidal, basket, chandelier, etc

Specific **electrophysiological** patterns



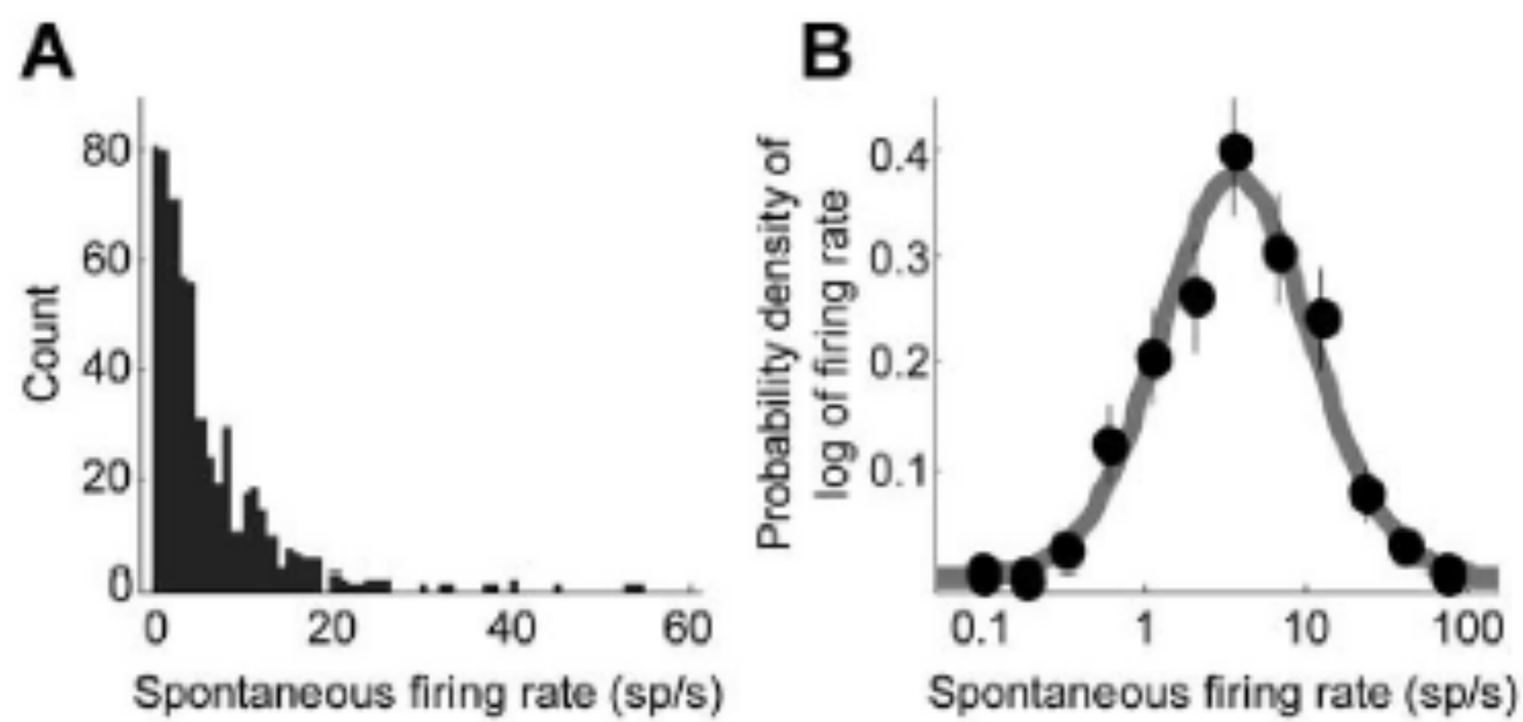
# Cortical signatures during self-sustained activity (SSA)

SSA

Subject is awake but **not submitted to sensory of behavioural tasks**

- **Slow** (< 1 Hz) and **high amplitude** network **oscillations**;
- Neurons with **low firing rates**
- **Non-Gaussian** firing rate distribution

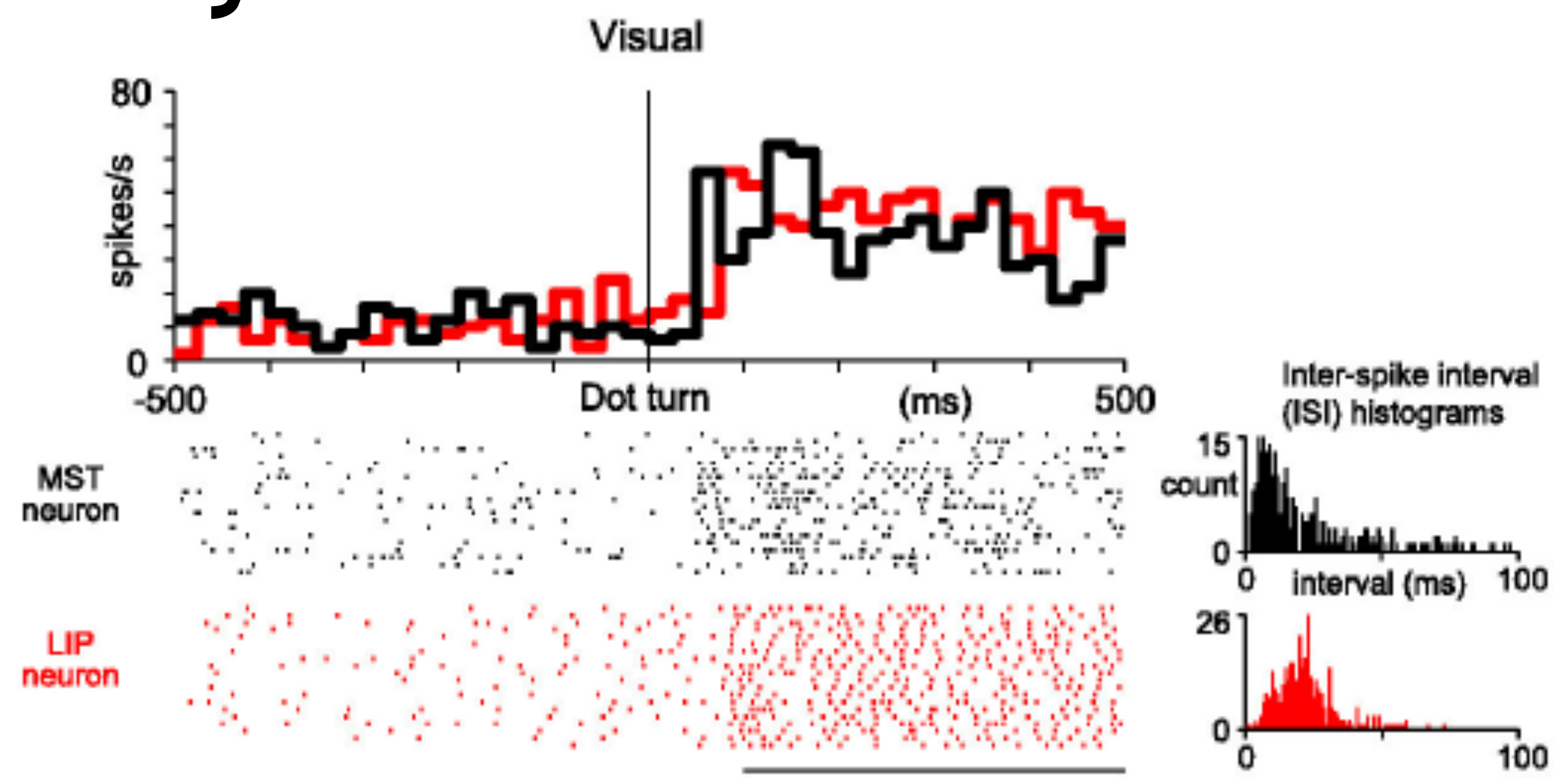
Data from auditory cortex



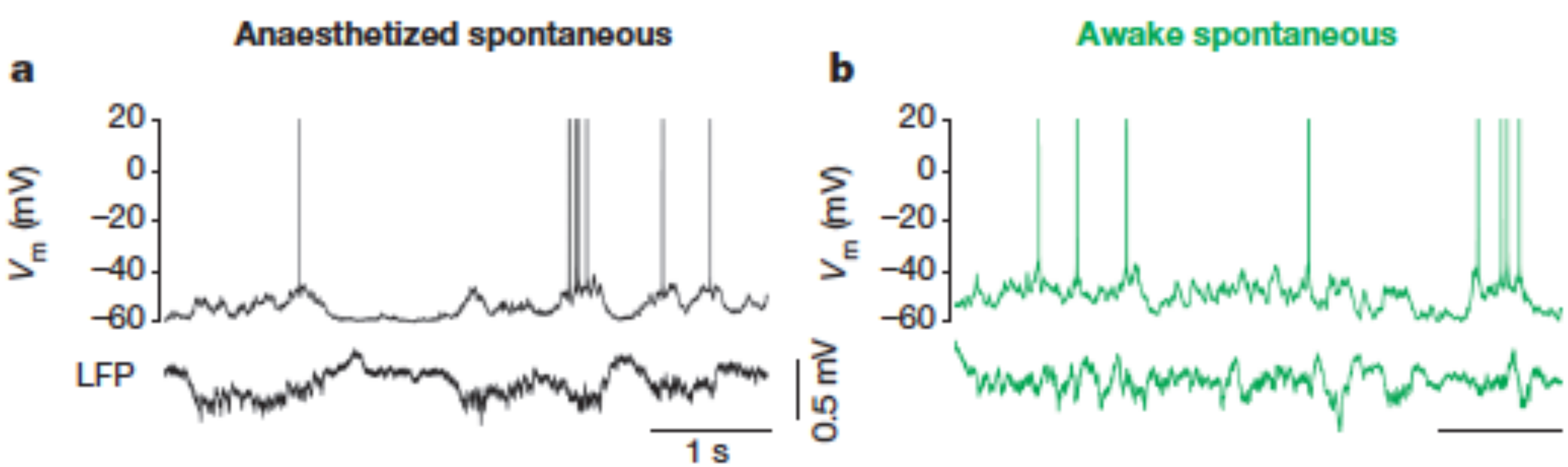

(B and C) Firing rates of most neurons were low and followed a lognormal distribution.

Hromádka et al., PLoS Biology 6:e16, 2008

- **Irregularity**




Maimon and Assad, Neuron 62:426-440, 2009




Haider et al., Nature 493:97-102, 2013

## What has been done recently?

- Classification of neuronal spiking patterns
- Improved knowledge of cortical structure
- Different hypotheses to explain cortical dynamics

## Motivation

Despite growing data sets

Relation between

- Cortical activity
- Electrophysiological classes
- Cortical structure

is poorly understood

It is important to have a model that reproduces **all** of the structured-activity of the cortex

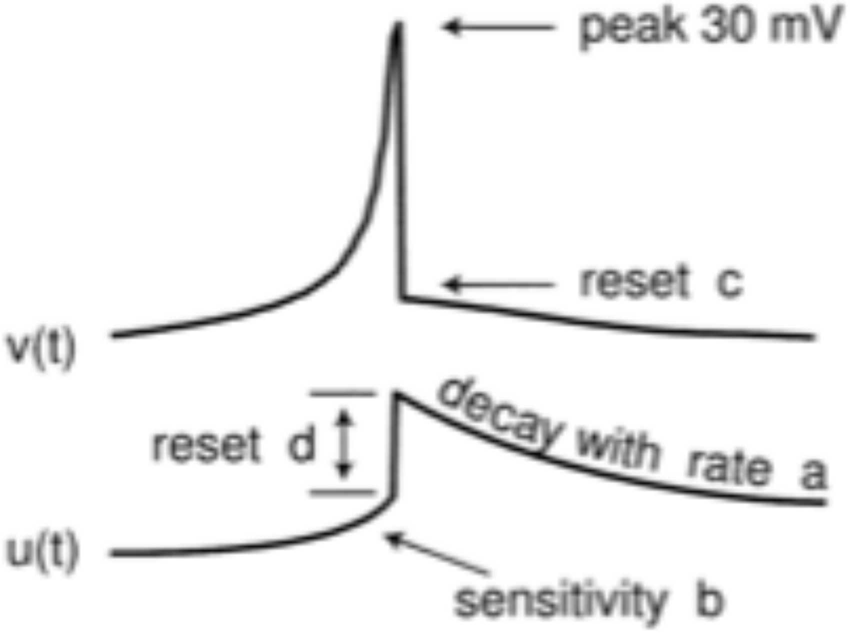
# Methods

## Neurons

### Izhikevich model

$$\begin{cases} \dot{v} = 0.04v^2 + 5v - u + I \\ \dot{u} = a(bv - u) \end{cases}$$

$$if\ v = 30mV, then\ \begin{cases} v \leftarrow c \\ u \leftarrow u + d \end{cases}$$

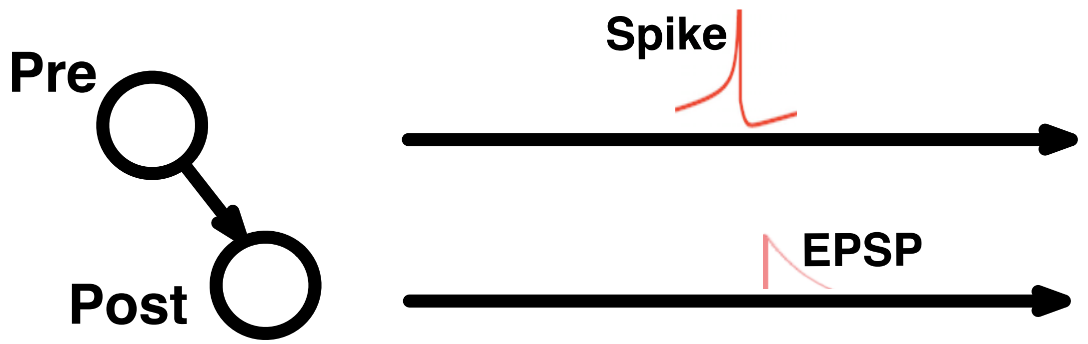



Izhikevich, E. M. (2003).

## Synapses

$$I_{syn} = g_{syn}(t)(V - E_{syn})$$

$$\begin{matrix} if\ presynaptic\ cell\ spike \\ otherwise \end{matrix} \begin{cases} g_{syn} \leftarrow g_{syn} + g_{max} \\ \tau \dfrac{dg_{syn}}{dt} = -g_{syn}(t) \end{cases}$$

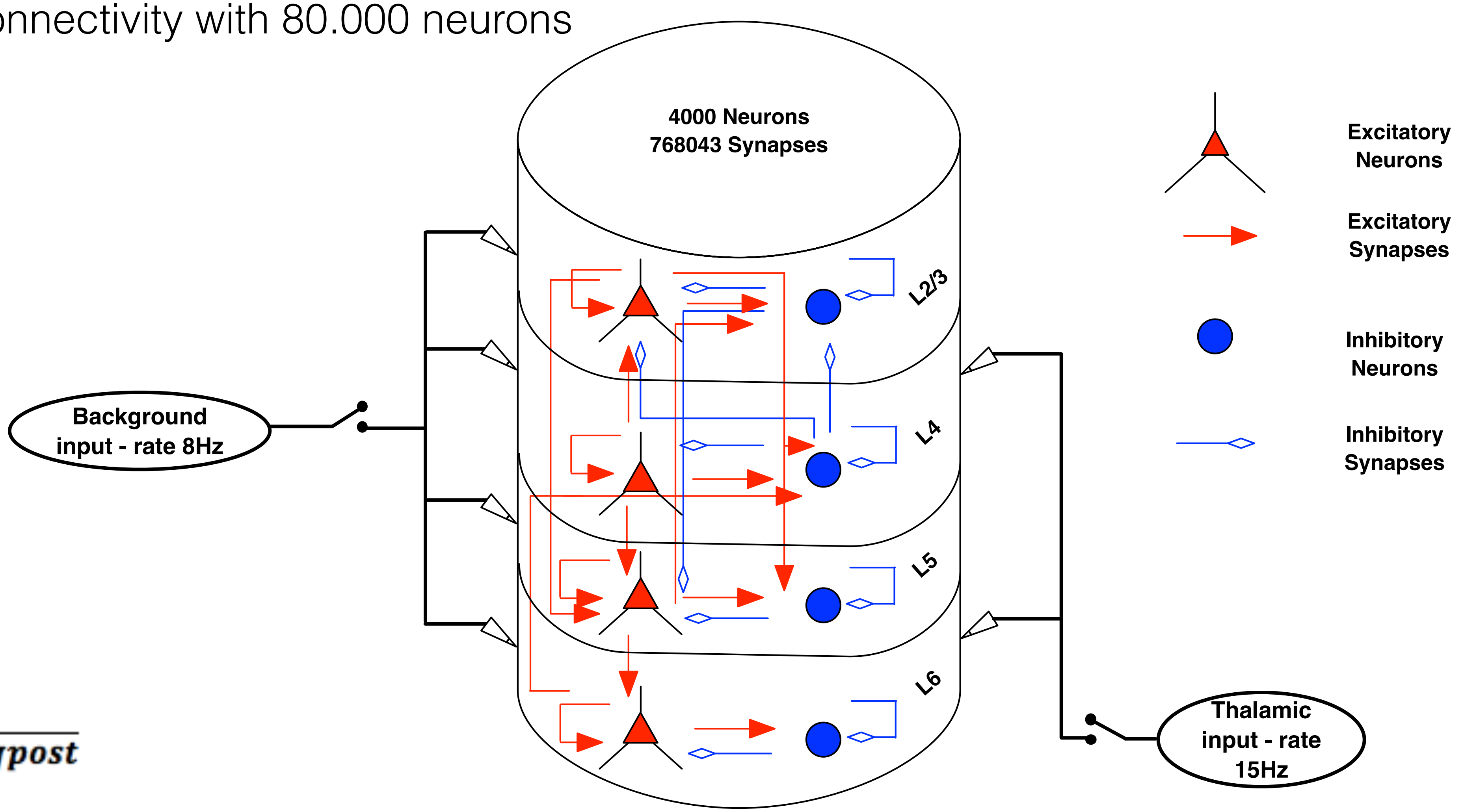



**Exc:** $g_{max} = g_{ex}$
**Inh:** $g_{max} = g_{in}$

# Methods

## Model

- Integrated connectivity map (Potjans and Diesmann, 2014)
- Full-scale 1mm² microcircuit connectivity with 80.000 neurons




Probability $$C_{N^{pre},N^{post}} = \frac{K}{N^{pre}N^{post}}$$

Only connections with probabilities >0.04 are shown

# Methods

## Building the model

- 4000 Neurons - 80% excitatory and 20% inhibitory
- Divide them proportionally into layers
- Connect following wiring rule

## Spatial location

- Cell's spatial location is determined by it's layer
- Assume maximum delay is set to 10ms

**Connectivity**

| to \ from | L23e | L23i | L4e | L4i | L5e | L5i | L6e | L6i |
|---|---|---|---|---|---|---|---|---|
| L23e | 0.101 | 0.169 | 0.044 | 0.082 | 0.032 | 0 | 0.008 | 0 |
| L23i | 0.135 | 0.137 | 0.032 | 0.052 | 0.075 | 0 | 0.004 | 0 |
| L4e | 0.008 | 0.006 | 0.050 | 0.135 | 0.007 | 0.0003 | 0.045 | 0 |
| L4i | 0.069 | 0.003 | 0.079 | 0.160 | 0.003 | 0 | 0.106 | 0 |
| L5e | 0.100 | 0.062 | 0.051 | 0.006 | 0.083 | 0.373 | 0.020 | 0 |
| L5i | 0.055 | 0.027 | 0.026 | 0.002 | 0.060 | 0.316 | 0.009 | 0 |
| L6e | 0.016 | 0.007 | 0.021 | 0.017 | 0.057 | 0.020 | 0.040 | 0.255 |
| L6i | 0.036 | 0.001 | 0.003 | 0.001 | 0.028 | 0.008 | 0.066 | 0.144 |

# Methods

## Stimuli

### Scenario A

- in vivo
- cortico-cortical connections
- background input $v$=8Hz (poisson fixed rate)
- thalamic connections
- thalamic input $v$=15Hz (poisson fixed rate) (L4 and L6)

### Scenario B

- deafferentation
- turn off thalamic input
- only background input $v$=8Hz

# Methods

## Measurements

1. **Spike trains, membrane voltages**

2. **Individual and Mean population frequencies**

3. **ISI (interspike interval) -** Time interval between spikes.

4. **CV (coefficient of variation of a neuron's ISIs) -** Ratio of standard deviation to the mean.
   (Gabbiani and Koch, 1998; Dayan and Abbott, 2001; Laing and Lord, 2009)

$$CV_i = \frac{\sigma_{\mathrm{ISI_i}}}{\overline{\mathrm{ISI}}_i}$$

5. **Synchrony -** Normalized to be between 0 and 1.
   (Golomb et. al., 2001)

$$\chi^2(N) = \frac{\sigma_V^2}{\frac{1}{N}\sum_{i=1}^{N}\sigma_{V_i}^2}$$

# Results

## Scenario A

Experiment: Parameter search

- We look for (cortical signatures):

  - Collective low spiking frequency (< 1 Hz)
  - Irregularity in the individual neuronal spikes
  - Asynchronous activity
  - Large sub-threshold fluctuations


$$\Delta g_{ex} = 1 \text{ and } \Delta g_{in} = 1$$

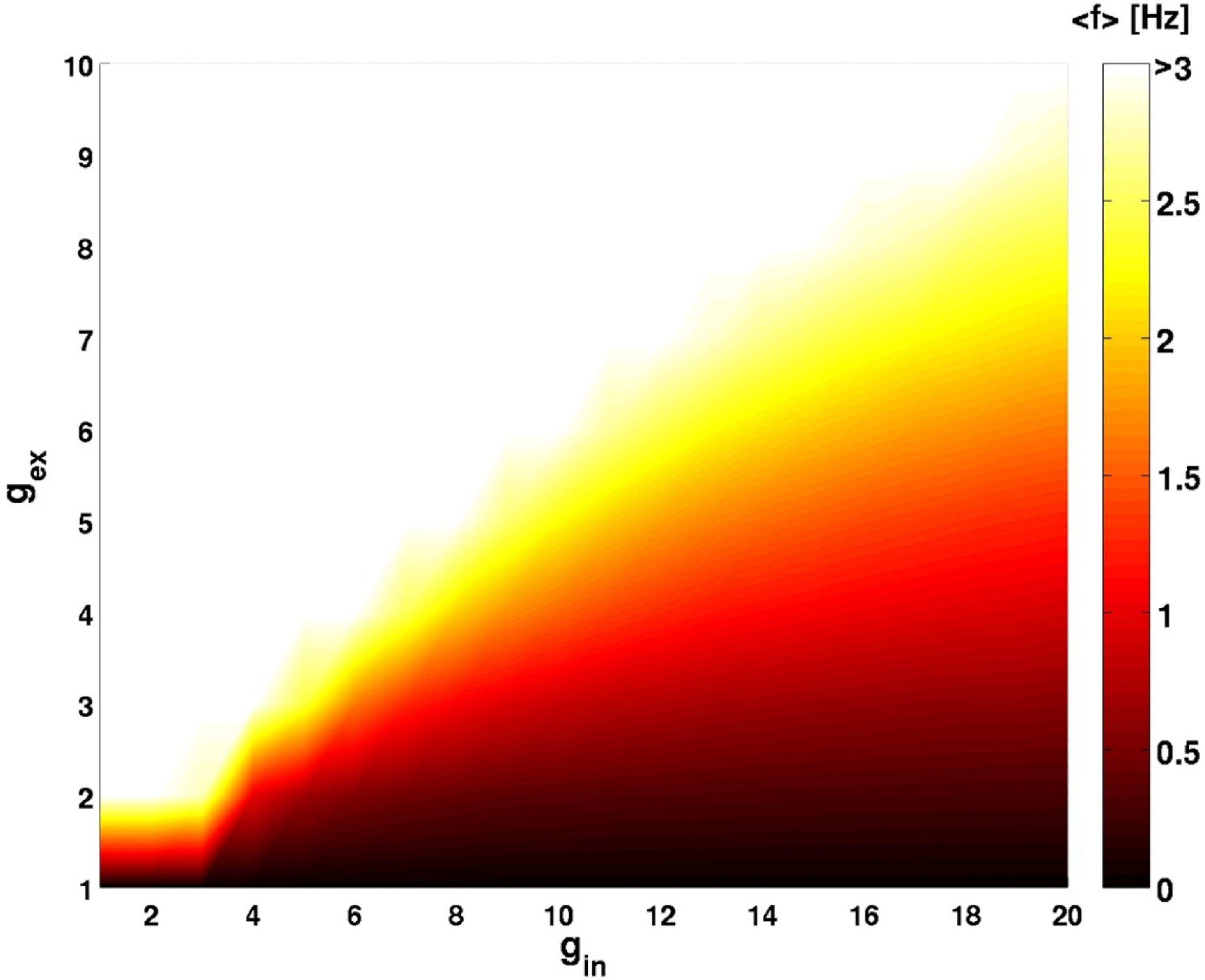
Simulation Parameters

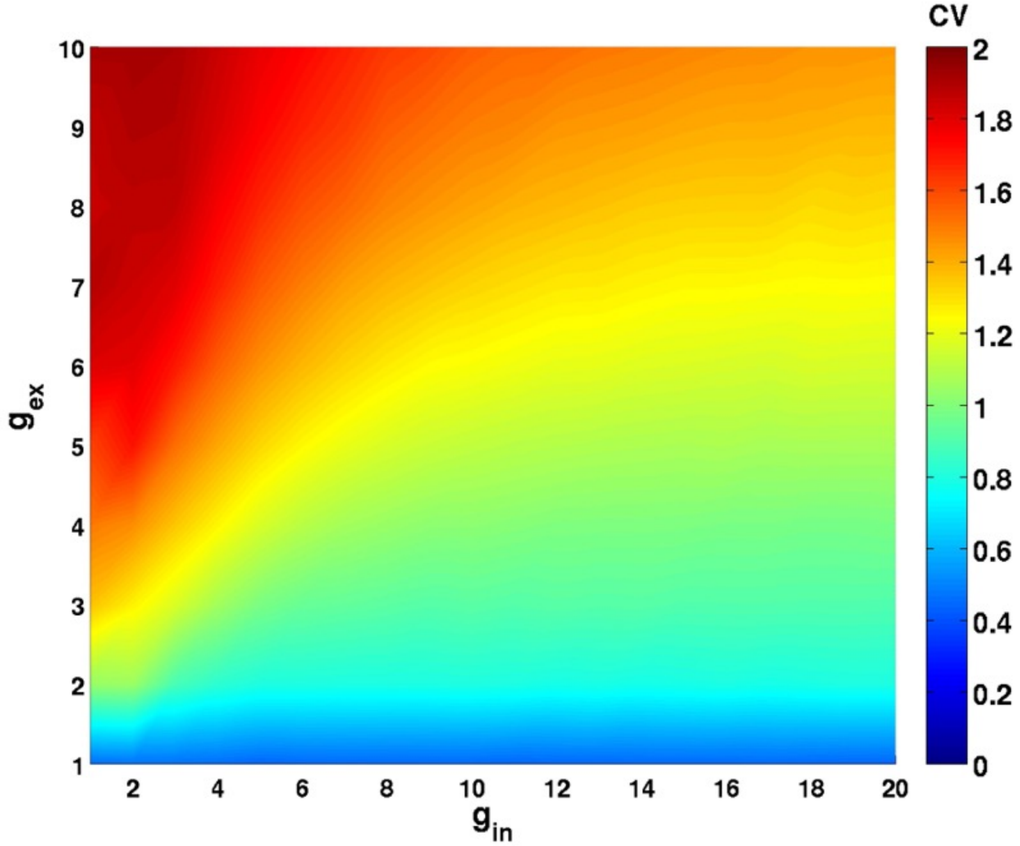
$T_{simulation}$ = 1000 ms
30 different seeds

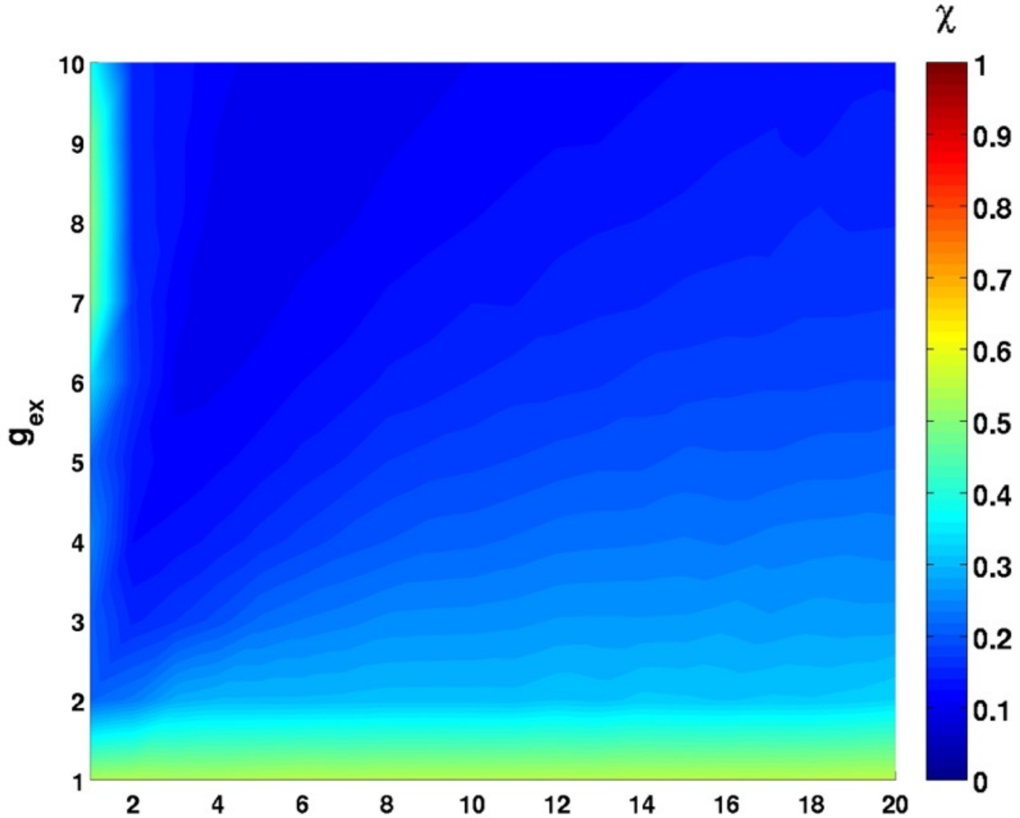
# Results

## Scenario A

Experiment: Parameter search



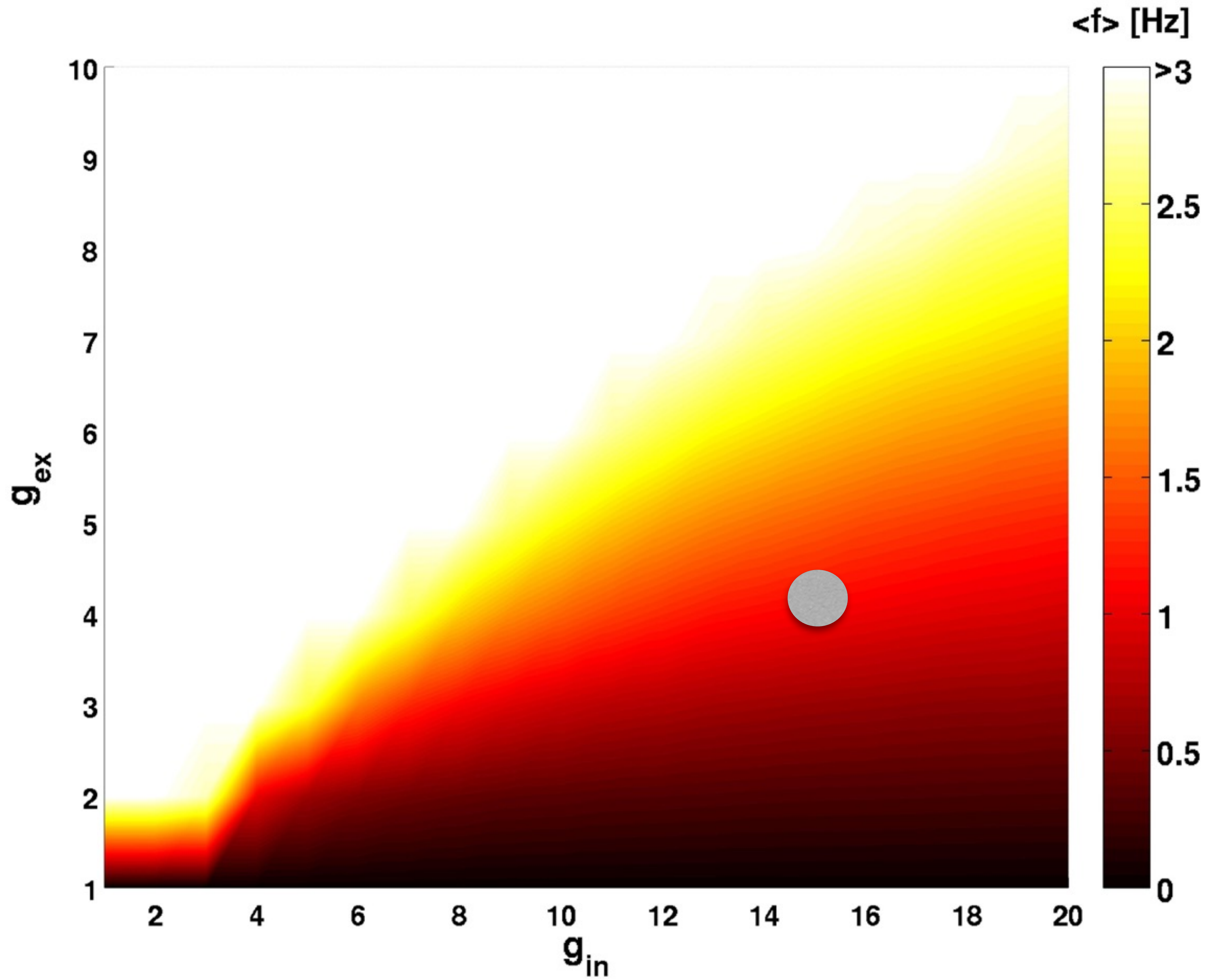



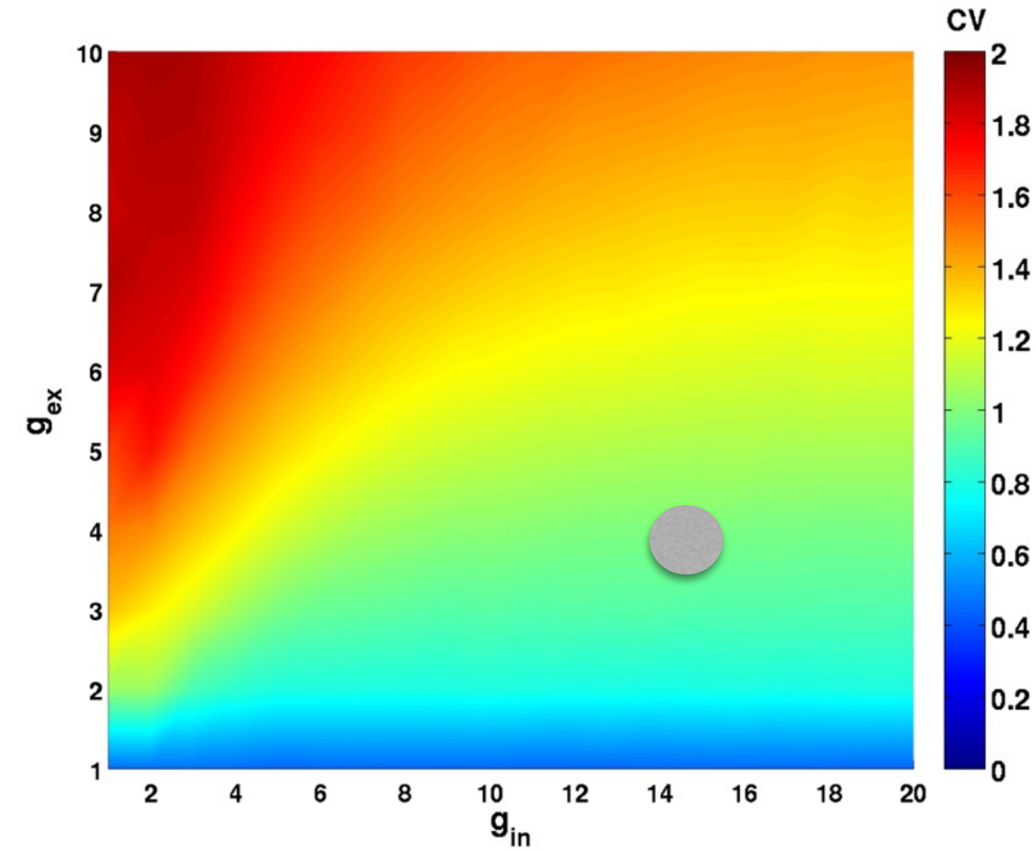



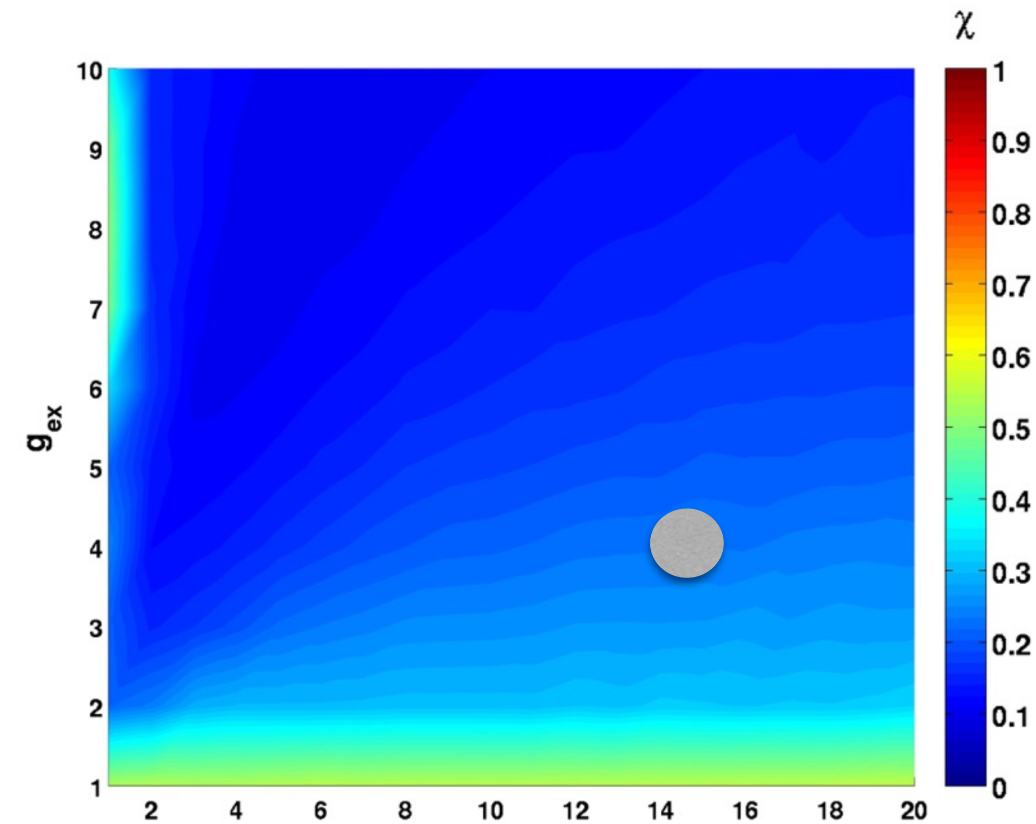
# Results

## Scenario A

Experiment: Parameter search

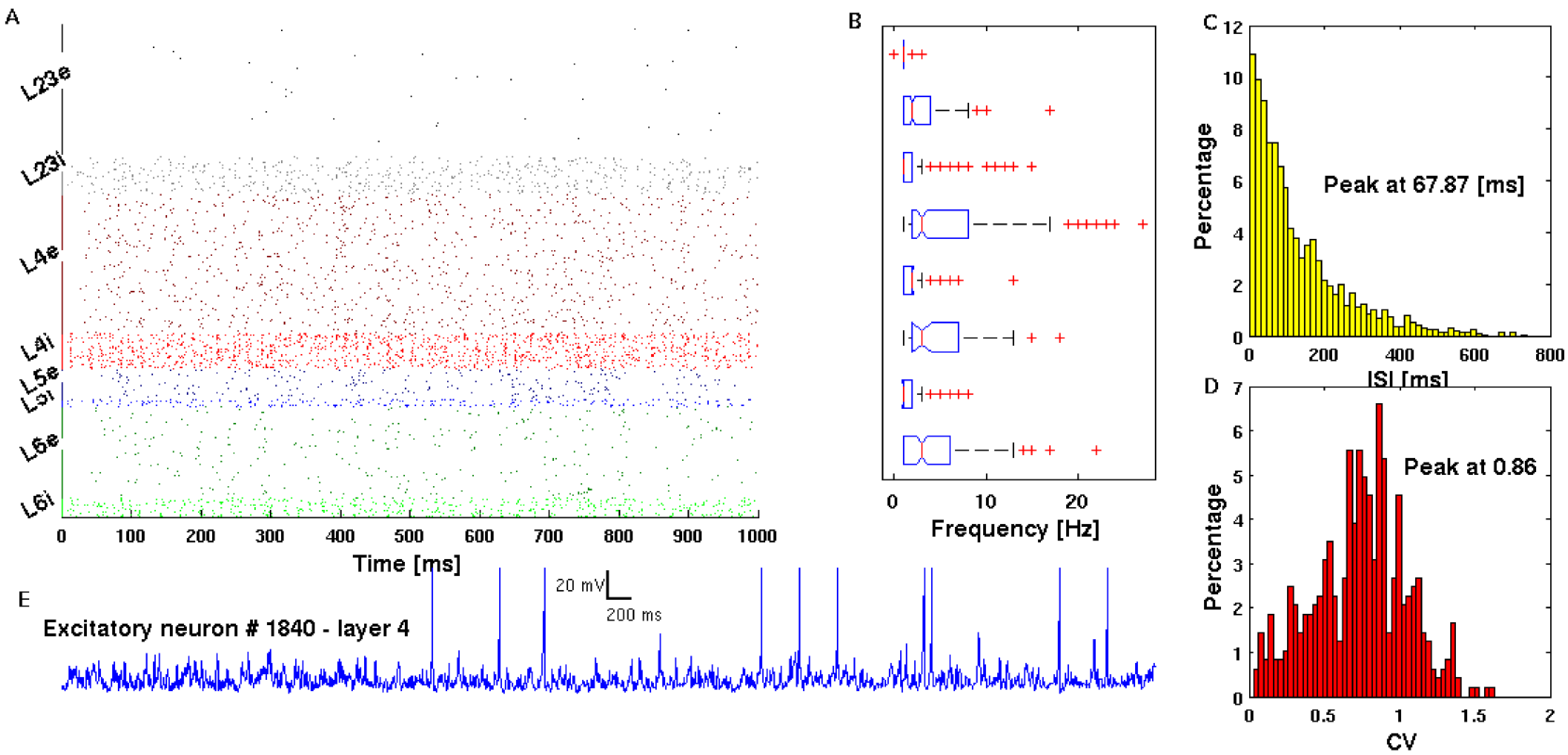


# Results

($g_{ex} = 4, g_{in} = 15$)



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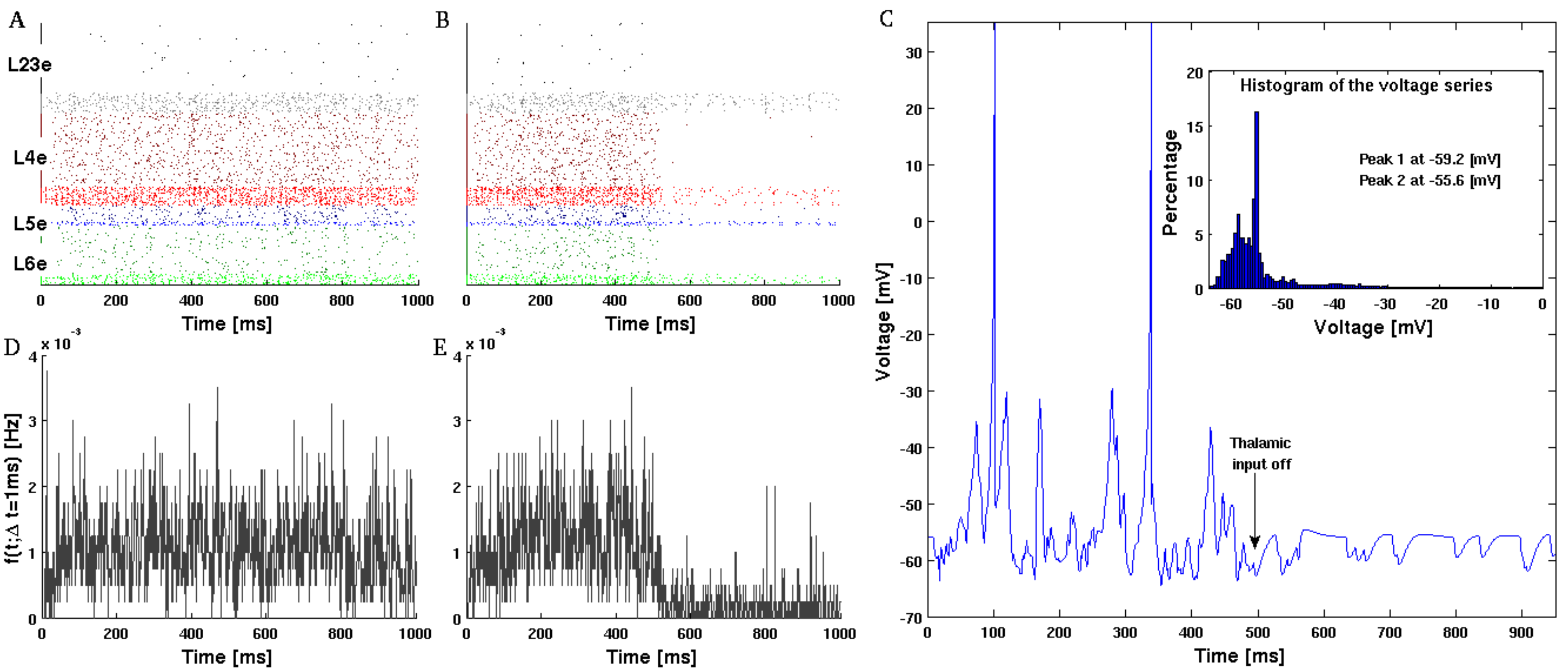
# Results

$(g_{ex} = 4, g_{in} = 15)$ Thalamic input is turned off at 500 ms

## Scenario A X Scenario B




- Similar to 'UP' and 'DOWN' states (two preferable subthreshold states during anesthesia)

Steriade et al., (1993); Sanchez-Vives et al., (2000)

# Summary and Conclusions

- Model of local cortical network shows realistic behavior
- Agreement with experimental recordings
- The model is being used to study structure-activity relationships
- NeuroMat members may use the model as a toy model

# References


- Binzegger, T., Douglas, R. J., & Martin, K. A. (2004).
- Brette et al., (2007).
- Brunel N., (2000).
- (Dayan and Abbott, 2001)
- Douglas and Martin, (2004).
- Gabbiani and Koch, 1998;
- (Golomb et. al., 2001)
- Izhikevich, E. M. (2003).
- Izhikevich, E. M., & Edelman, G. M. (2008).
- Laing and Lord, 2009
- Mountcastle, V. B. (1997).
- Potjans, T. C., & Diesmann, M. (2014).
- Sanchez-Vives et al., (2000)
- Steriade et al., (1993);
- Wester and Contreras (2012).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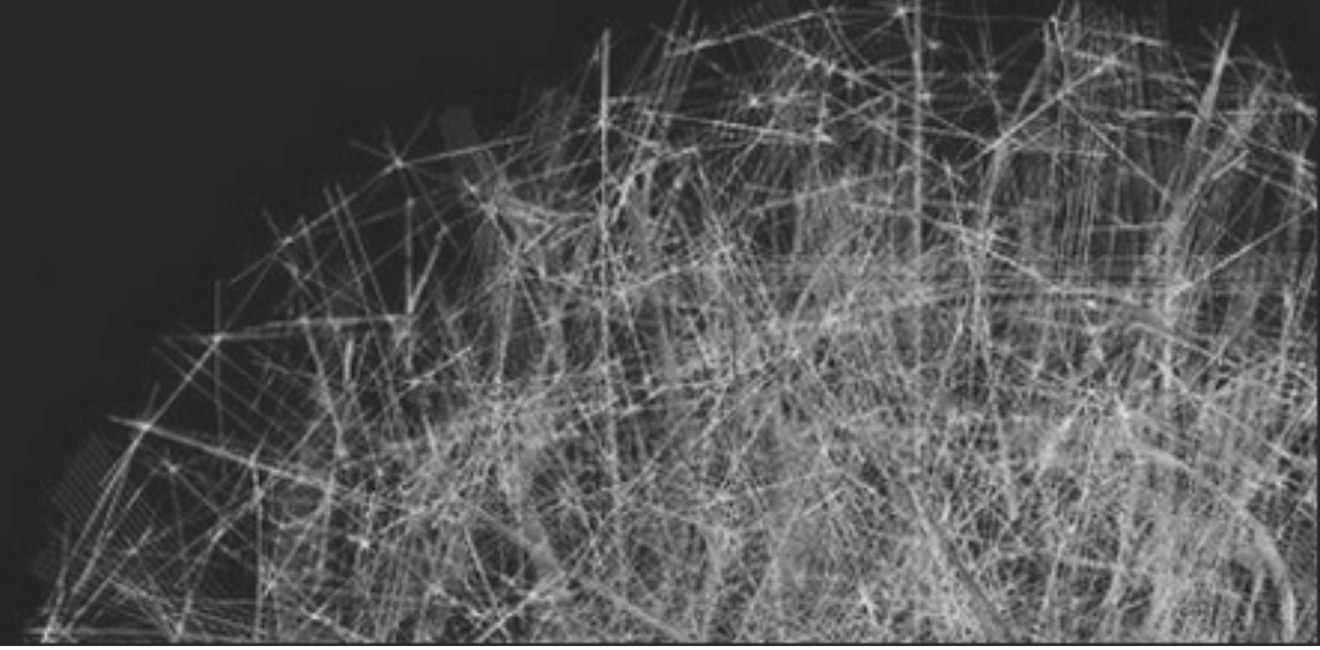

Thank you very much!

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