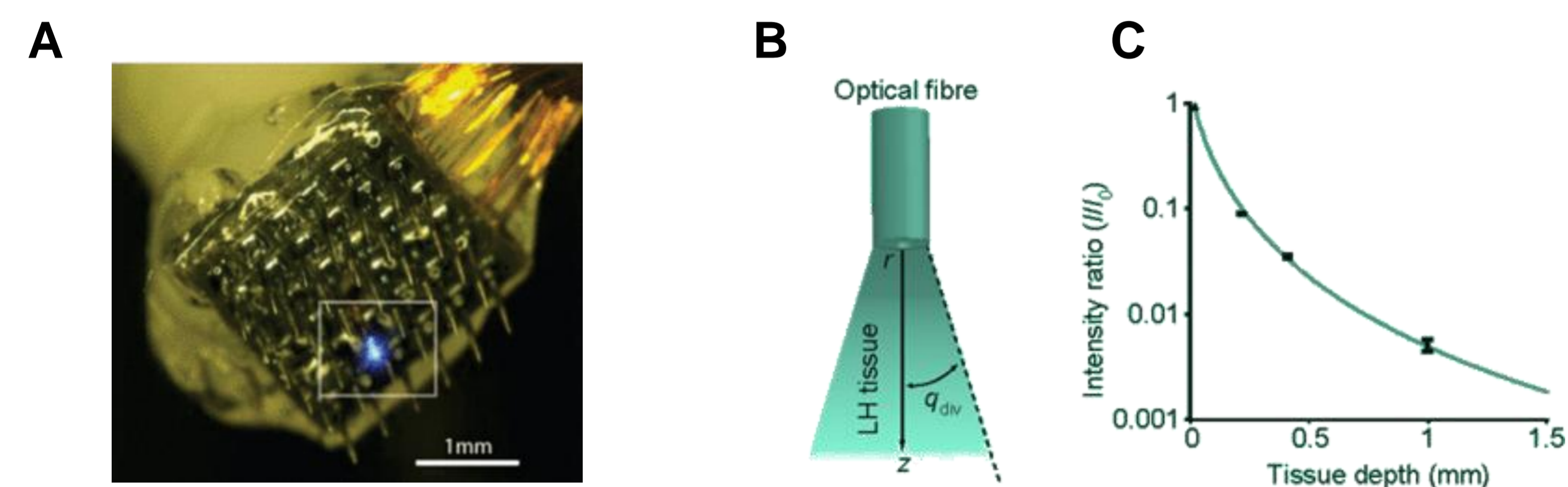


## 1. Introduction

Optogenetics is a potent tool for perturbing ongoing cortical dynamics. However, only small numbers of neurons can be recorded simultaneously. Here we present a biomimetic spiking network model of macaque M1 cortex in order to explore network-level effects of optogenetic stimulation – namely, how synaptic connections modulate the optogenetic stimulus response, and how optogenetic stimulation affects interlaminar information flow.

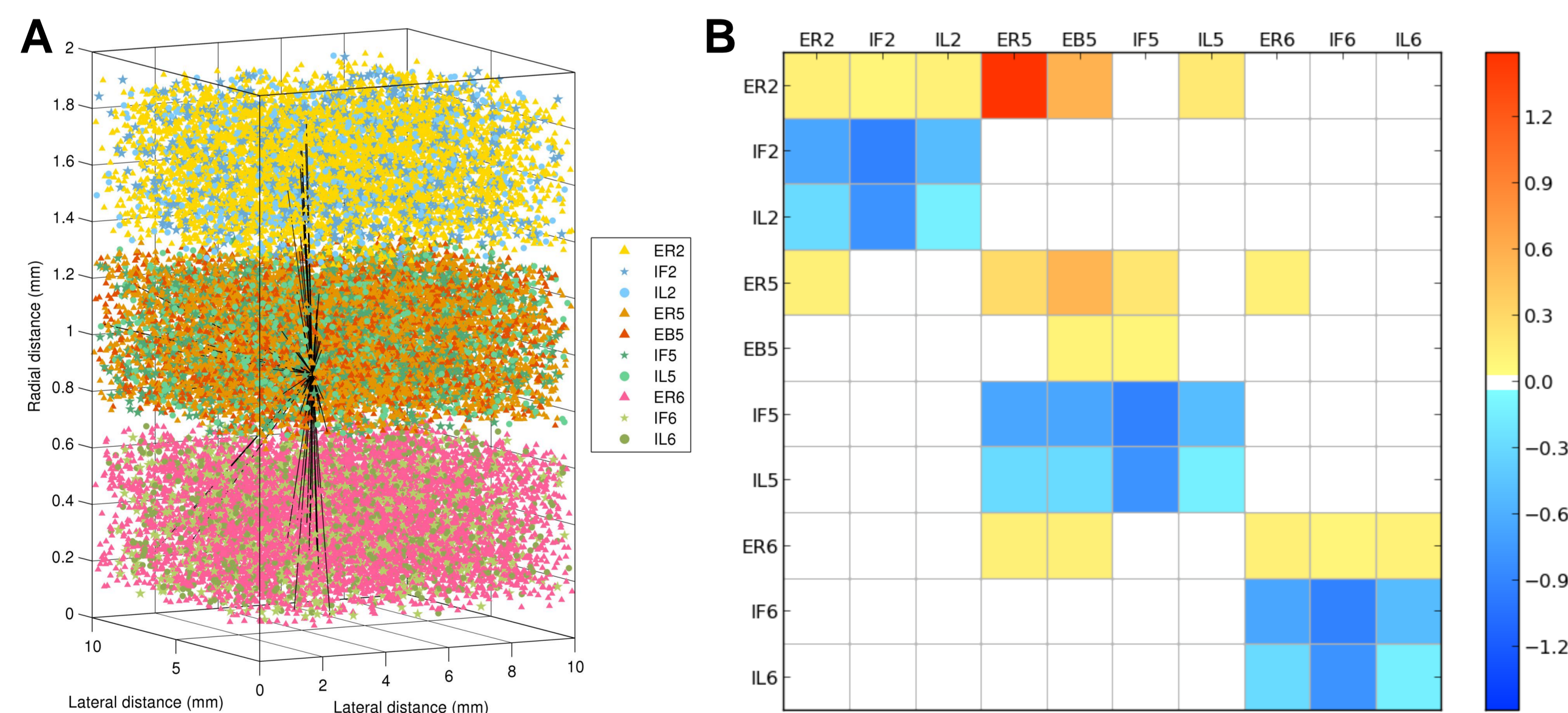
## 2. Methods

Experimental data (Fig. 1) were recorded from M1 in a male macaque. Optogenetic stimulation targeted excitatory neurons, likely preferentially affecting deeper layers, via the excitatory opsin C1V1TT, with either continuous (200 ms) or periodic (20, 40, or 80 Hz) pulses of green light (561 nm) [1].



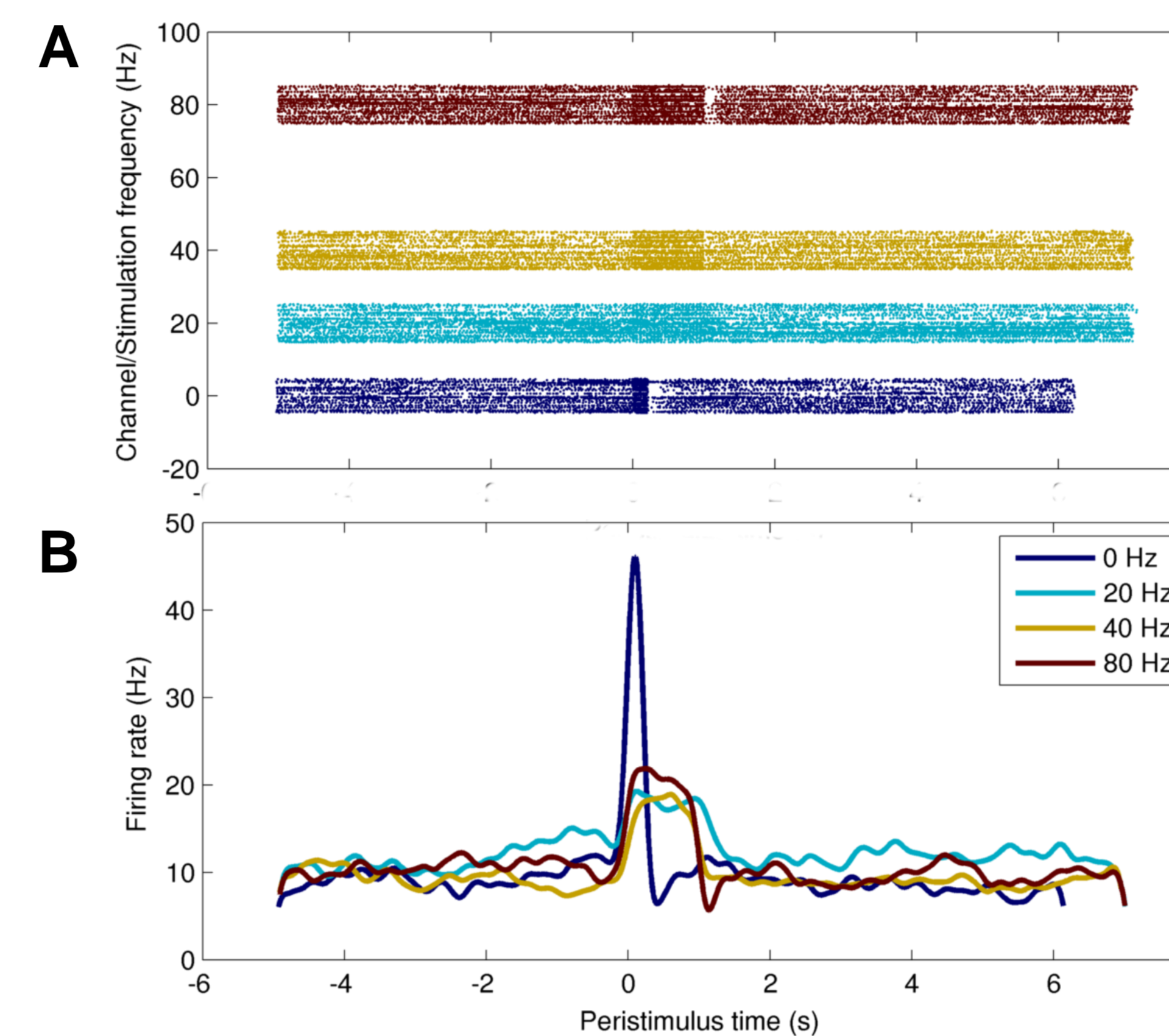
**Fig. 1:** Schematic of the experimental method. (A) A combined electrode-optrode, similar to the one used for optogenetic stimulation and spike recording. (B) Attenuation of light in brain tissue. (C) Lateral spread of light. (Figure based on [2] and [3].)

The simulation (Fig. 2) consisted of six-layered primary motor cortex comprised of 24,800 spiking Izhikevich neurons [4], with connectivities drawn from empirical data; a similar model has previously been shown to produce realistic firing rates and spectra [5].

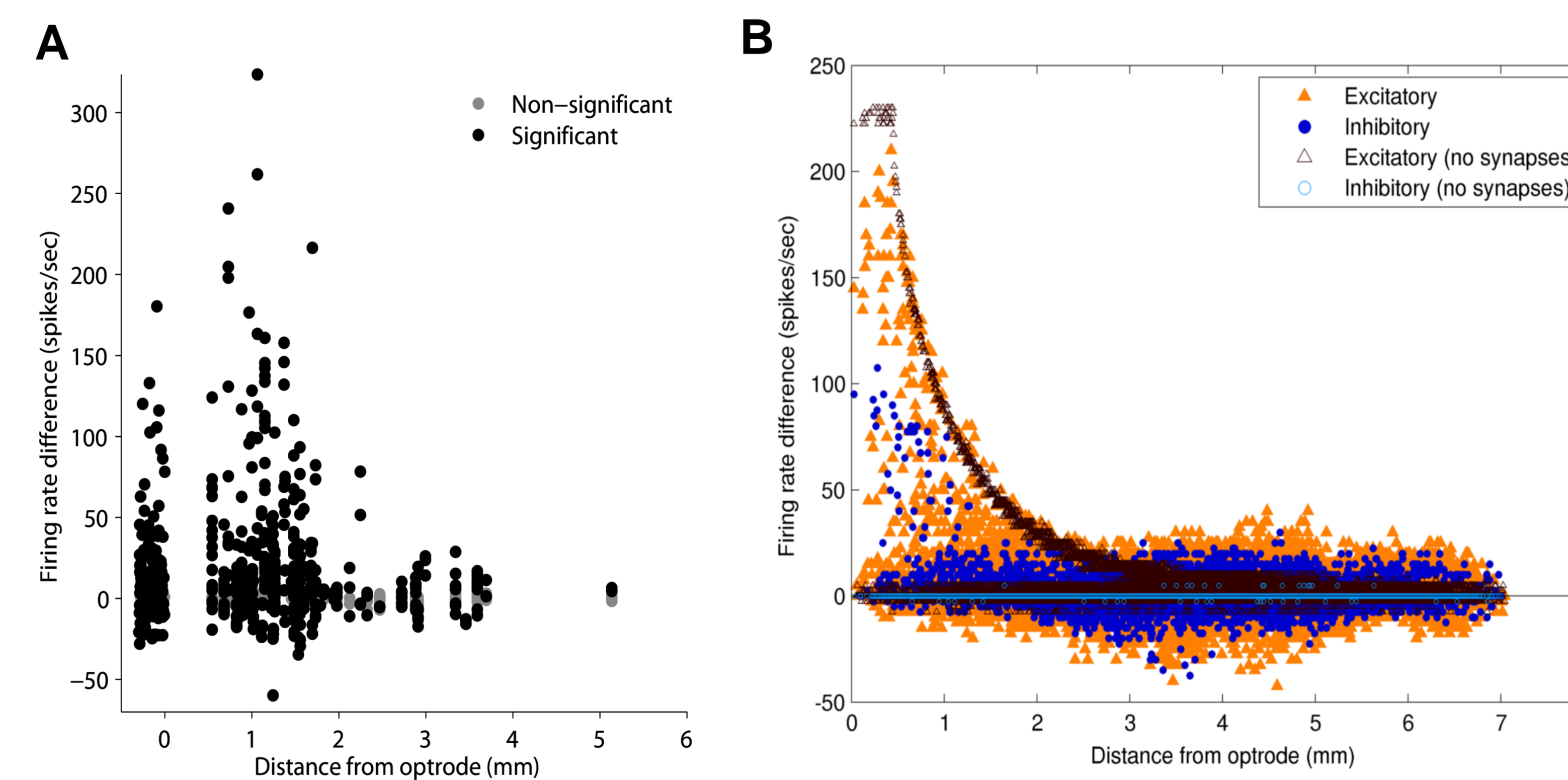


**Fig. 2:** (A) Layout of the model. The efferent connections from a single layer 5 pyramidal cell are shown (black lines). (B) Connectivity of the model. Color shows normalized effective connectivity (probability  $\times$  weight) from rows to columns, with red denoting excitation and blue denoting inhibition. E = excitatory pyramidal neuron; I = inhibitory interneuron; R = regular firing; B = bursting; F = fast-spiking; L = low-threshold spiking.

## 3. Results



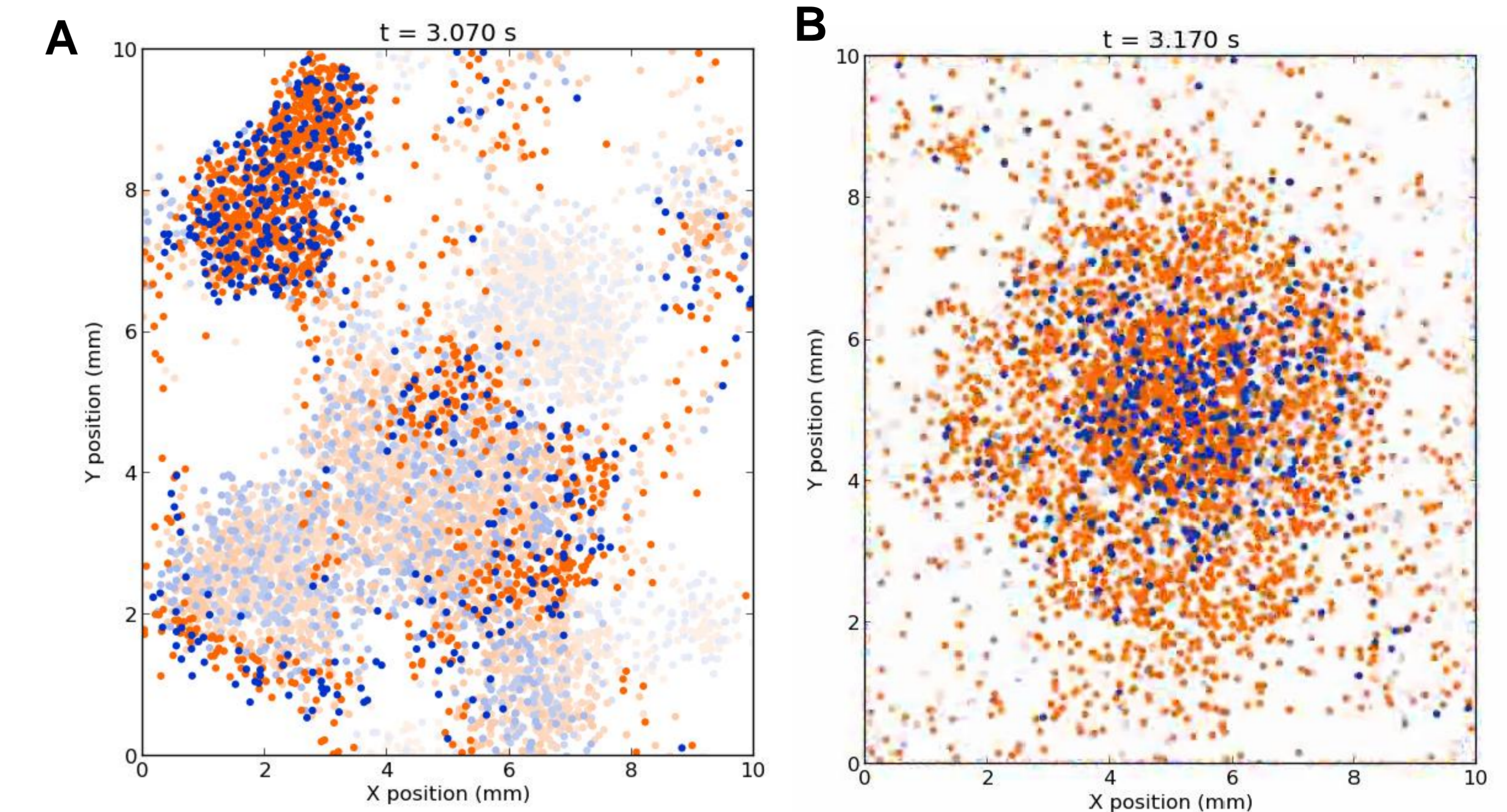
**Fig. 3:** Experimental data from the awake subject, showing (A) a spike raster and (B) a peristimulus time histogram. Four different optogenetic stimulation frequencies were used (colors), with roughly 50 single- or multi-unit activities available for each.



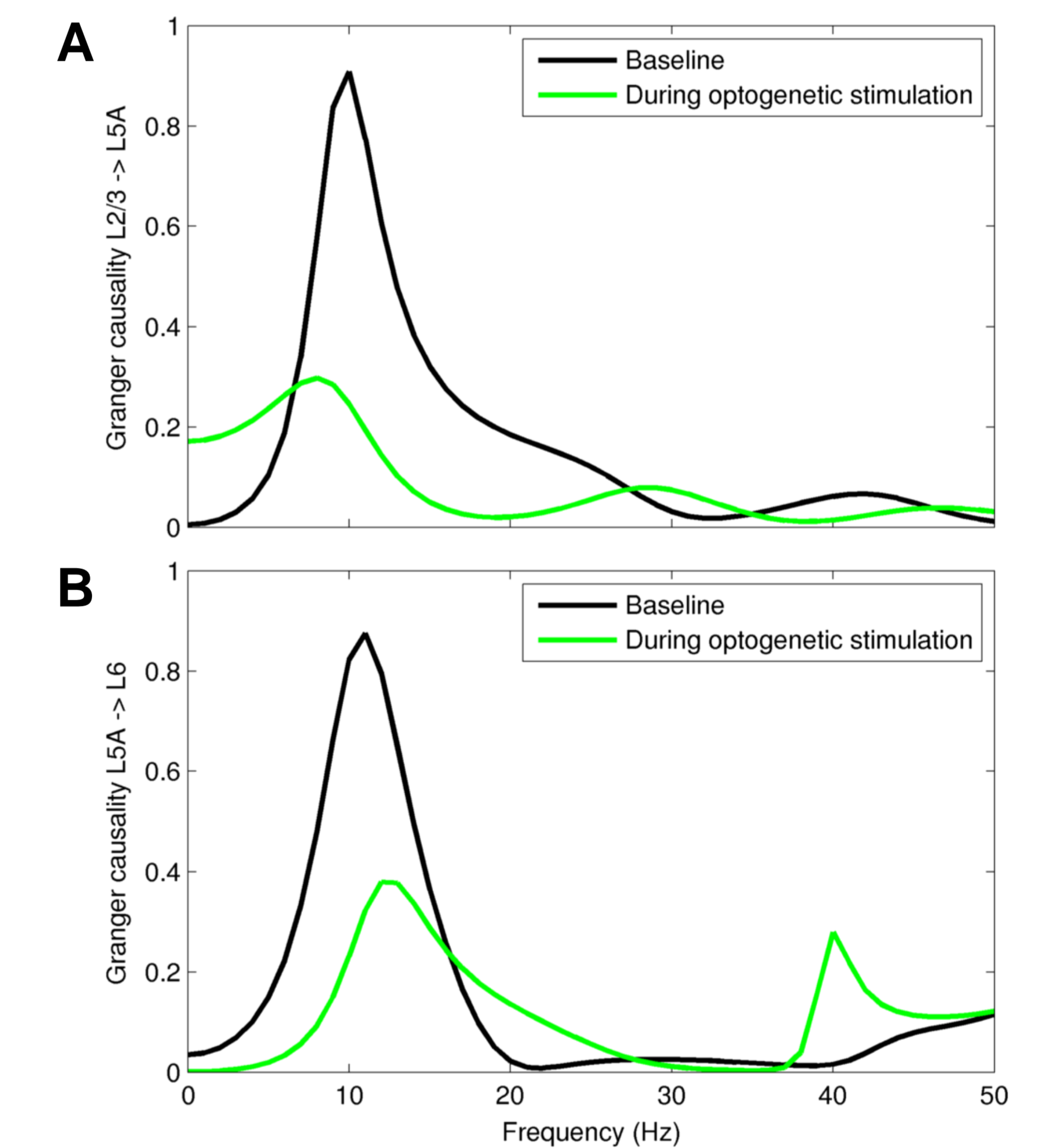
**Fig. 5:** (A) Experimental and (B) simulated responses to optogenetic stimulation. In both cases, firing rates decreased with lateral distance from the optrode. For the simulated response, filled dots show the response with connections; hollow markers show the response without connections.

## 4. Summary

- To our knowledge, this is the first network model of optogenetics.
- Synaptic connections modulate the network's response to optogenetic stimulation: by increasing the radius of activation, and by increasing response heterogeneity (including inhibition of some cells).
- Optogenetic stimulation may be used to modulate information flow: for example, 40 Hz stimulation suppresses causality in the  $\mu$  rhythm band.
- Future work will investigate if the model can be used to predict the effects of specific optogenetic stimulation protocols.



**Fig. 4:** Spatial dynamics of the simulation. (A) Traveling waves in baseline activity, showing spiking in excitatory (orange) and inhibitory (blue) neurons. (B) Response to optogenetic stimulation, showing focal activation and diffuse activity at greater distances.



**Fig. 6:** Simulated Granger causality (A) from superficial to deep layers, and (B) within deep layers. Optogenetic stimulation perturbs the strong causality in the  $\mu$  rhythm band (10 Hz) and introduces causality at the stimulation frequency (40 Hz).

## References

- [1] Mattis J, et al. (2001). *Nature Methods* 9:159–72.
- [2] Wang J, et al. (2011). *IEEE Engineering in Medicine and Biology*.
- [3] Adamantidis, et al. (2007). *Nature* 450:420–4.
- [4] Izhikevich EM, Edelman GM (2008). *Proc Natl Acad USA* 105:3593–8.
- [5] Kerr CC, et al. (2013). *Front Comput Neurosci* 7:1–14.

## Acknowledgement

This work was supported by DARPA Grant N66001-10-C-2008.

## Further information

E-mail: [cliffk@neurosim.downstate.edu](mailto:cliffk@neurosim.downstate.edu) | Web: [neurosimlab.org](http://neurosimlab.org)