

# Bayesian Inference of Neural Activity and Connectivity from All-Optical Interrogation of a Neural Circuit

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## Problem + Project Goals

All-optical techniques (simultaneous + *in vivo*)

1. 2-photon optogenetics → drive spikes in neurons
2. Calcium imaging → record fluorescence at cellular resolution

Goal: infer **circuit mapping** and individual neuron **spiking activity** from this data

## Approach + Methodology

Global Bayesian inference strategy where we **jointly infer distributions** over the spikes and unknown connections

Why is this possible?

- GPU computing
- Automatic differentiation libraries
- Variational autoencoders

## Conclusions

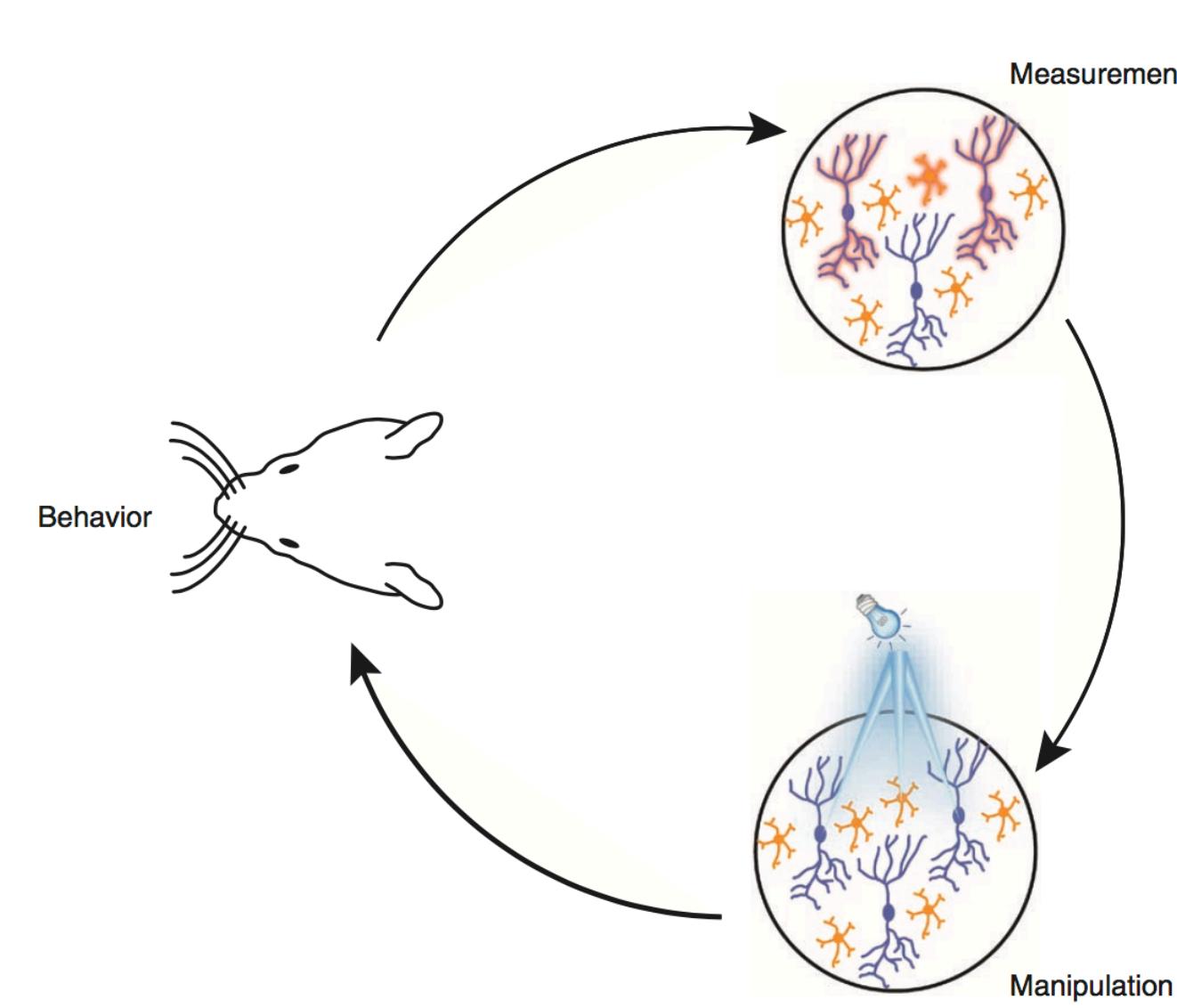
- Data shows evidence of sparse connectivity
- Inferred weights are consistent with known properties of neural circuits
- Joint inference is better than a pipeline

**This is the first fully Bayesian model of calcium imaging designed for perturbation data that is able to extract posteriors over such a wide range of parameters with such efficiency**

## 1 Data + Variational Inference

### Optogenetic Experiment

- Mouse layer 2/3 of V1
- GCaMP6s calcium imaging, C1V1 opsin
- Stimulate five random cells twice per second, observe activity in rest of network
- Spontaneous data recording



### Bayes' Rule

$$P(z|x) = \frac{P(x|z)P(z)}{P(x)} \quad \text{posterior}$$

latent variables  $z$        $P(z)$  prior  
generative model       $P(x|z)$  likelihood  
data       $P(x,z)$  joint  
 $P(x|z)P(z)$   
 $P(z|x)P(x)$

### Model Evidence

Log likelihood function where some parameters have been marginalized

$$P(x) = \int P(x|z)P(z)dz$$

- Computationally intractable
- Hinders application of Bayesian techniques to large-scale data

## 2 Model Framework

### Recognition Model

VI + DNN, create posterior  $Q(z|x)$  intended to approximate  $P(z|x)$

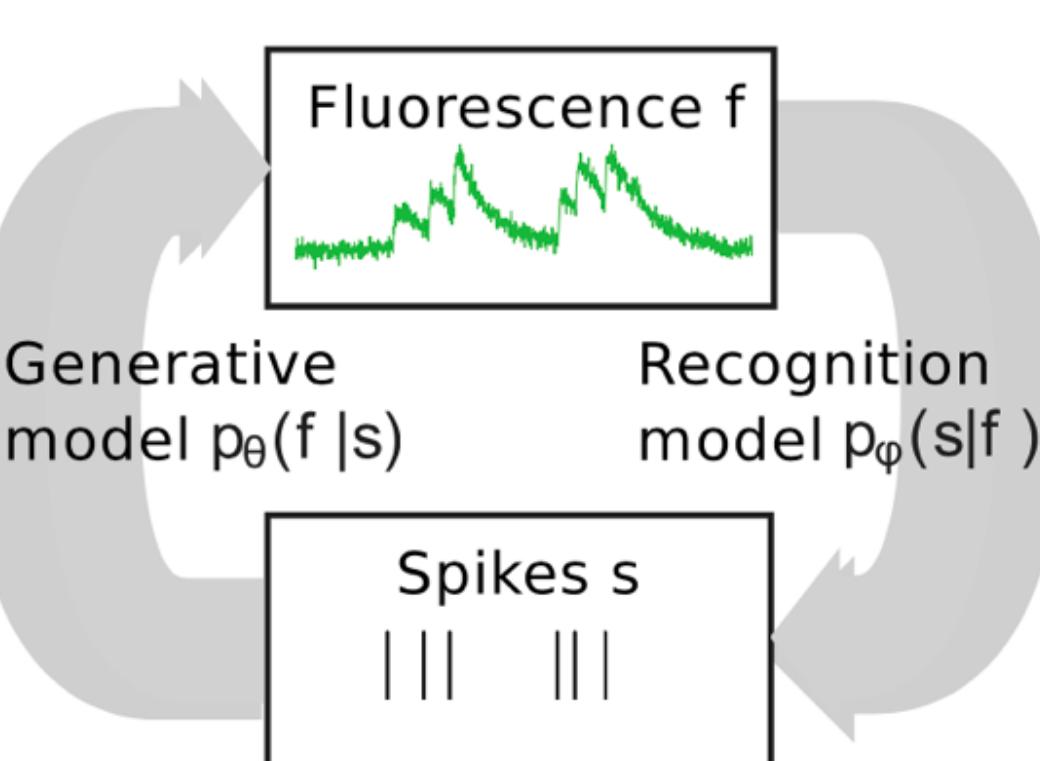
$$\log P(x) \geq E_{Q(z|x)}[\log P(x, z) - \log Q(z|x)]$$

Factorize the approximate posterior over the spikes

$$Q(s(t)|v(t)) = \text{Bernoulli}(s(t); \sigma(v(t)))$$

$$v(t) = \text{MLP}(f(t-T:t+T)) + D^e W^{se} e(t) + b^s$$

NN that takes a window of traces and nonlinearly maps:  
20 features → 2 standard layers → single value



### Generative Model

$$P(f(t)) = N(f(t); r(t), \Sigma^f)$$

Fluorescence signals at time  $t$

Reconstruction with Gaussian noise

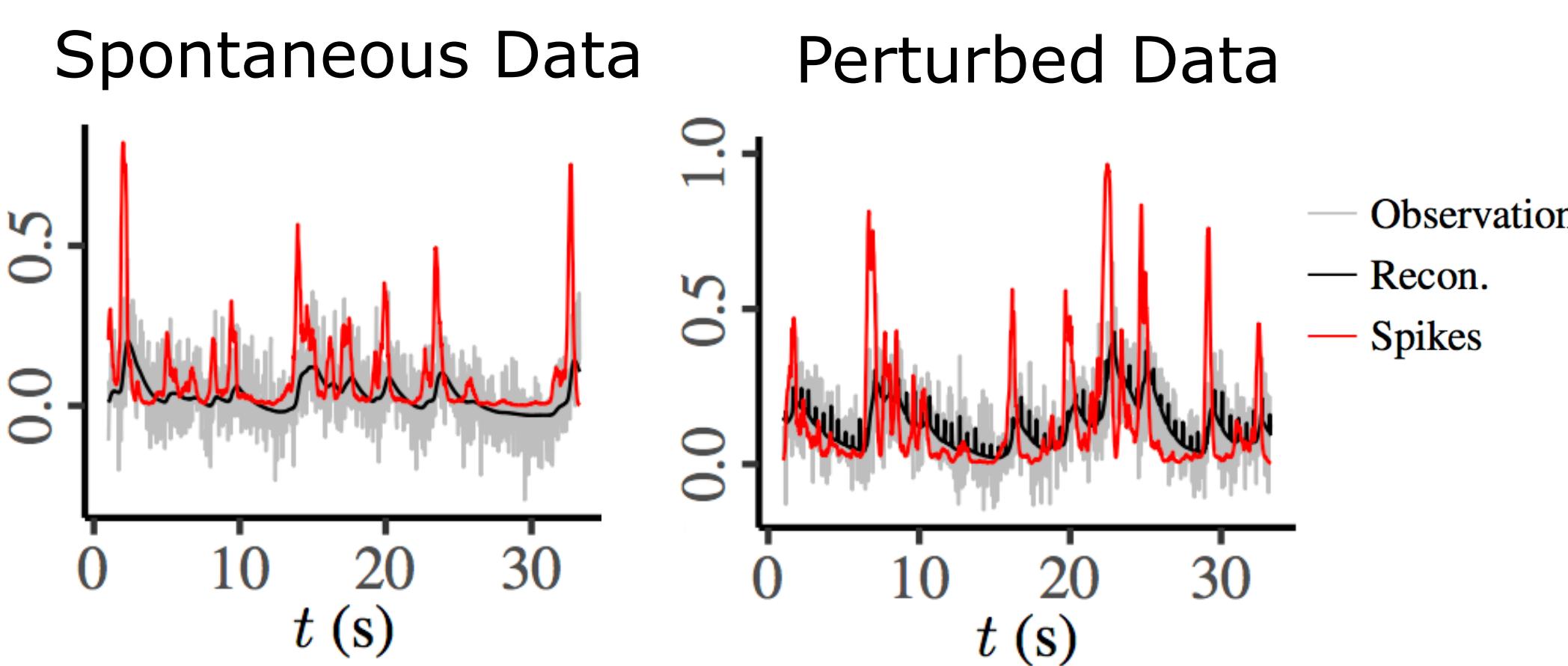
Learned, diagonal covariance matrix

- ① Generate spikes at times step  $t$

- ② Generate calcium fluorescence signals from the spikes

## 3 Results

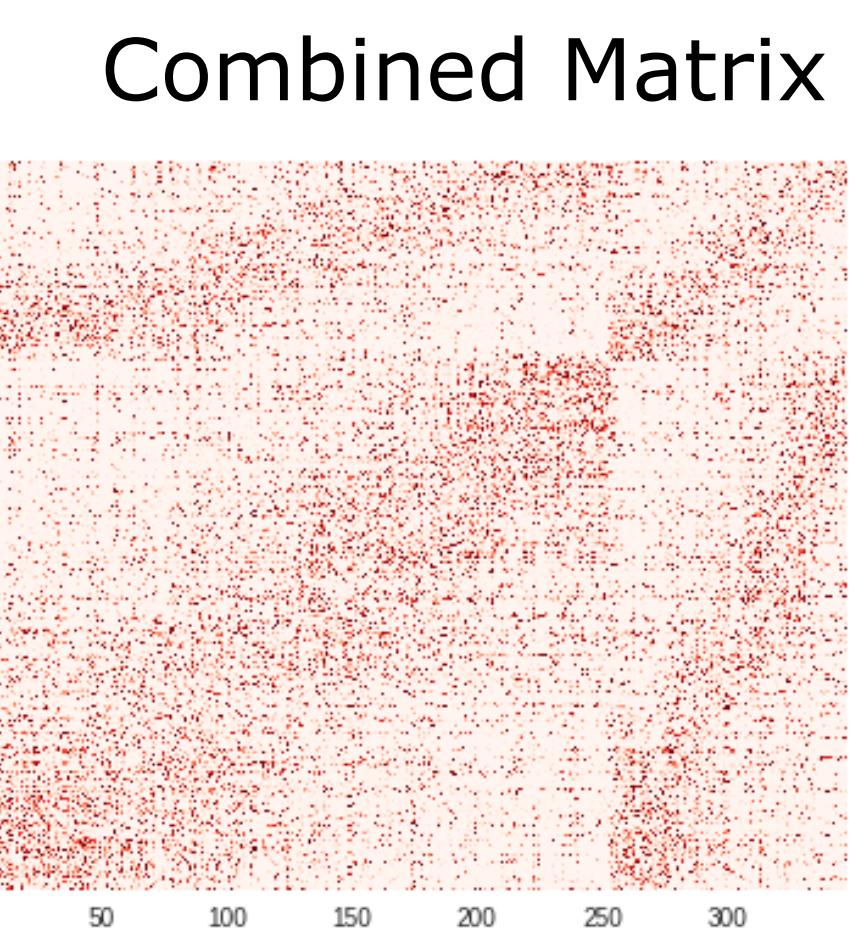
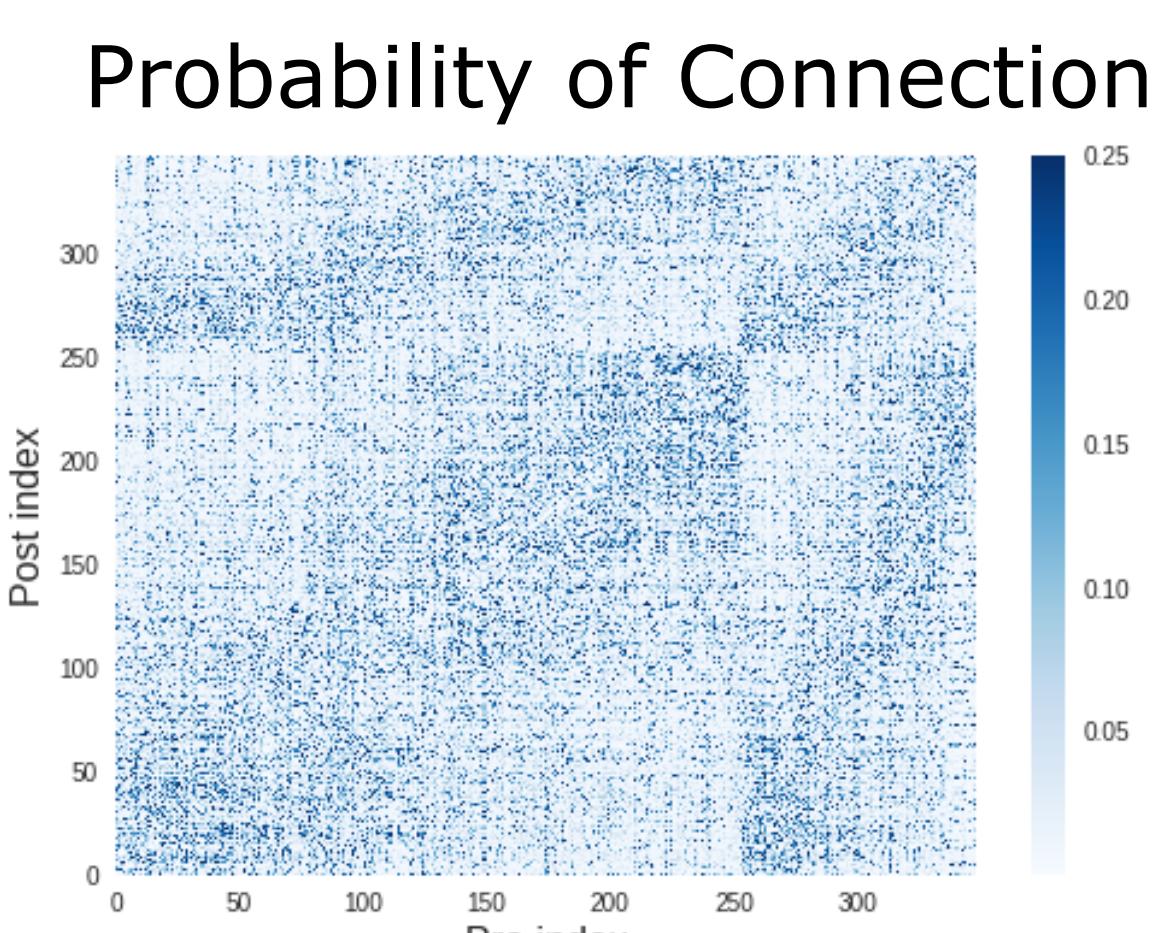
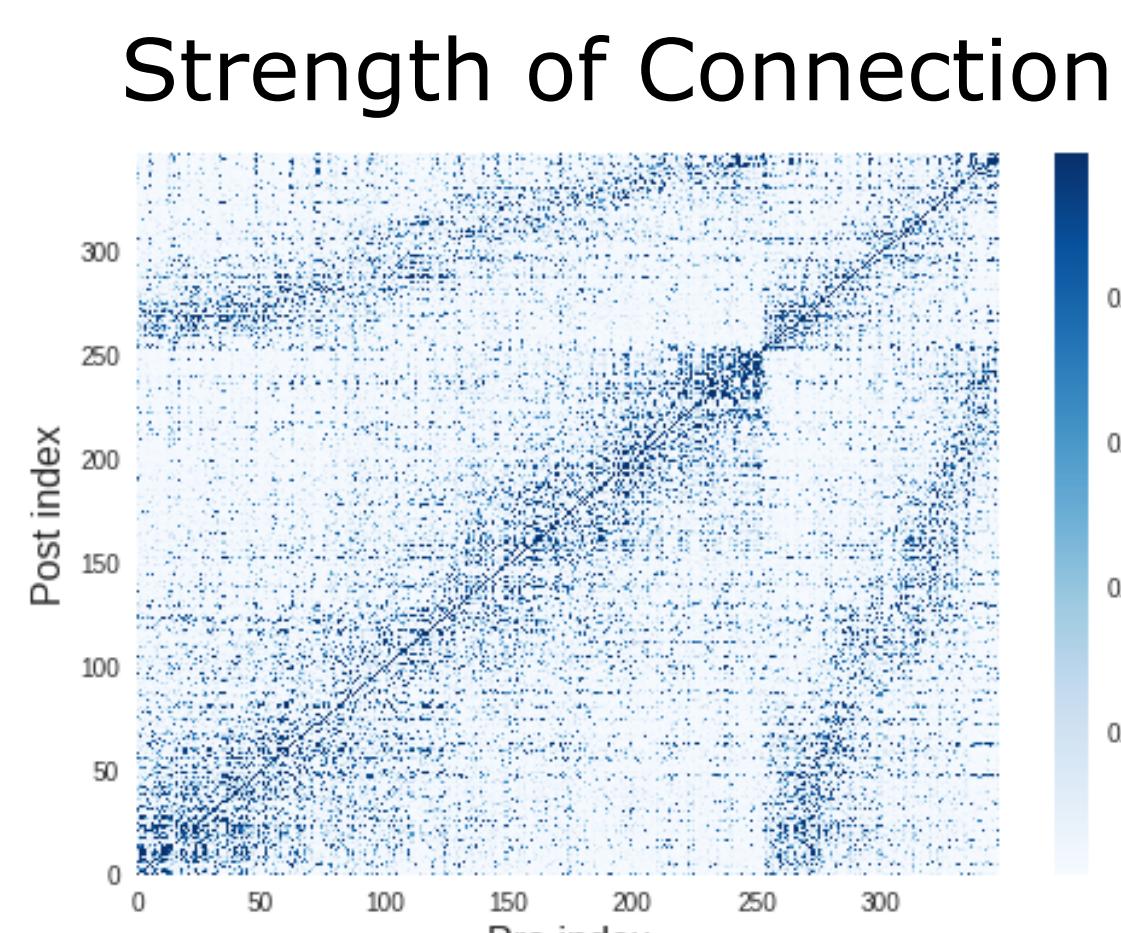
### Spike Inference



### Self Stimulation-Triggered Averages

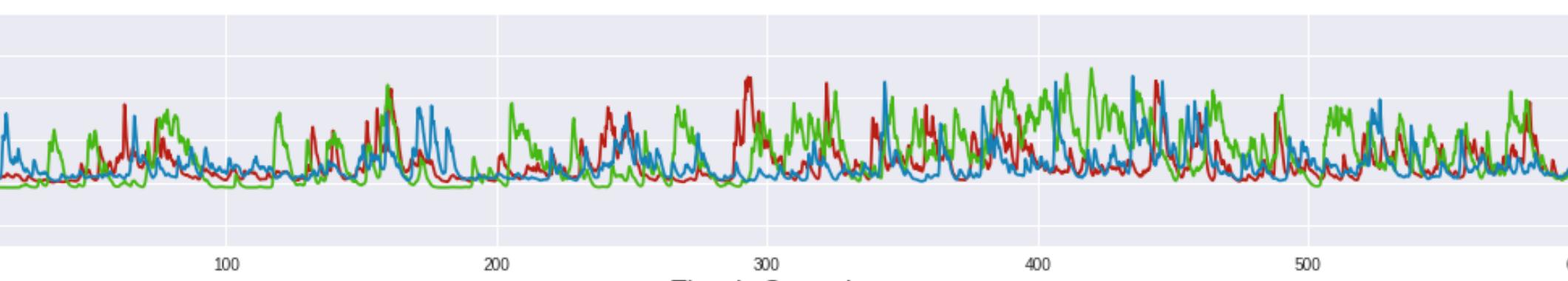


### Synaptic Connectivity Matrices

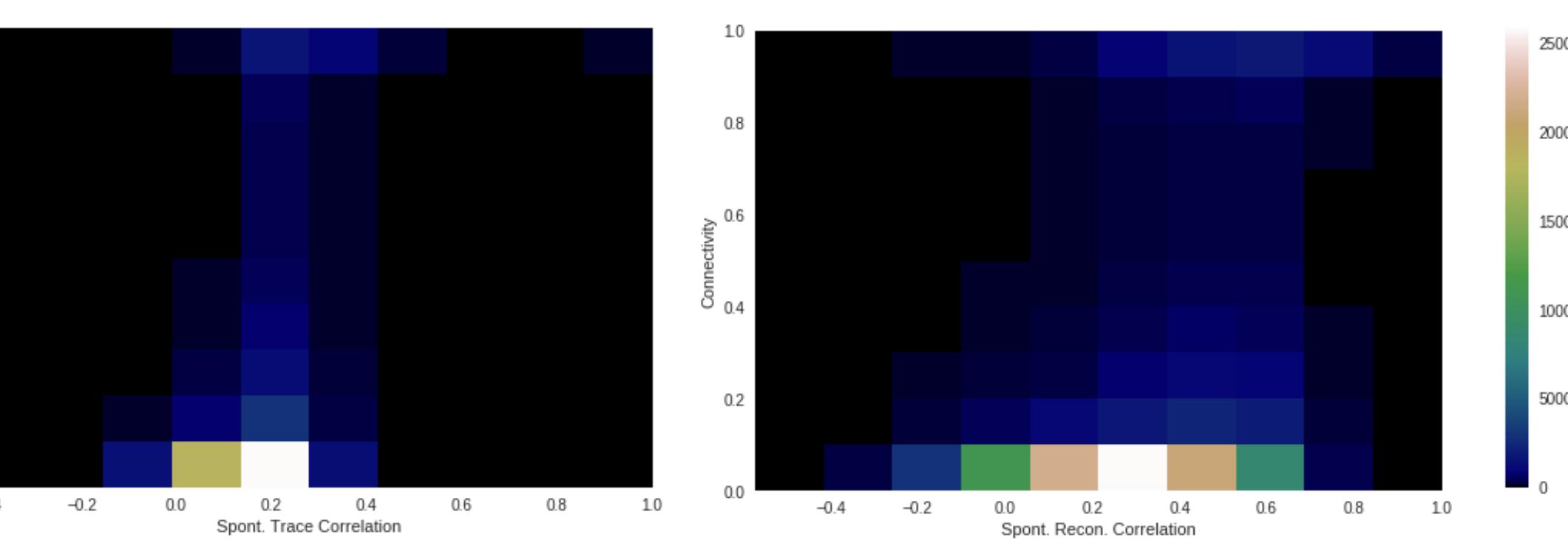


### Confirming Synapse Predictions + Need for Sparser Inferences

#### Reconstructed Traces of Connected Neurons



#### Correlation Coefficients



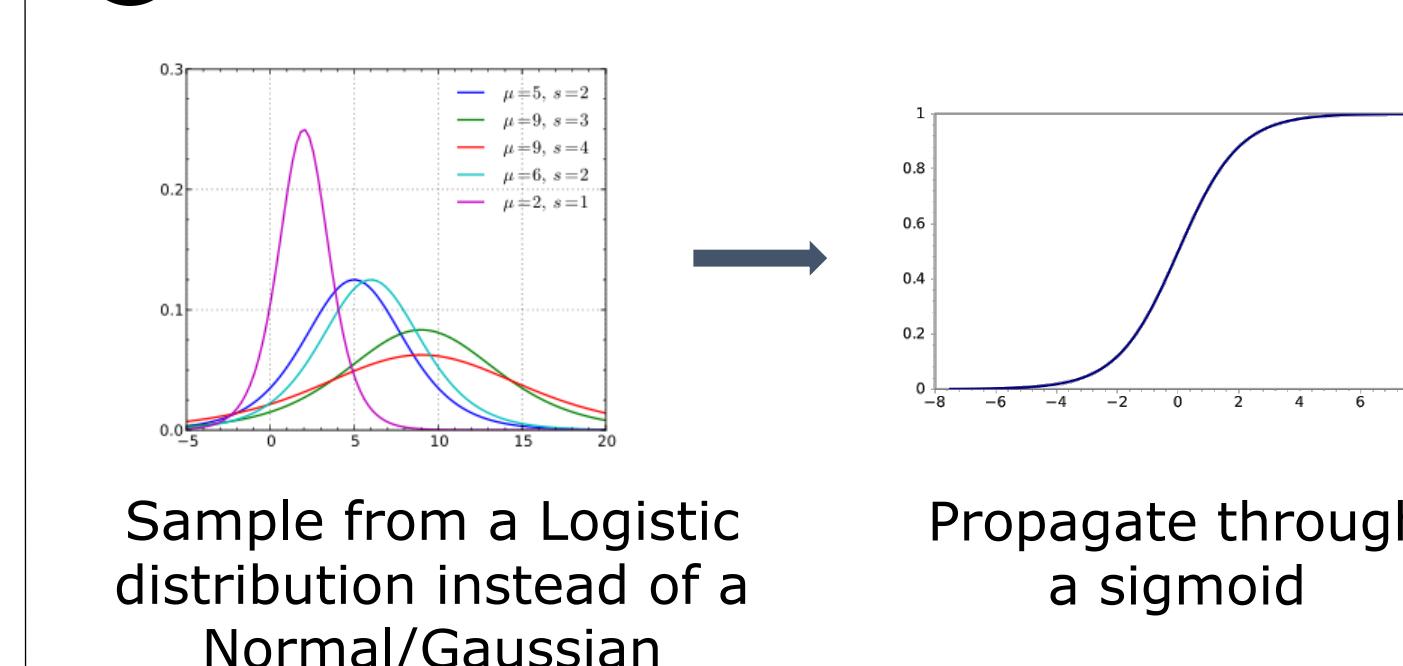
## 4 Next Steps

### Improving the Model

- ① Upsampling to increase the resolution of the spike probabilities

Calcium Traces	Perturbations
$[0.32 \ 0.22]$	$[1 \ 0]$
$[0.57 \ 0.09]$	$[0 \ 1]$
$\downarrow$ linear interpolation	$\downarrow$ interpolate with zeros
$[0.32 \ 0.22]$	$[1 \ 0]$
$[0.445 \ 0.155]$	$[0 \ 0]$
$[0.57 \ 0.09]$	$[0 \ 1]$

- ② Gumbel method



This work was supported by Howard Hughes Medical Institute and Janelia Research Campus as part of the Janelia Undergraduate Scholars Program. We thank Adam Packer, Thomas Mrsic-Flogel, and others for providing the necessary data to make this project possible.

### Acknowledgements

- [1] Aitchison, L., Russell, L., Packer, A., Yan, J., Castonguay, P., Häusser, M., & Turaga, S. Model-based Bayesian inference of neural activity and connectivity from all-optical interrogation of a neural circuit. *NIPS* (2017, under review).
- [2] Speiser, A., Yan, J., Archer, E., Buesing, L., Turaga, S., & Macke J.H. Fast amortized inference of neural activity from calcium imaging data with variational autoencoders. *NIPS* (2017, under review).
- [3] Packer, A.M., Russell, L.E., Dagleish, H.W., & Häusser, M. Simultaneous all-optical manipulation and recording of neural circuit activity with cellular resolution *in vivo*. *Nature Methods*. vol. 12, no. 2, pp. 140–146, (2015).

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### Adaptation

Refactor model to **plug-and-play** spike-inference and fitting methods

Optogenetic + observational datasets

### References