

# 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*)
- 2-photon optogenetics → drive spikes in neurons
  - 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***

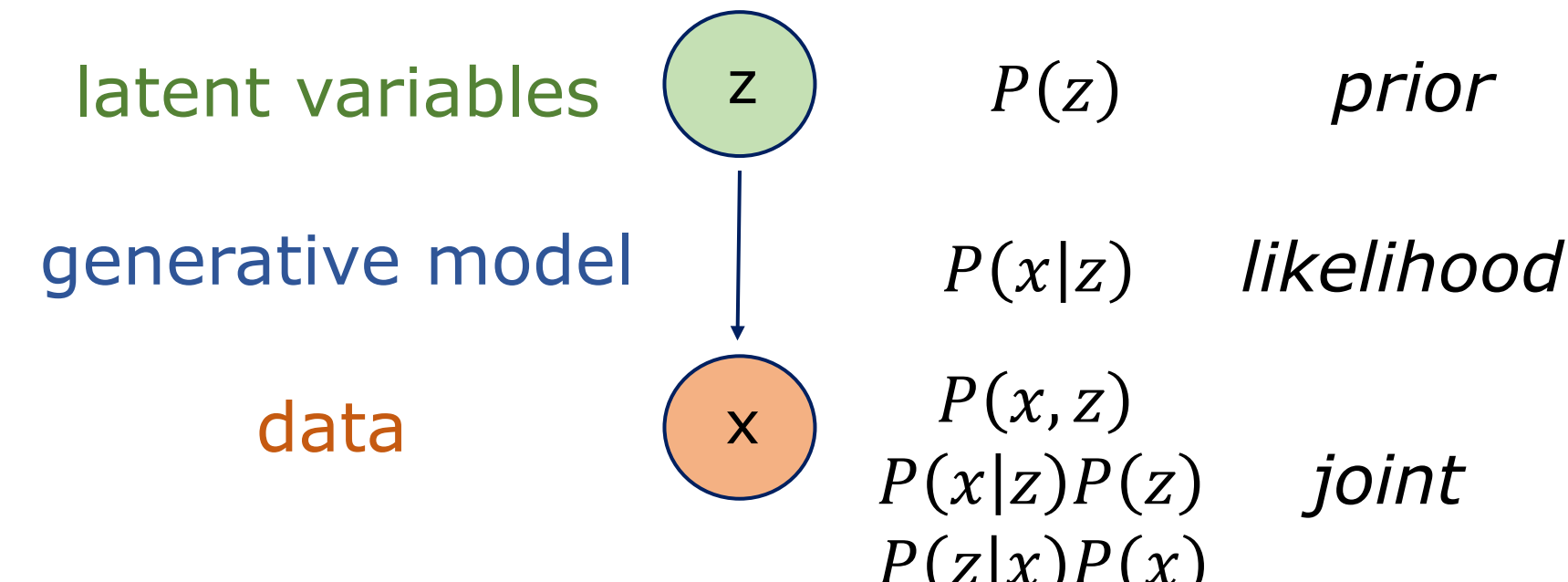
## 1 Data + Variational Inference

### 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

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

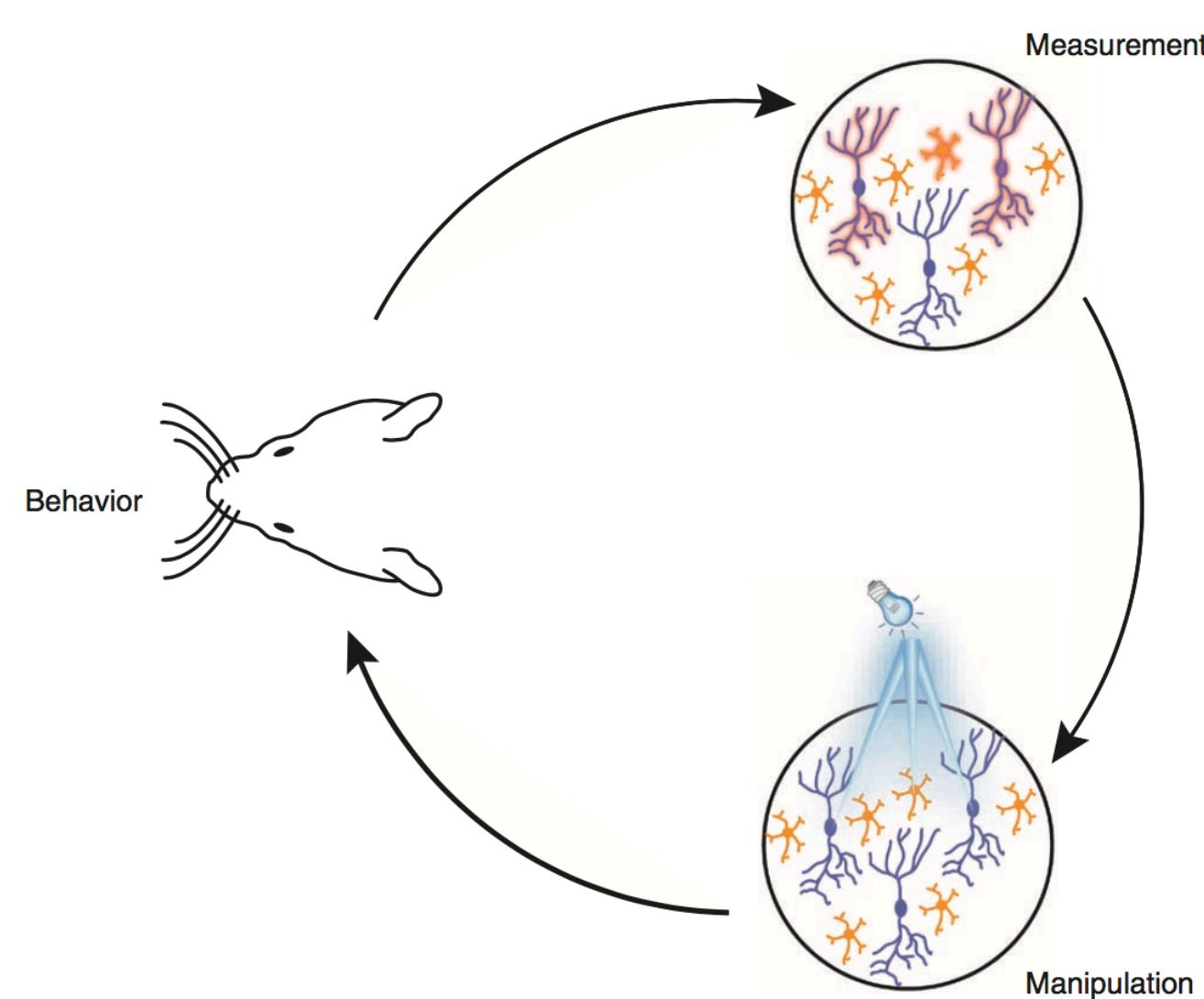


### Model Evidence

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
- VI solves this!



## 2 Model Framework

### Recognition Model

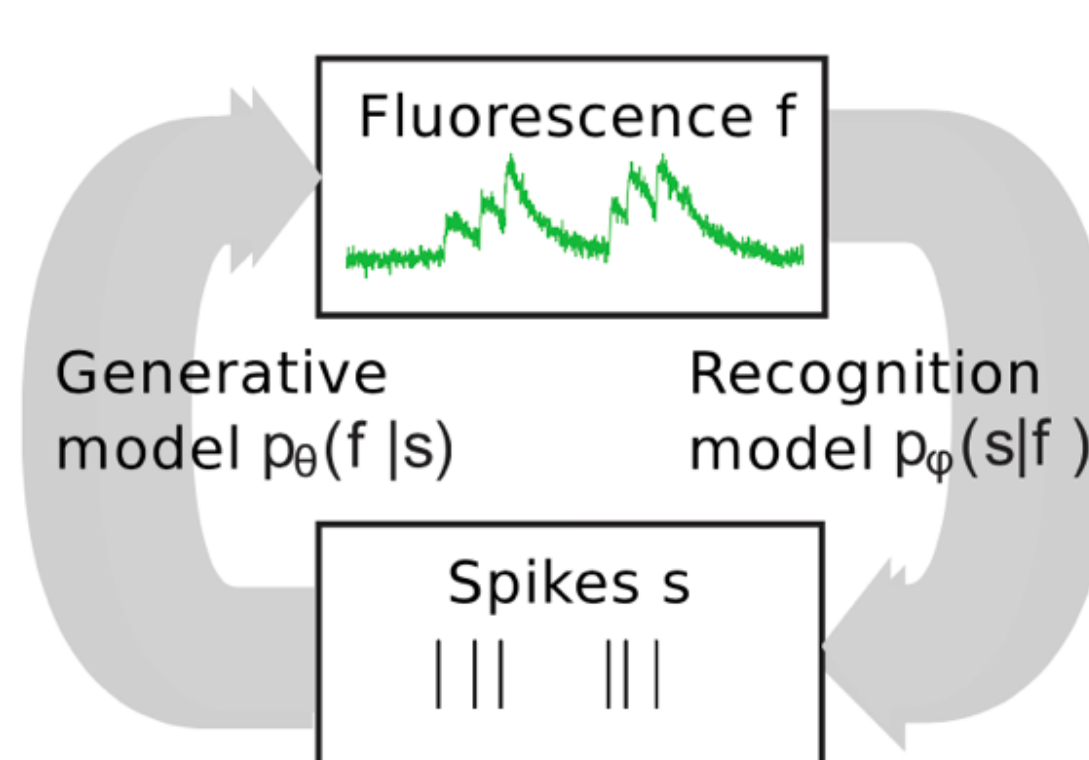
VI + DNN, create posterior  $Q(z|x)$  intended to approximate  $P(z|x)$

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

Factorize the approximate posterior over the spikes

$$Q(s(t)|v(t)) = \text{Bernoulli}(s(t); \sigma(v(t)))$$
$$v(t) = \underbrace{MLP(f(t - T:t + T))}_{\text{NN that takes a window of traces and nonlinearly maps: 20 features} \rightarrow 2 \text{ standard layers} \rightarrow \text{single value}} + D^e W^{se} e(t) + b^s$$

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



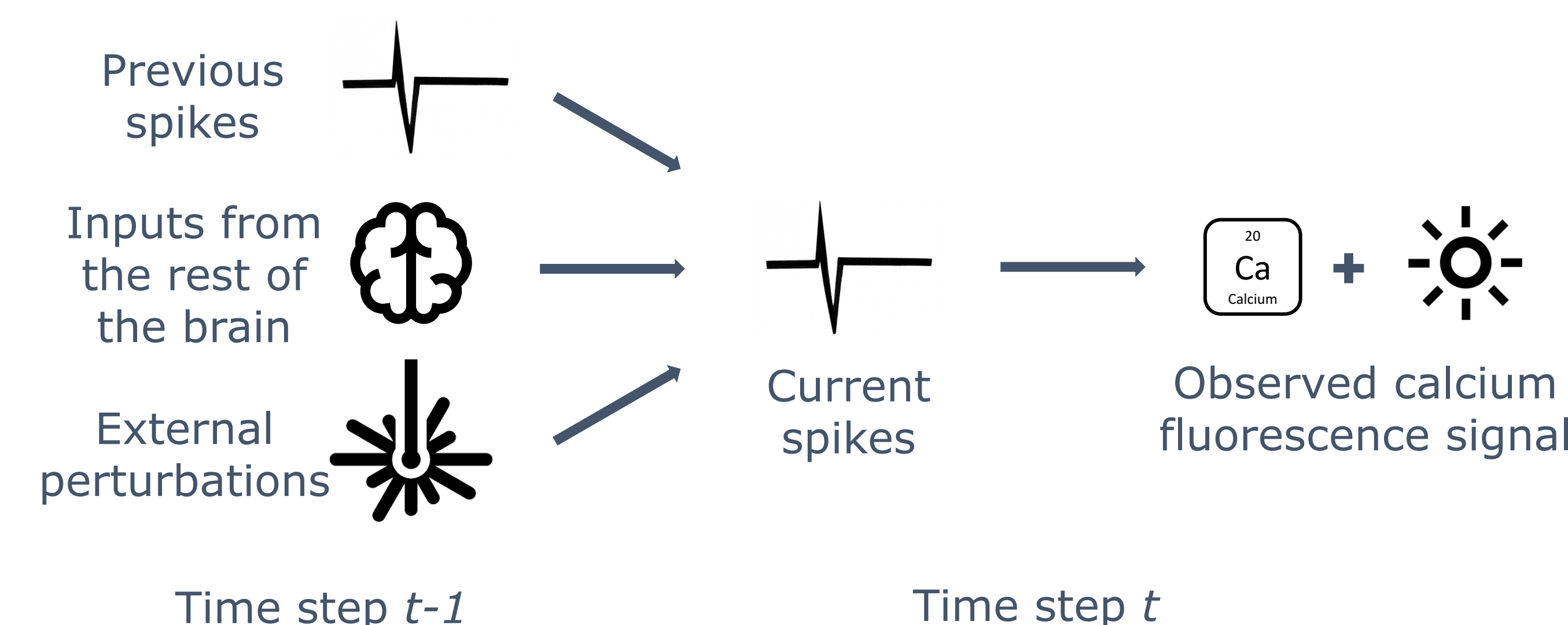
### Generative Model

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

Fluorescence signals at time  $t$  Reconstruction with Gaussian noise Learned, diagonal covariance matrix

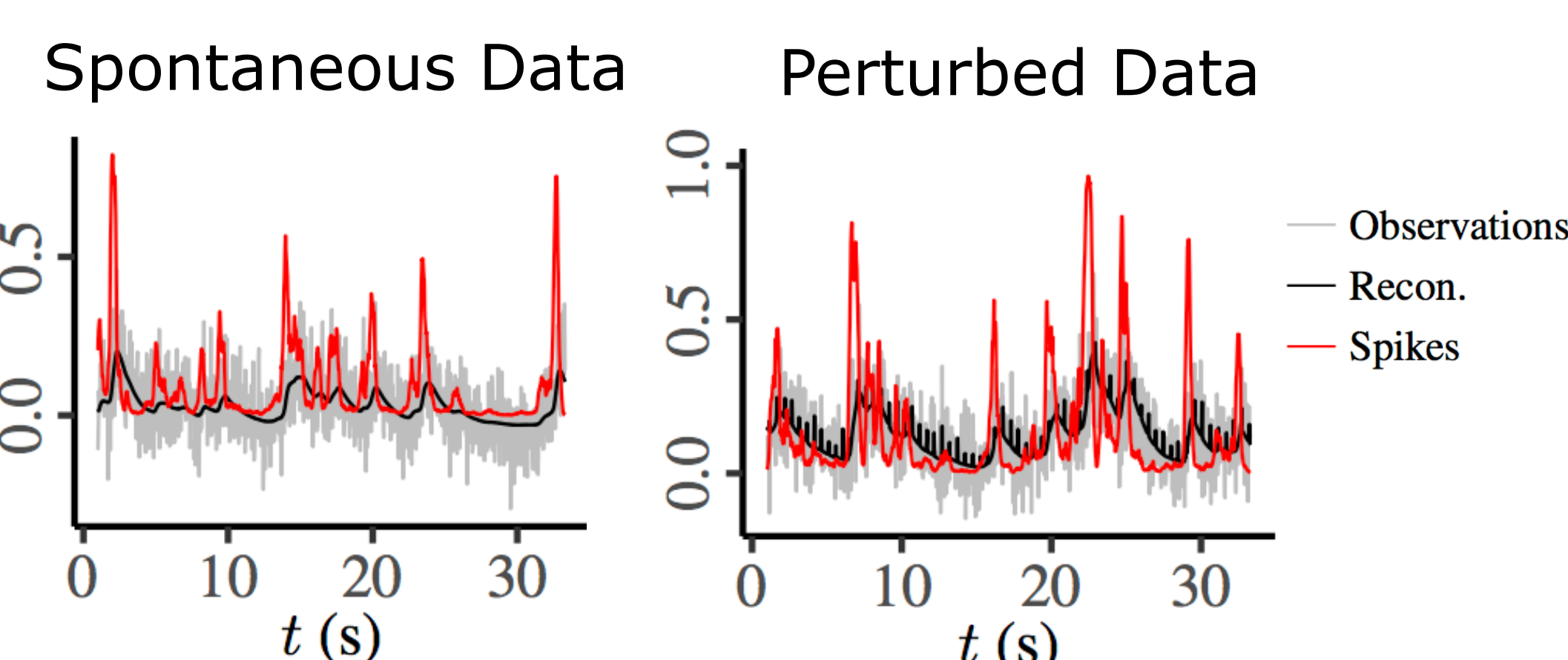
① Generate spikes at times step  $t$

② Generate calcium fluorescence signals from the spikes



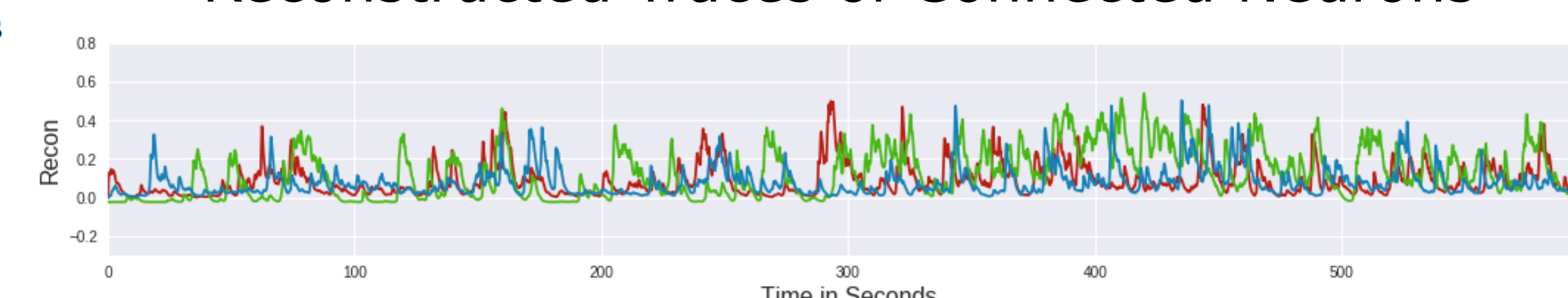
## 3 Results

### Spike Inference

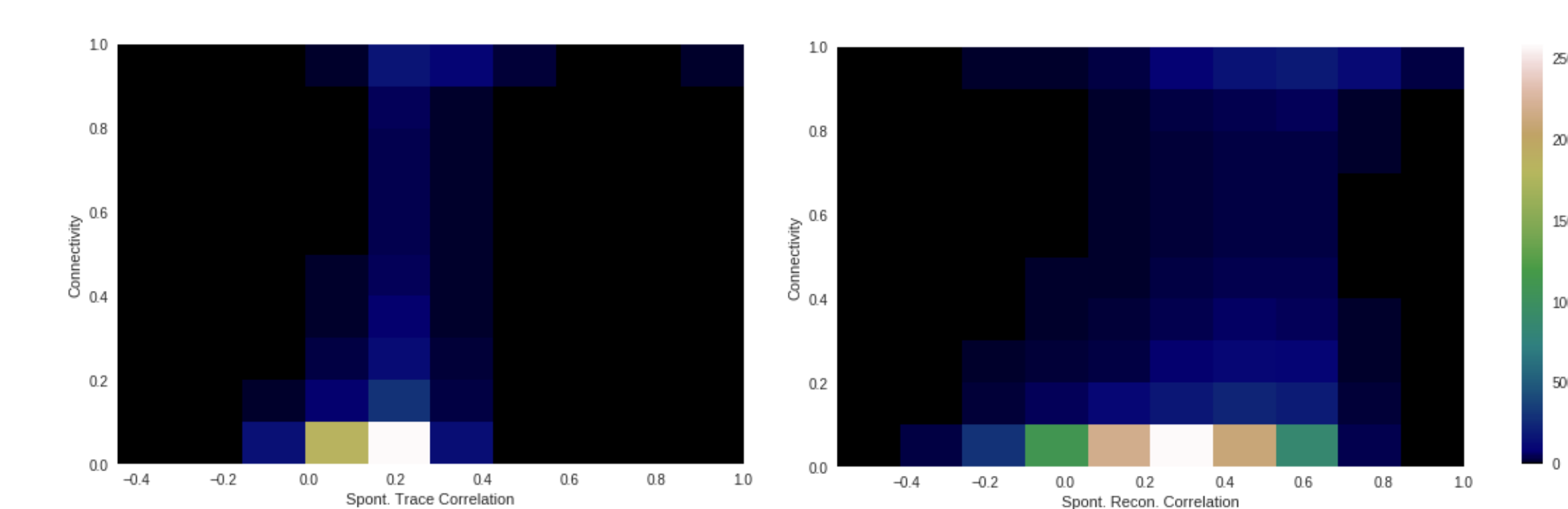


### Confirming Synapse Predictions + Need for Sparser Inferences

#### Reconstructed Traces of Connected Neurons

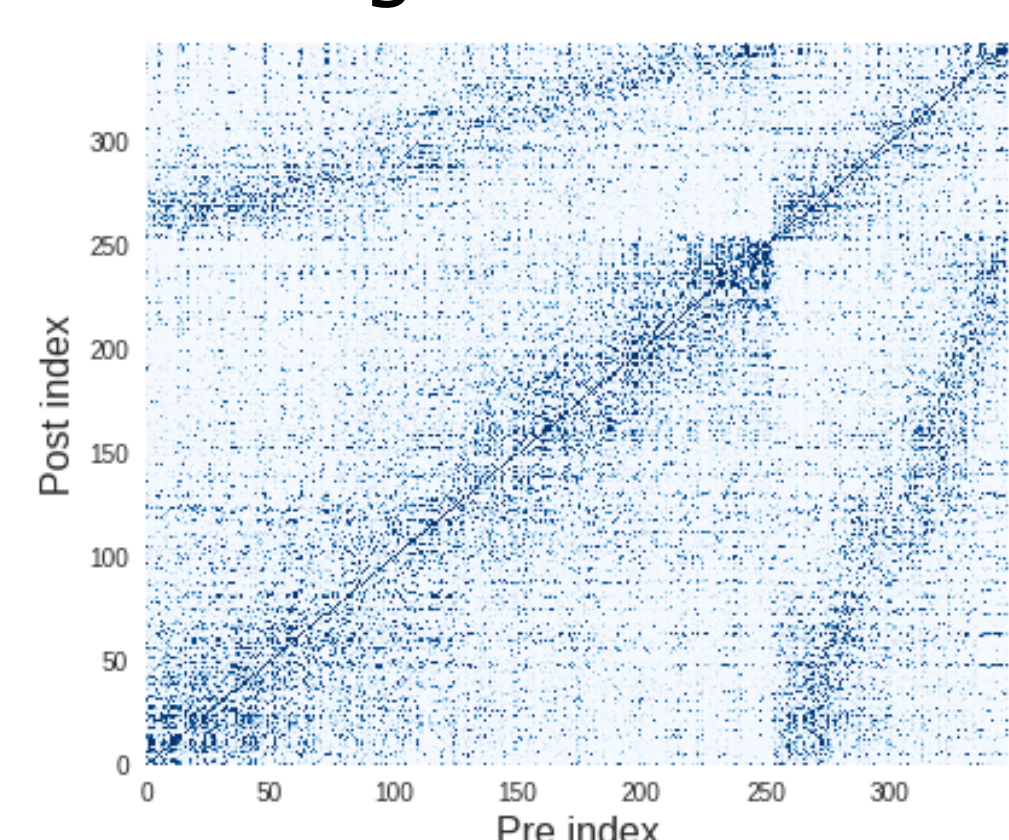


#### Correlation Coefficients

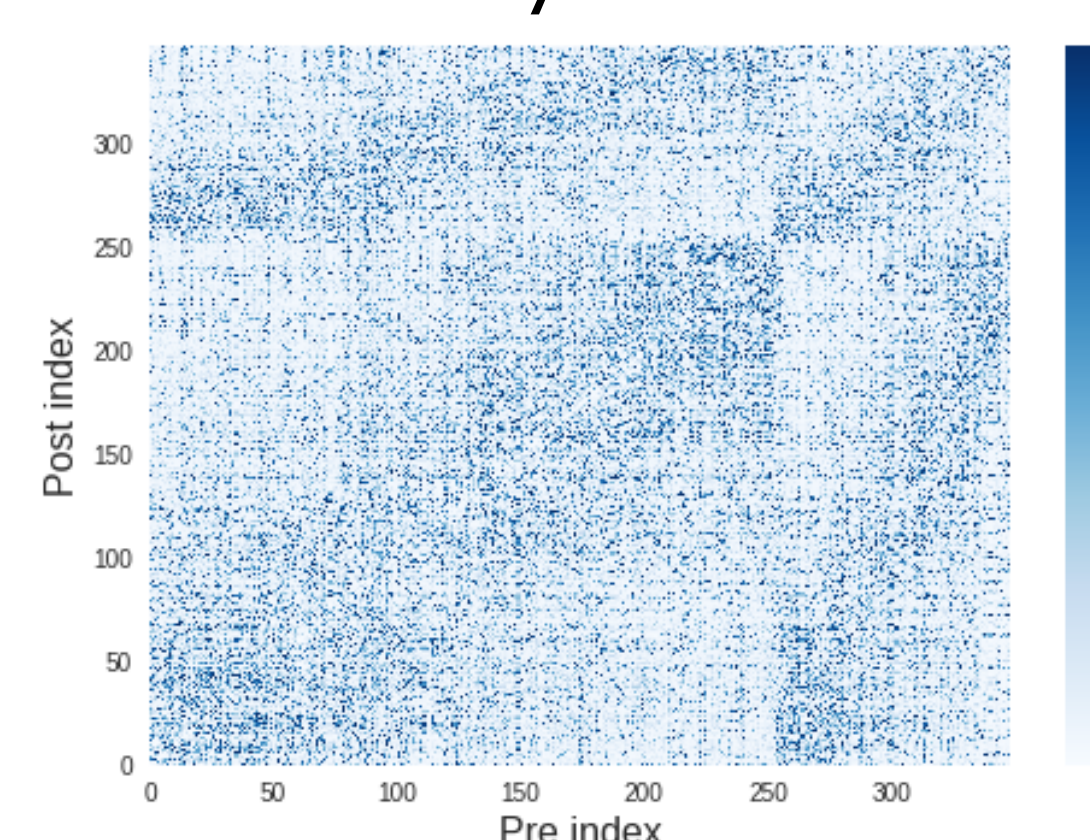


### Synaptic Connectivity Matrices

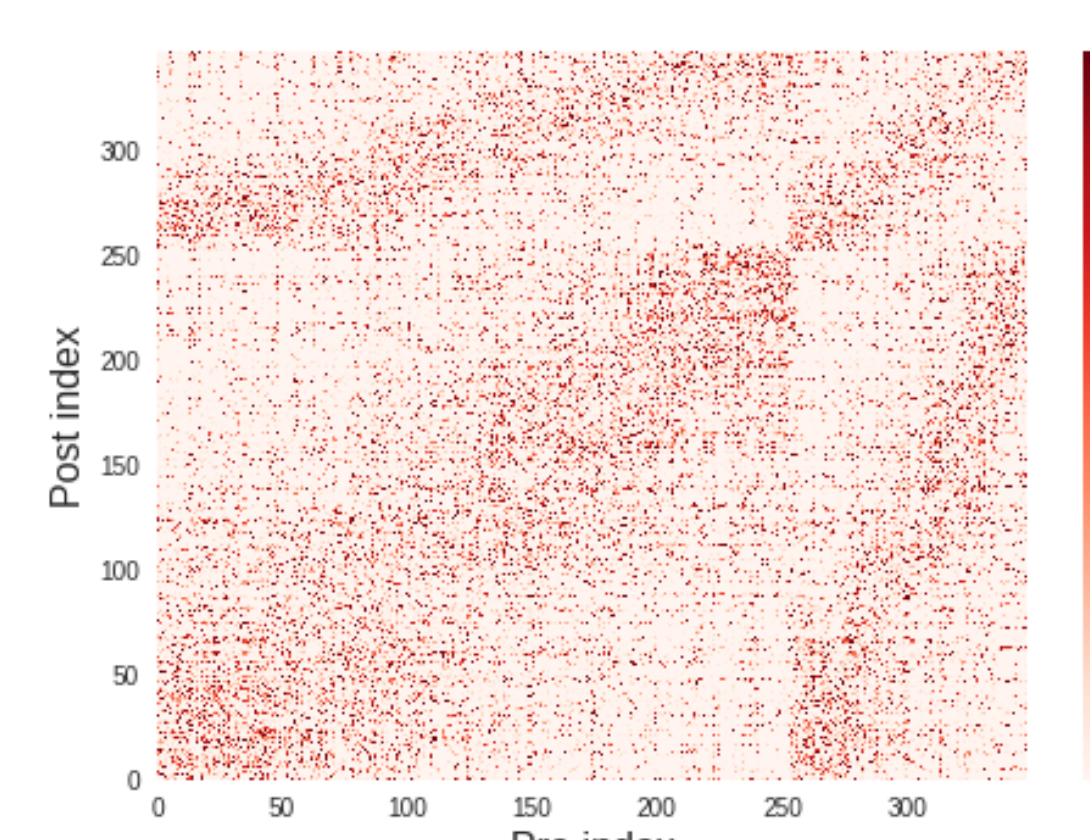
#### Strength of Connection



#### Probability of Connection



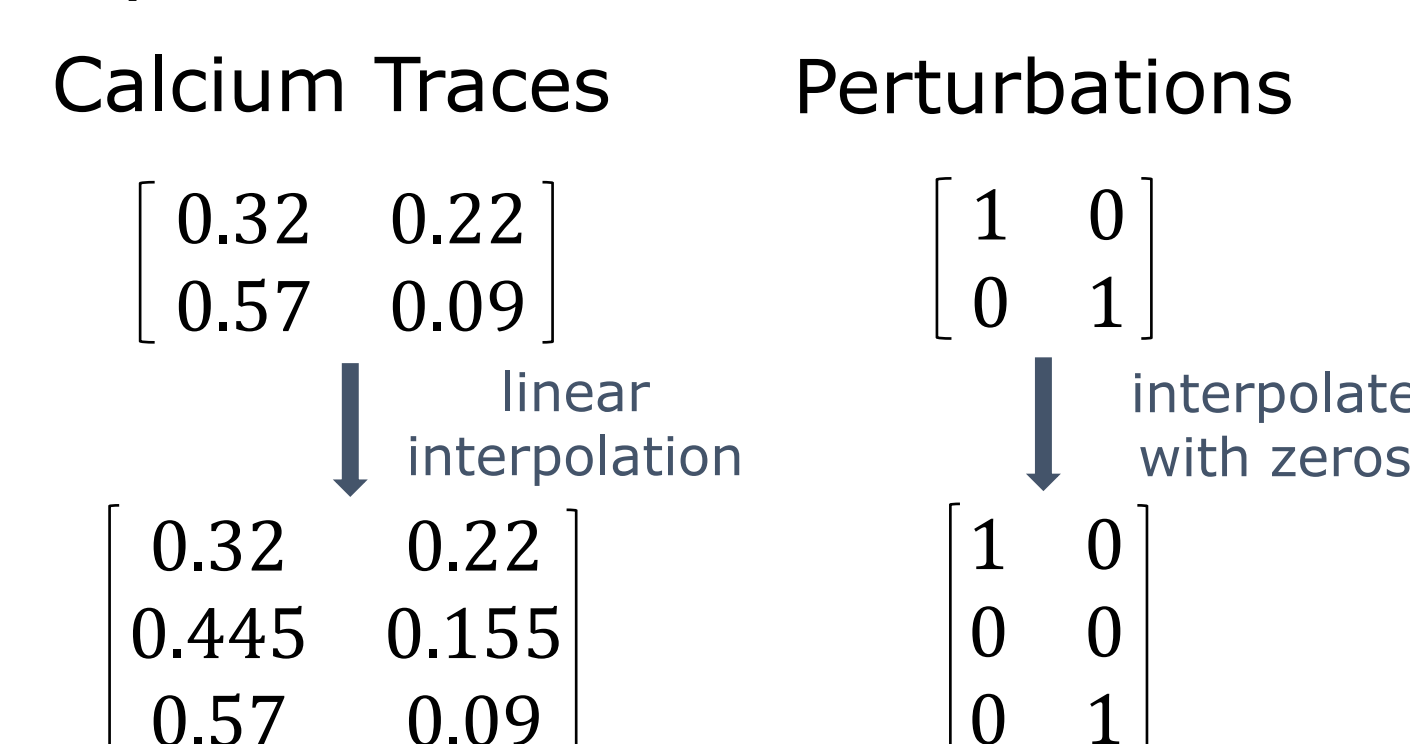
#### Combined Matrix



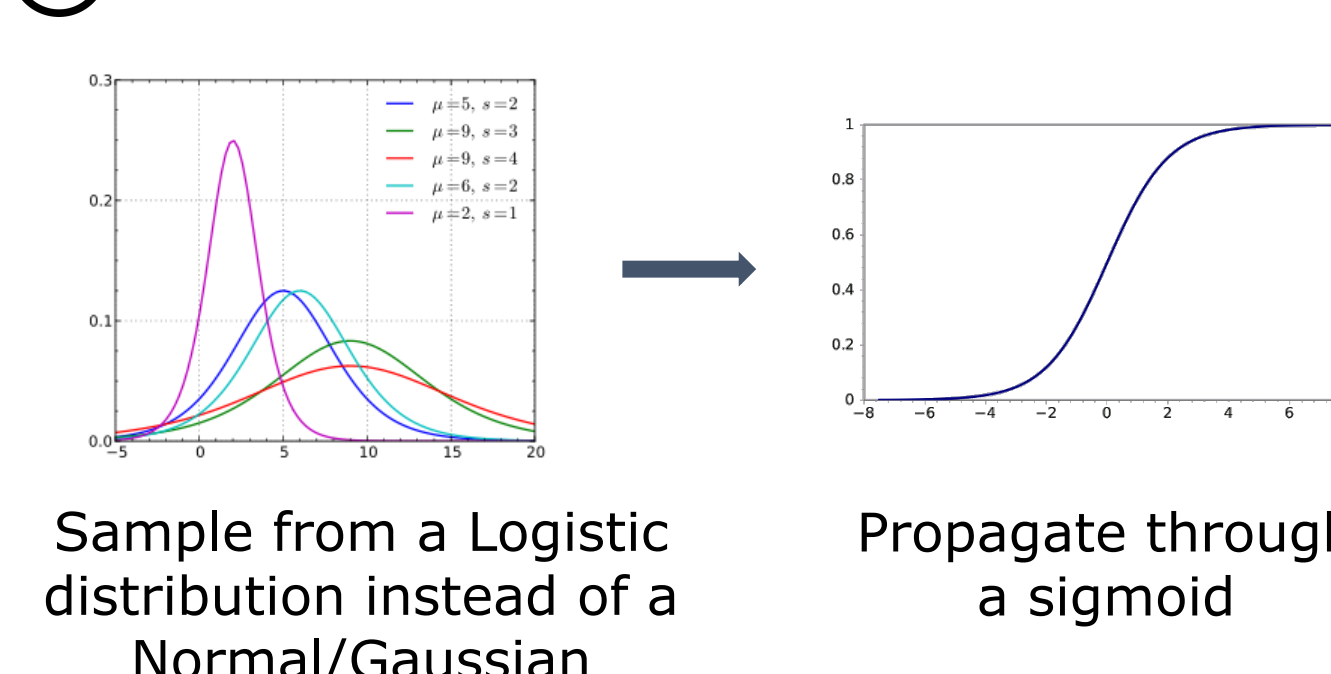
## 4 Next Steps

### Improving the Model

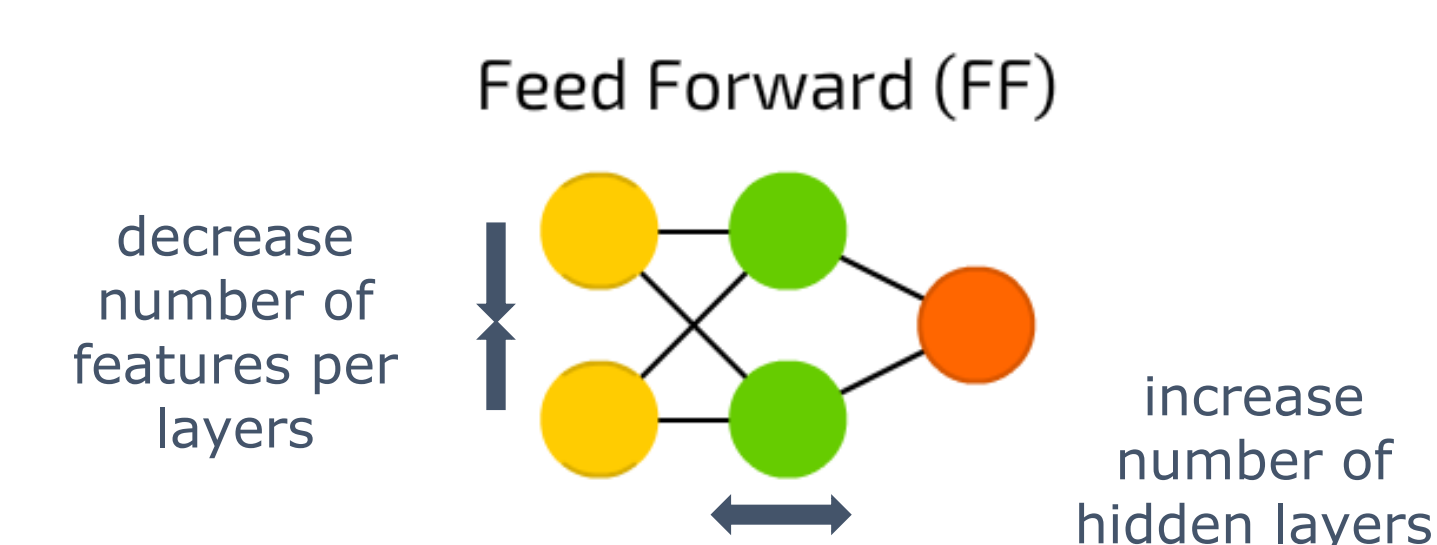
① Upsampling to increase the resolution of the spike probabilities



② Gumbel method



③ Expand convolutional neural network in recognition model



④ Nonlinear generative model

- Linear: instant rise, exponential decay
- Nonlinear: incorporate intracellular dynamics of calcium in neurons
- Possible with Gumbel

### Adaptation

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

Optogenetic + observational datasets

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### References

- [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).
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- [3] Packer, A.M., Russell, L.E., Dalgleish, 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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