# One-hot Generalized Linear Model for Switching Brain State Discovery

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# 1 Introduction

# Task

- Exposing meaningful and interpretable neural interactions is critical to understanding neural circuits.
- Inferred neural interactions from neural signals primarily reflect functional connectivities.
- A classical one-state generalized linear model (GLM) is only able to find a static functional connectivity graph.
- But in a long experiment, subject animals may experience different stages defined by the experiment, stimuli, or behavioral states, and hence functional connectivities can change over time.

# Previous works and our contribution

- To model dynamically changing functional connectivities, prior work employs state-switching GLM with hidden Markov models (i.e., HMM-GLMs).
- However, this lacks biological plausibility, as functional interactions are shaped and confined by the underlying anatomical connectome.
- Our new one-hot HMM-GLM can model the dynamically changing functional connectivity confined by an underlying anatomical connectome, and provide stable and interpretable state transitions.

# 2 Method

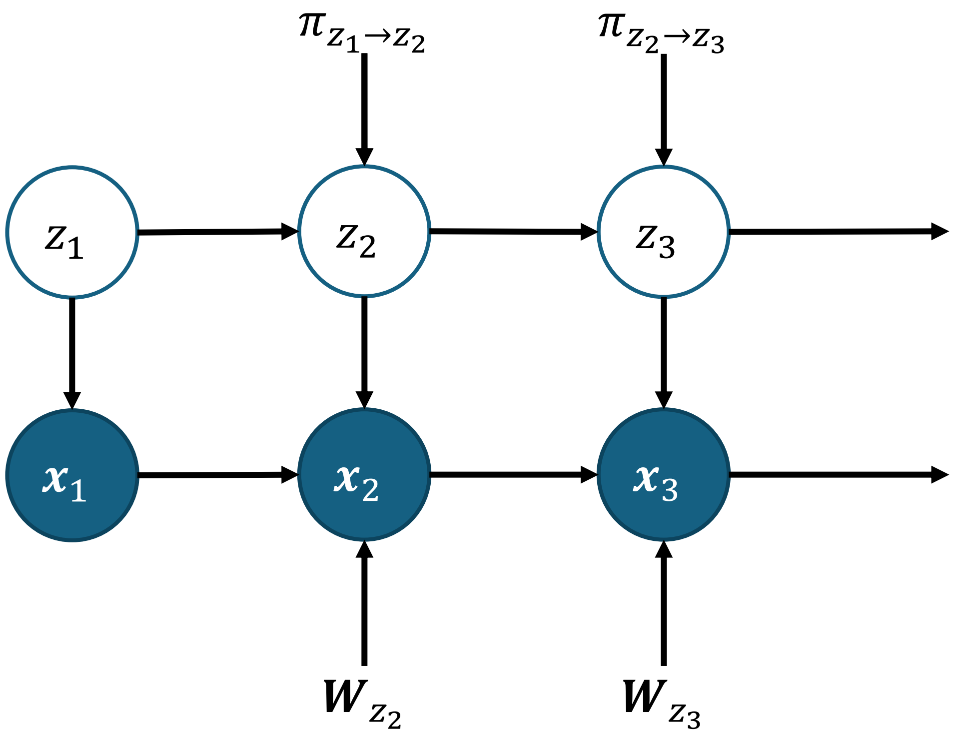
# Classic one-state GLM

- Spike train data $\boldsymbol{X} \in \mathbb{N}^{T \times N}$, $N$ neurons, $T$ time bins.
- Firing rates of the $n$-th neuron at the $t$-th time bin

$$f_{t,n} = \sigma\left(b_n + \sum_{n'=1}^{N} w_{n \leftarrow n'} \cdot \left(\sum_{k=1}^{K} x_{t-k,n'}\, \phi_k\right)\right)$$

- Spike count $x_{t,n} \sim \mathrm{Poisson}(f_{t,n})$.
- $\sigma$ is a non-linear function (e.g., Softplus).
- $b_n$ is the background intensity of the $n$-th neuron.
- $w_{n \leftarrow n'}$ is the weight of influence from neuron $n'$ to neuron $n$.
- $\boldsymbol{\phi} \in \mathbb{R}_+^K$ is the basis function summarizing history spikes.

# Naïve HMM-GLM (HG)

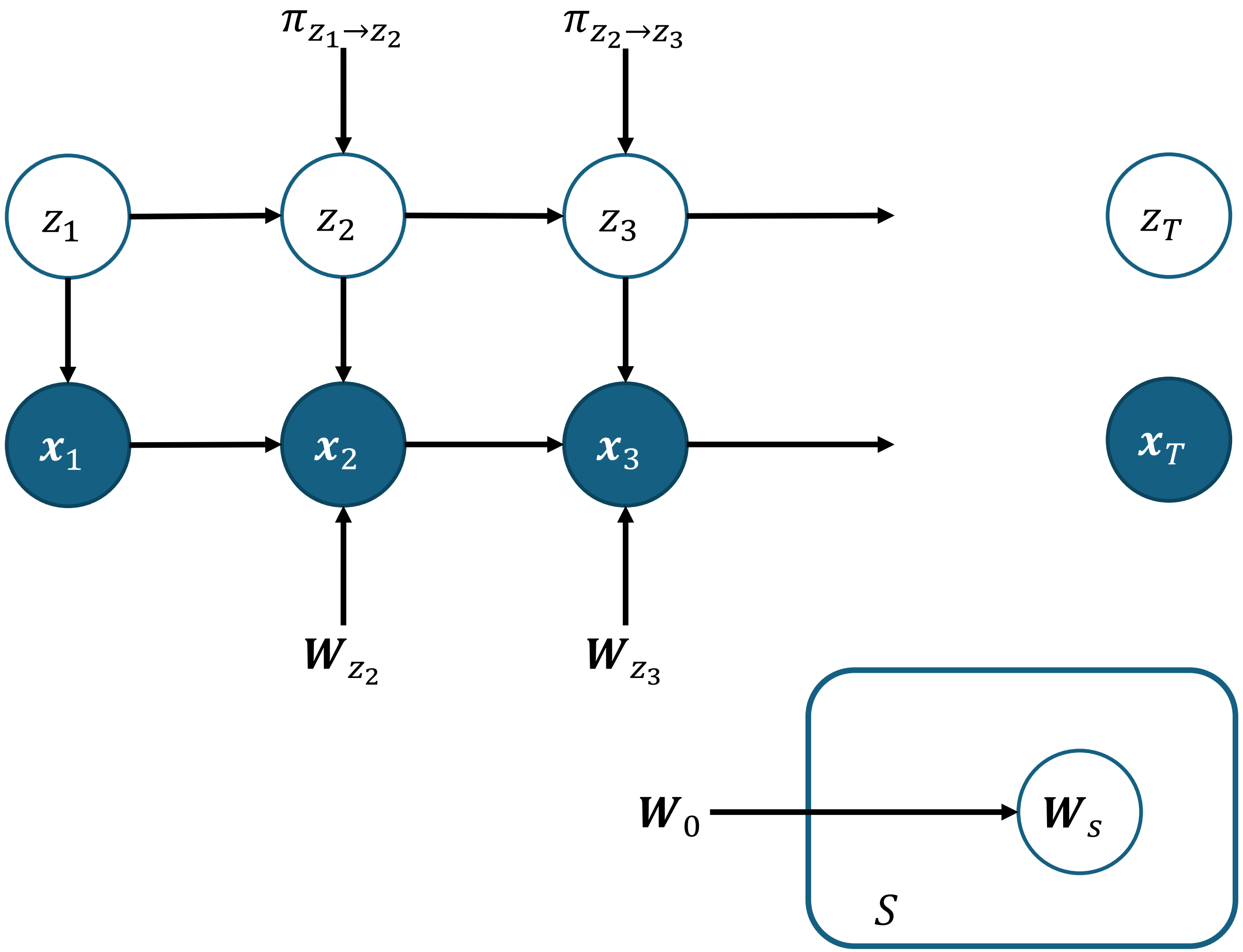



- $S$ states, $N$ neurons, $T$ time bins.
- $\{\boldsymbol{x}_t \in \mathbb{N}^N\}_{t=1}^T$ is the spike count for the $N$ neurons
- $\{z_t \in \{1,2,\dots,S\}\}_{t=1}^T$ is the state index
- $\boldsymbol{\Pi} \in \mathbb{R}^{S\times S}$ is the state transition matrix
- $\{\boldsymbol{W}_s \in \mathbb{R}^{N\times N}\}_{s=1}^S$ is the weight matrix

$$f_{t,n} = \sigma\left(b_n + \sum_{n'=1}^{N} w_{z_t, n \leftarrow n'} \cdot \left(\sum_{k=1}^{K} x_{t-k,n'} \, \phi_k\right)\right)$$

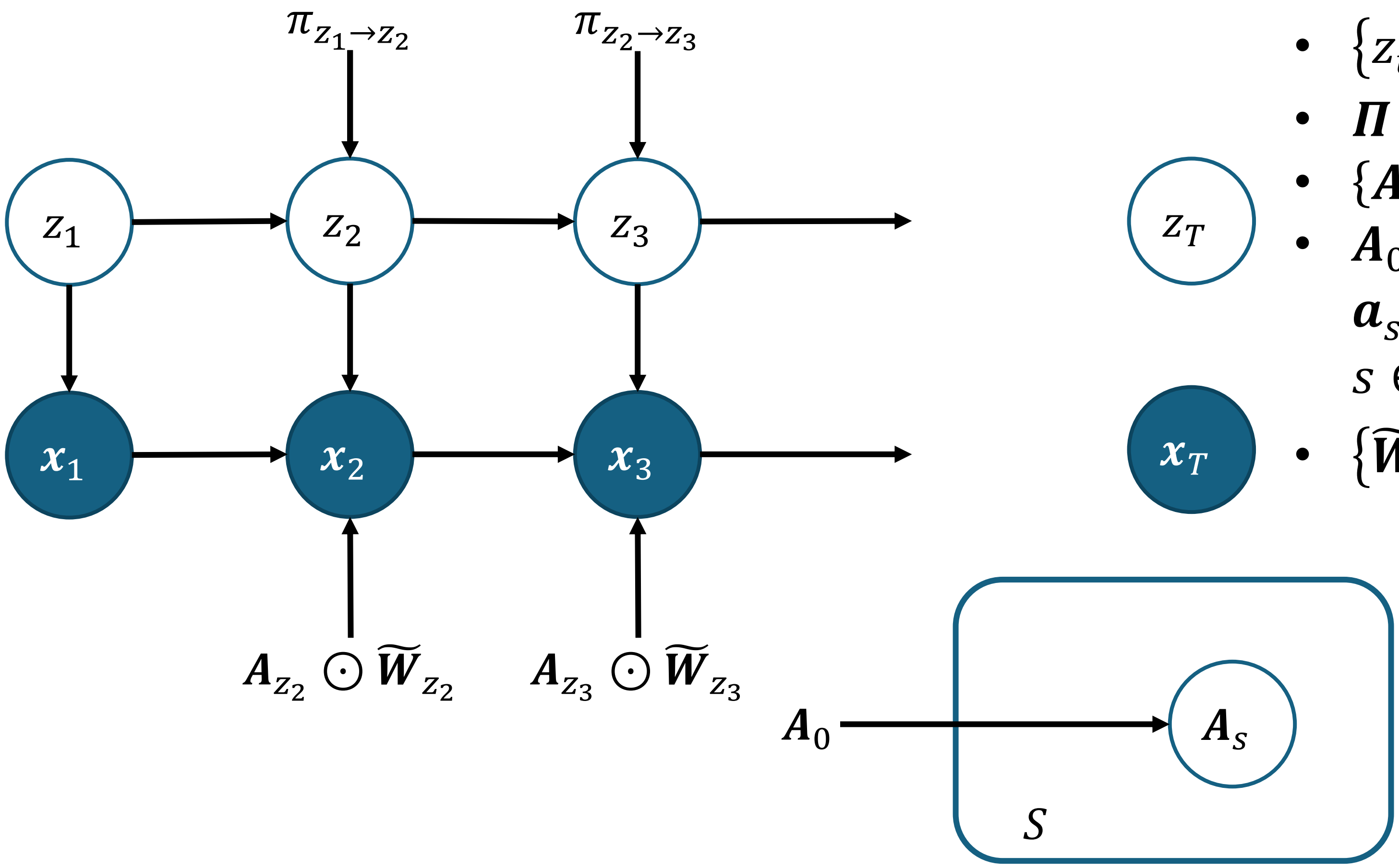
- $f_{t,n}$: Firing rates of neuron $n$ at time $t$
- $\sigma$: Nonlinear activation $\sigma: \mathbb{R} \to \mathbb{R}_+$
- $b_n$: Background intensity of neuron $n$
- $w_{z_t, n \leftarrow n'}$: Weight from neuron $n'$ to neuron $n$ in state $z_t$
- $x_{t-k,n'}$: Spiking history of neuron $n'$ before time $t$

# Gaussian HMM-GLM (GHG)




- $S$ states, $N$ neurons, $T$ time bins.
- $\{\boldsymbol{x}_t \in \mathbb{N}^N\}_{t=1}^T$ is the spike count for the $N$ neurons
- $\{z_t \in \{1,2,\dots,S\}\}_{t=1}^T$ is the state index
- $\boldsymbol{\Pi} \in \mathbb{R}^{S\times S}$ is the state transition matrix
- $\{\boldsymbol{A}_s \in \{-1,0,1\}^{N\times N}\}_{s=1}^S$ is the adjacency matrix
- $\boldsymbol{W}_0 \in \mathbb{R}^{N\times N}$ is the Gaussian prior of $\boldsymbol{W}_s$, $w_{s,n\leftarrow n'} \sim \mathcal{N}\left(w_{0,n\leftarrow n'}, \sigma^2\right)$, i.i.d. for $s \in \{1,\dots,S\}$
- $\{\boldsymbol{W}_s \in \mathbb{R}^{N\times N}\}_{s=1}^S$ is the weight matrix

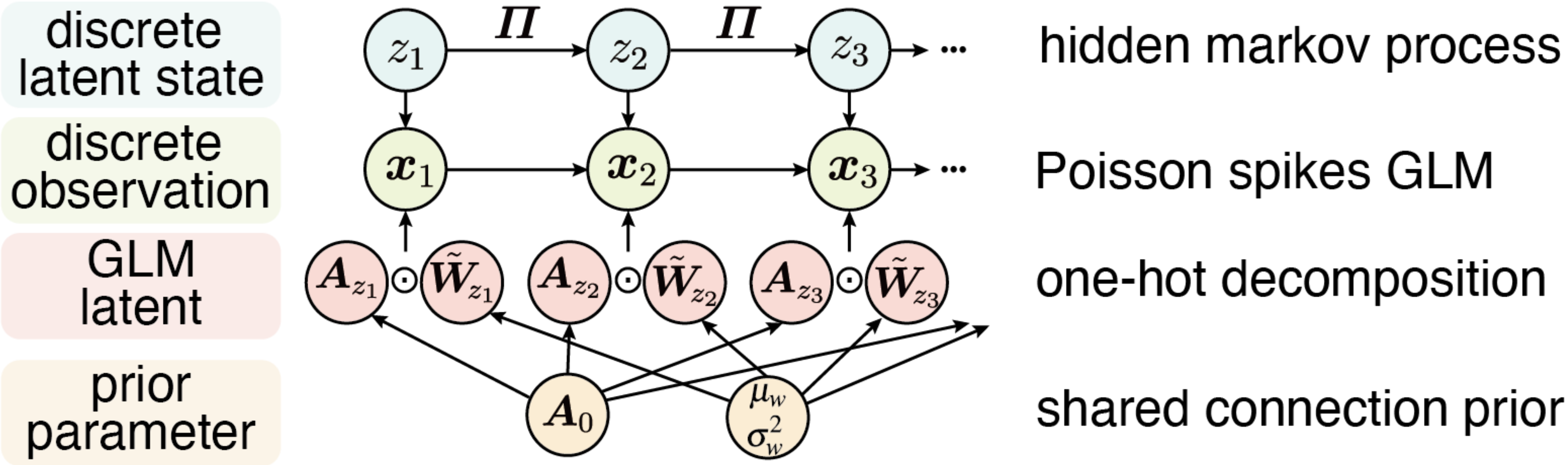
# One-hot HMM-GLM (OHG)

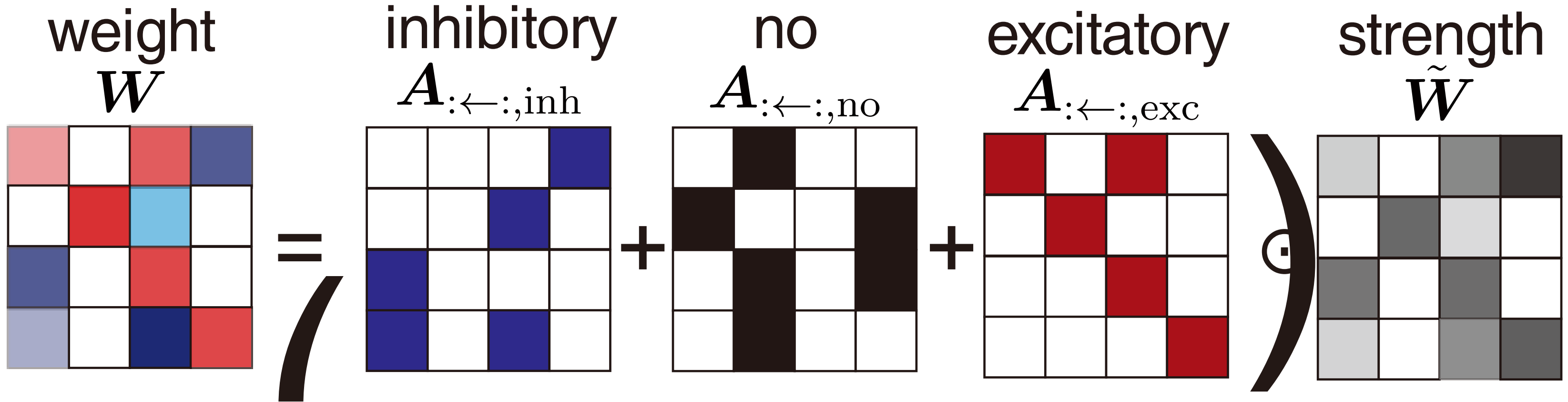



- $\{\boldsymbol{x}_t \in \mathbb{N}^N\}_{t=1}^T$ is the spike count for the $N$ neurons
- $\{z_t \in \{1,2,\dots,S\}\}_{t=1}^T$ is the state index
- $\boldsymbol{\Pi} \in \mathbb{R}^{S\times S}$ is the state transition matrix
- $\{\boldsymbol{A}_s \in (\Delta^2)^{N\times N}\}_{s=1}^S$ is the adjacency matrix
- $\boldsymbol{A}_0 \in (\Delta^2)^{N\times N}$ is the Gumbel-softmax prior of $\boldsymbol{A}_s$, $\boldsymbol{a}_{s,n\leftarrow n'} \sim \text{Gumbel} - \text{Softmax}(\boldsymbol{a}_{0,n\leftarrow n'}, \tau)$, i.i.d. for $s \in \{1,\dots,S\}$
- $\{\widetilde{\boldsymbol{W}}_s \in (0,\infty)^{N\times N}\}_{s=1}^S$ is the strength matrix

$$w_{s,n\leftarrow n'} = \left[(-1)a_{s,n\leftarrow n',\text{inh}} + (+1)a_{s,n\leftarrow n',\text{exc}}\right] \cdot \widetilde{w}_{s,n\leftarrow n'}$$

# One-hot HMM-GLM, complete illustration



# 3 Inference

# E-step, forward-backward algorithm

- Define $\gamma_{z_t}(t) \coloneqq p\left(z_t \middle| \boldsymbol{X}; \theta^{\text{old}}\right)$, $\xi_{z_{t-1},z_t}(t) \coloneqq p\left(z_{t-1}, z_t \middle| \boldsymbol{X}; \theta^{\text{old}}\right)$
- Define $\alpha_{z_t}(t) \coloneqq p(\boldsymbol{x}_1, \dots, \boldsymbol{x}_t, z_t)$
- Define $\beta_{z_t}(t) \coloneqq p(z_{t+1}, \dots, z_T | \boldsymbol{x}_1, \dots, \boldsymbol{x}_t, z_t)$
- Then, $\alpha_{z_t}(t)$ and $\beta_{z_t}(t)$ can be computed iteratively as

$$\begin{cases} \alpha_{z_t}(t) = p(\boldsymbol{x}_t | \boldsymbol{x}_1, \dots, \boldsymbol{x}_{t-1}, z_t) \sum_{z_{t-1}=1}^{S} \alpha_{z_{t-1}}(t) p(z_t | z_{t-1}), & \alpha_{z_1}(1) = p(z_1) p(\boldsymbol{x}_1 | z_1) \\ \beta_{z_t}(t) = \sum_{z_{t+1}=1}^{S} \beta_{z_{t+1}}(t+1) p(\boldsymbol{x}_{t+1} | \boldsymbol{x}_1, \dots, \boldsymbol{x}_t, z_{t+1}) p(z_{t+1} | z_t), & \beta_{z_T}(T) = 1 \end{cases}$$

# M-step

- With the inferred posterior for $\boldsymbol{z}$, we can update $\boldsymbol{\theta}$ by maximizing

$$
\begin{aligned}
Q(\theta, \theta^{\text{old}}) =& \mathbb{E}_{p(\boldsymbol{z}|\boldsymbol{X};\theta^{\text{old}})} \ln p(\boldsymbol{X}, \boldsymbol{z}; \theta) = \sum_{\boldsymbol{z}} p(\boldsymbol{z}|\boldsymbol{X}; \theta^{\text{old}}) \ln p(\boldsymbol{X}, \boldsymbol{z}; \theta) \\
&= \sum_{z_1=1}^{S} \gamma_{z_1}(1) \ln p(z_1; \theta) + \sum_{t=2}^{T} \sum_{z_{t-1}=1}^{S} \sum_{z_t=1}^{S} \xi_{z_{t-1}, z_t}(t) \ln p(z_t|z_{t-1}; \theta) \\
&\quad + \sum_{t=1}^{T} \sum_{z_t=1}^{S} \gamma_{z_t}(t) \ln p(\boldsymbol{x}_t|\boldsymbol{x}_1, \ldots, \boldsymbol{x}_{t-1}, z_t; \theta).
\end{aligned}
$$

# 4 Experiments

# Synthetic

- $S = 5$ states, $N = 20$ neurons, $T = 5000$ time bins.
- Transition probability: $\pi_{s,s'} = 0.005 + 0.975 \cdot \mathbf{1}[s = s']$.
- 20 spike trains, 10 for training and 10 for test.
- Metrics:
  - Test log-likelihood (LL) ↑
  - State accuracy ↑
  - Weight error ↓
  - Connection accuracy ↑
  - Connection prior accuracy ↑

# Synthetic

Table 1: The quantitative results in terms of 5 metrics on the synthetic dataset.

| method | LL ↑ | state acc ↑ | weight error ↓ | adj acc ↑ | adj prior acc ↑ |
|---|---|---|---|---|---|
| GLM | -8.43(±0.18) | nan(±nan) | 24.71(±0.19) | 43.12(±0.46) | 44.81(±0.61) |
| HMM Corr | -22.53(±0.64) | 42.84(±1.47) | nan(±nan) | 34.04(±0.12) | 15.45(±2.49) |
| HMM Bern | -5.68(±0.23) | 87.95(±0.93) | nan(±nan) | 36.25(±0.25) | 40.70(±1.53) |
| HG | -5.49(±0.58) | 37.73(±2.80) | 109.67(±2.63) | 34.17(±0.08) | 40.91(±0.48) |
| HG-L1 | 9.14(±0.18) | 91.60(±0.96) | 23.14(±0.08) | 37.47(±0.18) | 48.44(±0.57) |
| GHG | 8.58(±0.19) | 91.80(±0.92) | 21.54(±0.15) | 42.53(±0.22) | 48.93(±0.54) |
| GHG-L1 | 9.77(±0.20) | 92.08(±0.89) | 14.16(±0.07) | 41.08(±0.22) | 46.98(±0.60) |
| OHG | **14.64**(±0.23) | **92.75**(±0.87) | **10.99**(±0.21) | **73.90**(±0.52) | **80.60**(±0.59) |

- OHG is the best in terms of all metrics

# Synthetic

- OHG gets clear and accurate connectivities.
- OHG explicitly discriminate a weak connection and a no connection

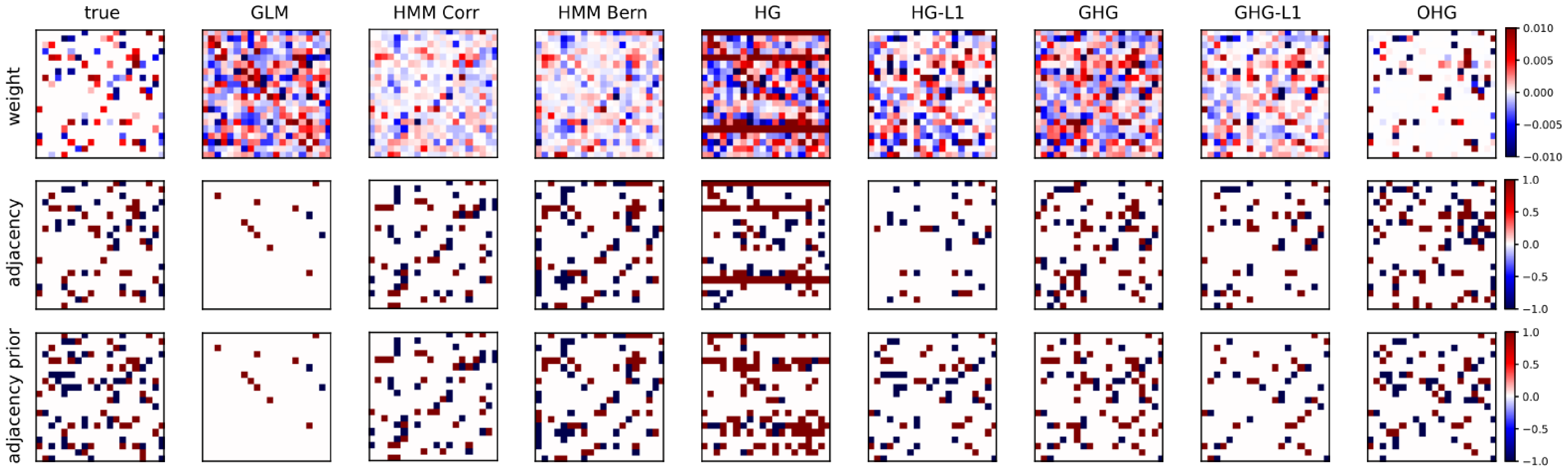



Figure 2: Visualization of weight $\boldsymbol{W}_2$ (top row) and adjacency $\boldsymbol{A}_2$ (middle row) corresponding to state 2 ($S = 5$ in total), and the adjacency prior $\boldsymbol{A}_0$ (bottom row) for all models learned from one trial of the synthetic dataset.

# Prefrontal cortex during a contingency task

- https://crcns.org/data-sets/pfc/pfc-6
- Neural spike trains were collected while a rat learned a behavioral contingency task.
- 5 seconds before trial start – 10 seconds after trial start.
- 750 time bins, bin size = 20 ms.
- First 2/3 trials are training, remaining 1/3 trials are test.
- Try different numbers of states $S \in \{2,3,4,5\}$.

# Prefrontal cortex during a contingency task

Table 2: The log-likelihood on the test set for different models and different numbers of states of the PFC-6 dataset. The result from the one-state GLM is -36.35(±0.00).

| method | 2 states | 3 states | 4 states | 5 states |
|---|---|---|---|---|
| HMM Corr | -37.11(±0.00) | -36.60(±0.00) | -36.53(±0.00) | -36.68(±0.00) |
| HMM Bern | -36.89(±0.00) | -36.57(±0.00) | -36.38(±0.00) | -36.38(±0.00) |
| HG | -37.30(±0.05) | -37.61(±0.17) | -37.22(±0.14) | -36.98(±0.19) |
| HG-L1 | -36.91(±0.01) | -36.90(±0.02) | -36.73(±0.09) | -36.63(±0.13) |
| GHG | -37.17(±0.00) | -37.11(±0.01) | -37.12(±0.00) | -37.11(±0.00) |
| GHG-L1 | -36.94(±0.00) | -36.88(±0.00) | -36.83(±0.00) | -36.77(±0.00) |
| OHG | **-35.92**(±0.02) | **-35.79**(±0.02) | **-35.77**(±0.03) | **-35.71**(±0.03) |

# Prefrontal cortex during a contingency task

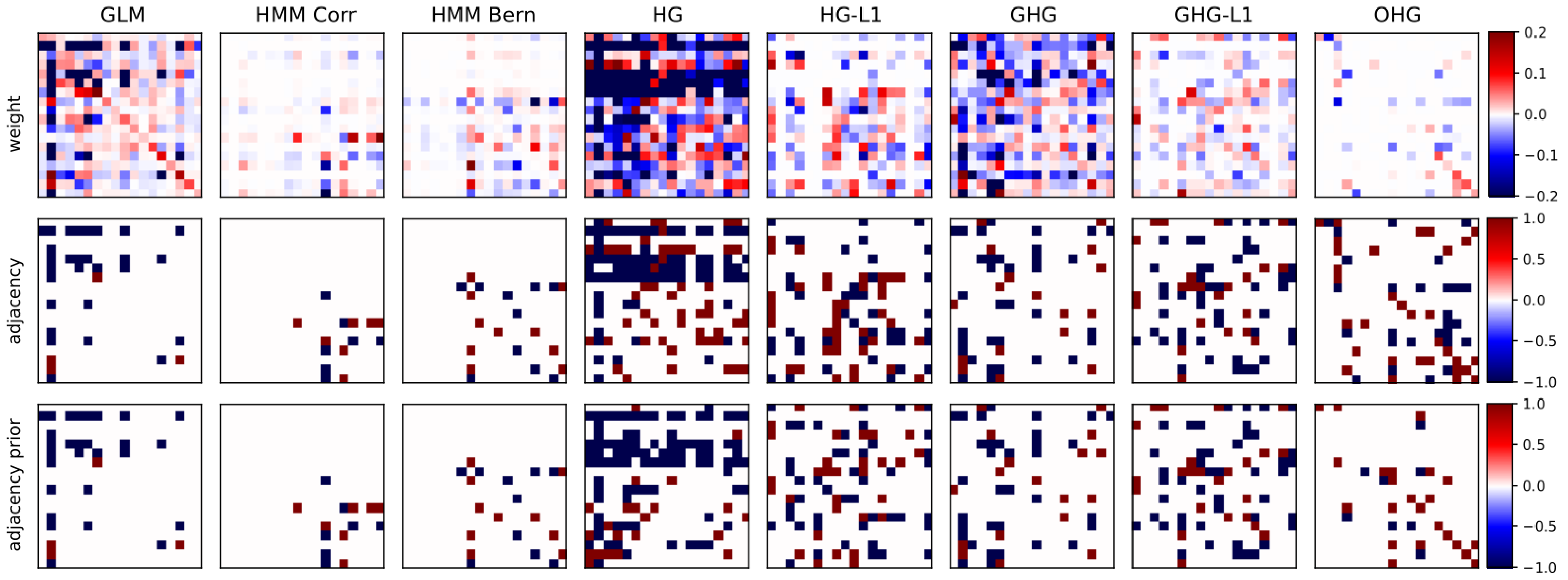
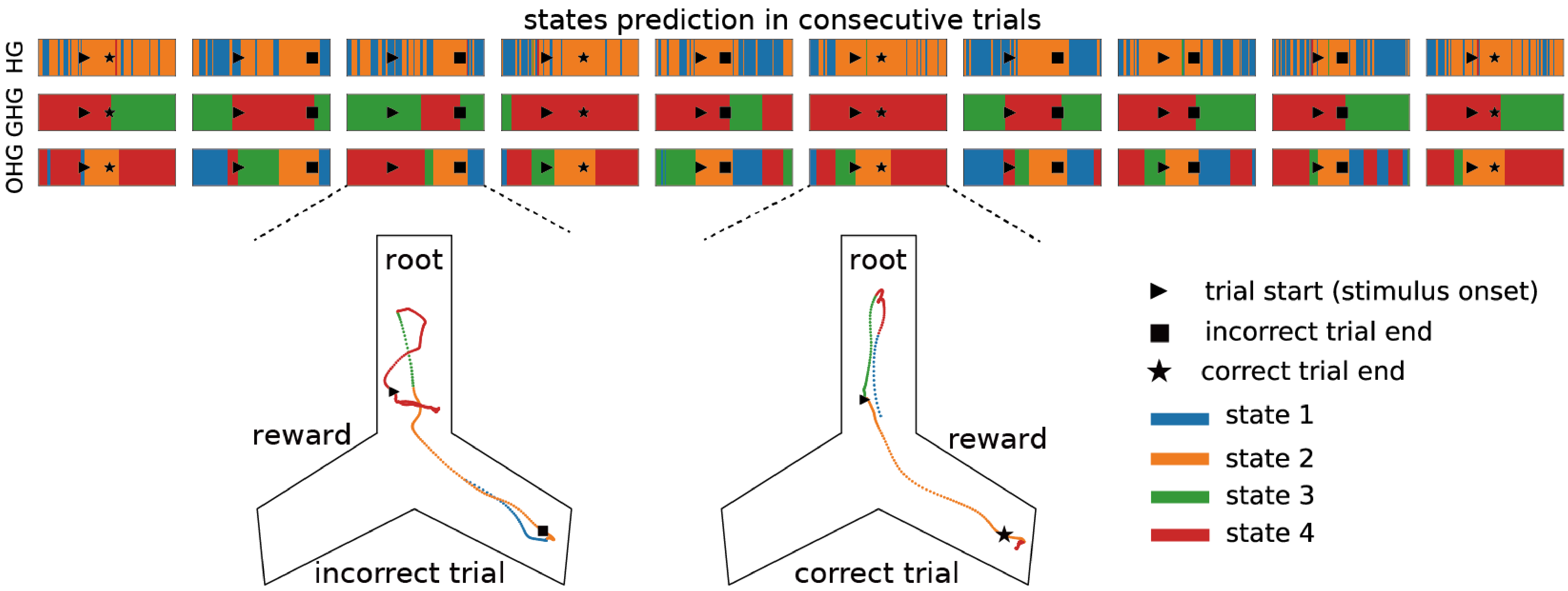


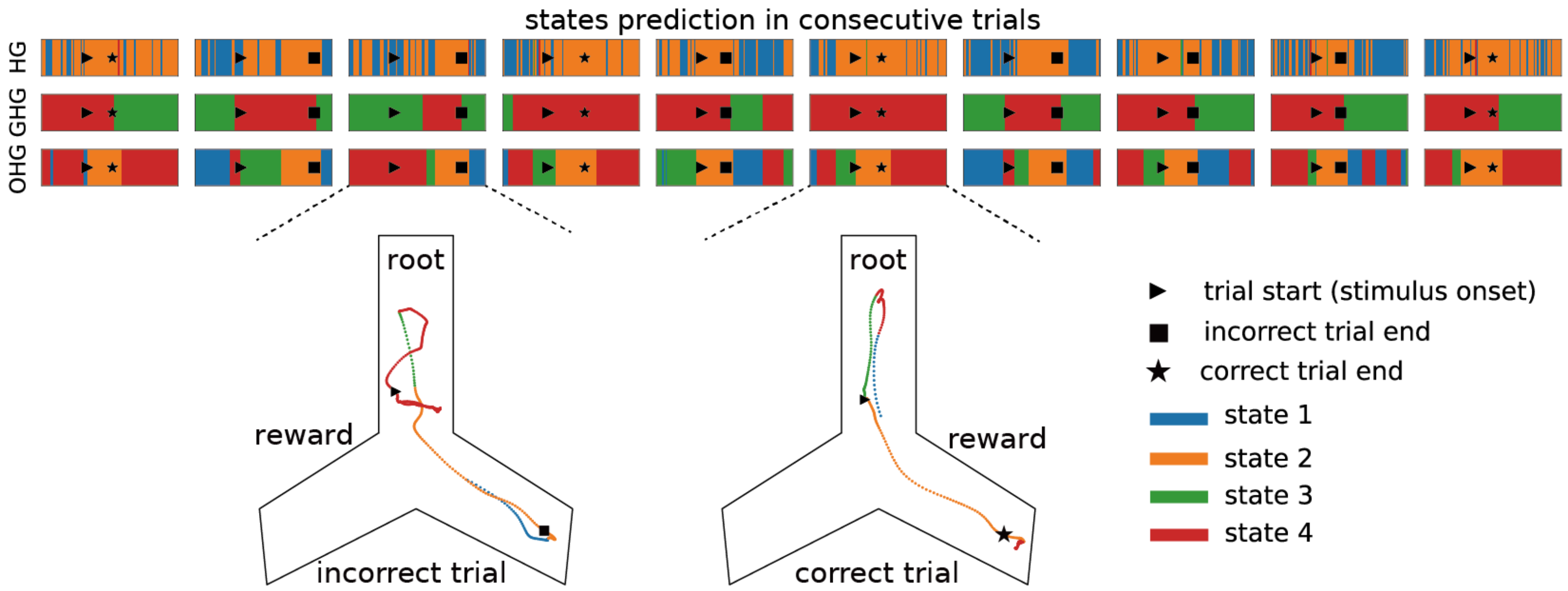

Figure 3: Visualization of weight $\boldsymbol{W}_4$ (top row) and adjacency $\boldsymbol{A}_4$ (middle row) corresponding to state 4 ($S = 4$ in total), and the adjacency prior $\boldsymbol{A}_0$ (bottom row) for all models learned from the PFC-6 dataset.

# Prefrontal cortex during a contingency task



# Prefrontal cortex during a contingency task

- HG: fast switches, limited interpretability
- GHG: $S = 4$ states are assumed, but GHG only infers two effective states
- OHG: 4 stable explainable states
  - Red: back to the root
  - Green: go to the turning point
  - Orange: reach a target
  - Incorrect trial: no reward, blue state
  - Correct trial: reward, red state

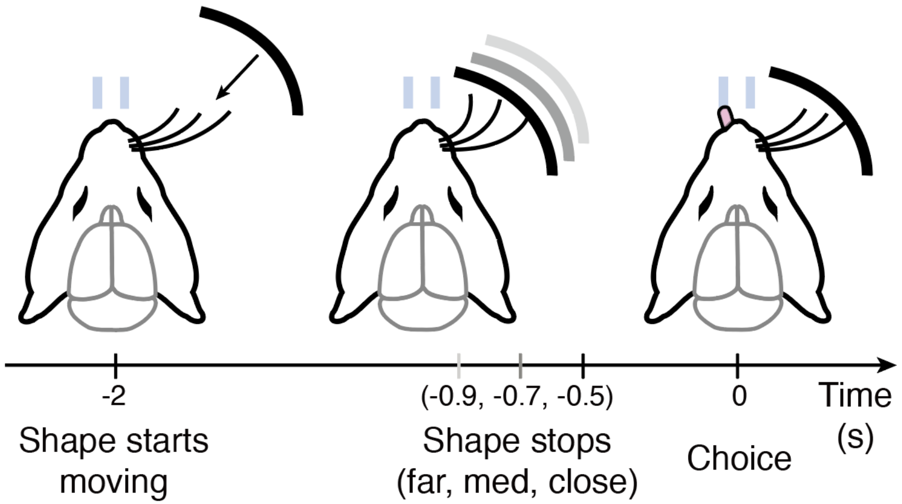


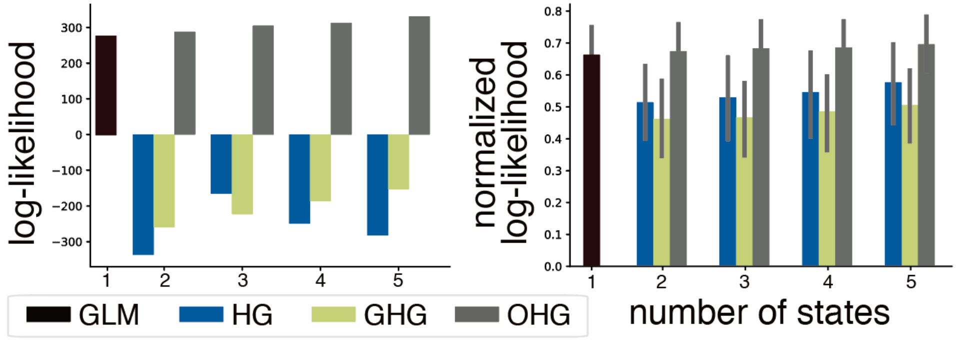
# Barrel cortex during whisking

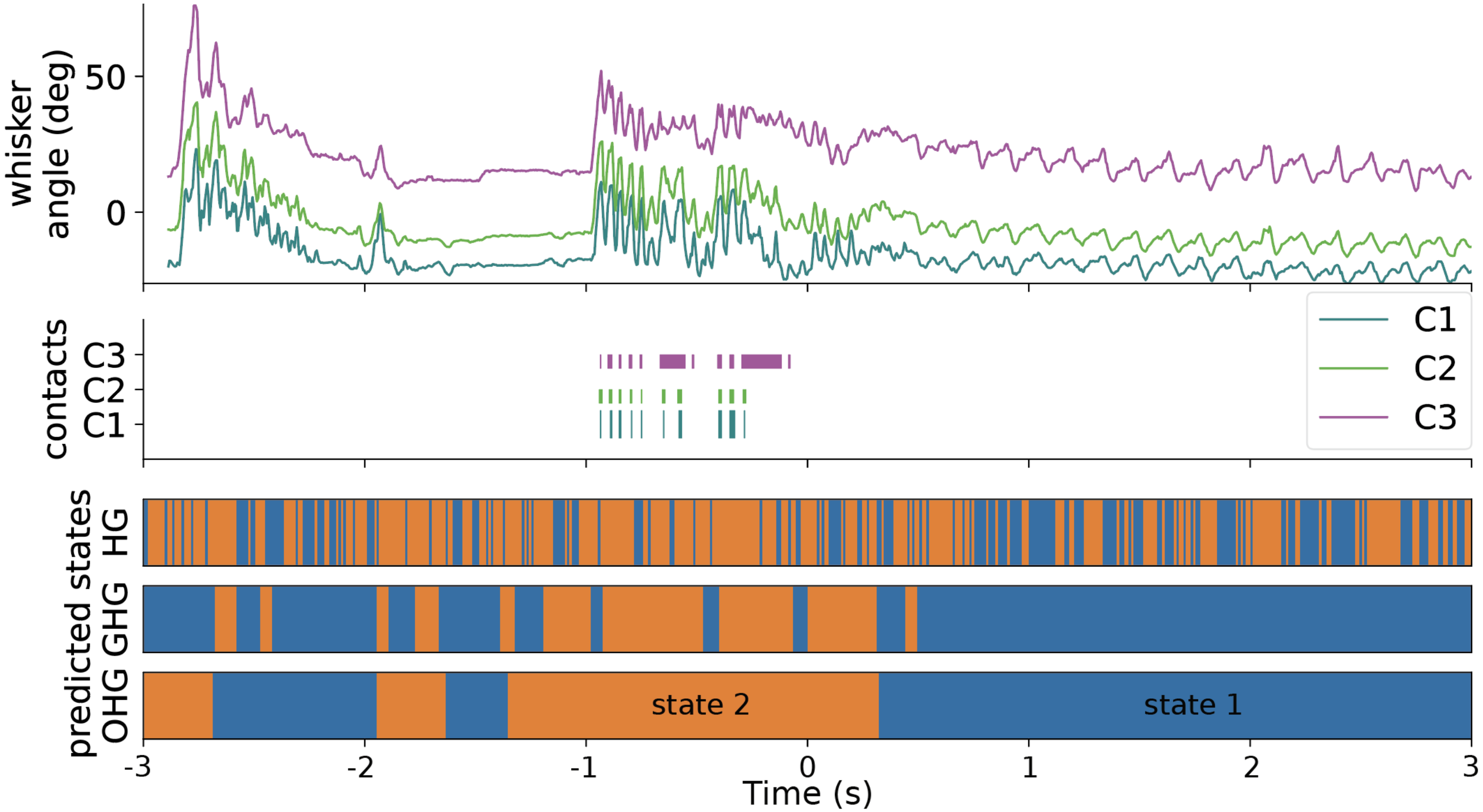
- Electrode recordings of the somatosensory (barrel) cortex in mice during a shape discrimination task (Rodgers et al., 2021; Rodgers, 2022; Nogueira et al., 2023).
- 27 sessions from 5 mice.
- Number of neurons $N$ ranges from 20 to 44.
- 6 seconds for each trial. Bin size = 3 ms.
- 750 time bins, bin size = 20 ms.
- 10 of 30 trials are randomly selected for test.
- Try different numbers of states $S \in \{2,3,4,5\}$.

# Barrel cortex during whisking

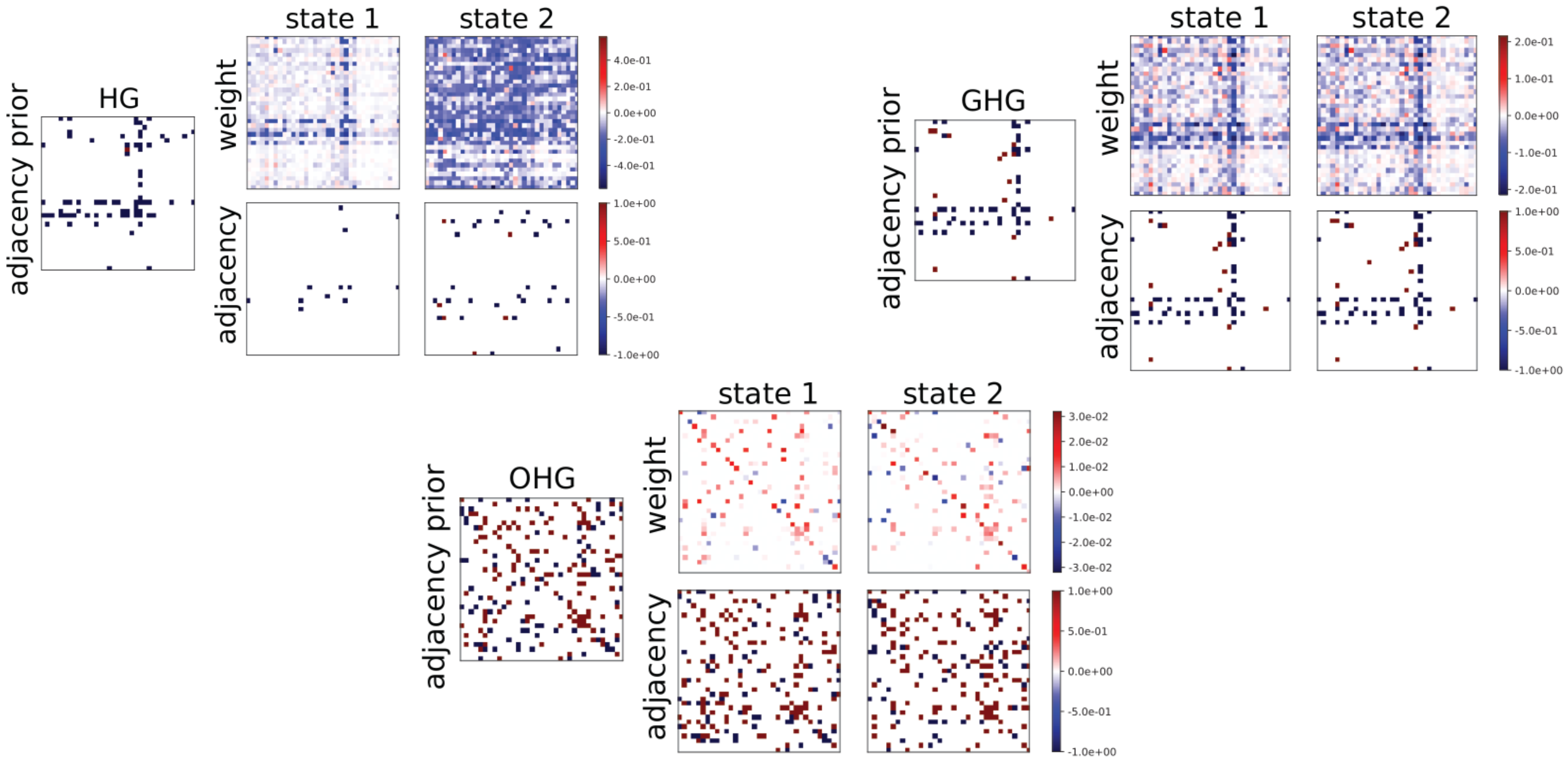
- OHG state 2 corresponds contacts
- OHG provides stable states prediction



# Barrel cortex during whisking



# Summary

- The newly proposed one-hot HMM-GLM decomposes the traditional weight matrix in GLMs into a discrete connection matrix with type and a positive-valued strength matrix. Such a decomposition is critical when applied to state-switching neural interaction discovery.
- The regulated connection matrices $\boldsymbol{A}_s$ in our OHG with their shared prior $\boldsymbol{A}_0$ should inform us about underlying anatomical connectome and thus uncover the “more likely” physical interactions between neurons.
- The less restricted strength matrices $\widetilde{\boldsymbol{W}}$ in OHG will provide us with sufficient traceability to capture functional variations across multiple brain states.

# Thanks for listening!