INFERRING CORTICAL NETWORK STRUCTURE FROM PATTERNS OF CORRELATED ACTIVITY ACROSS CELL TYPES

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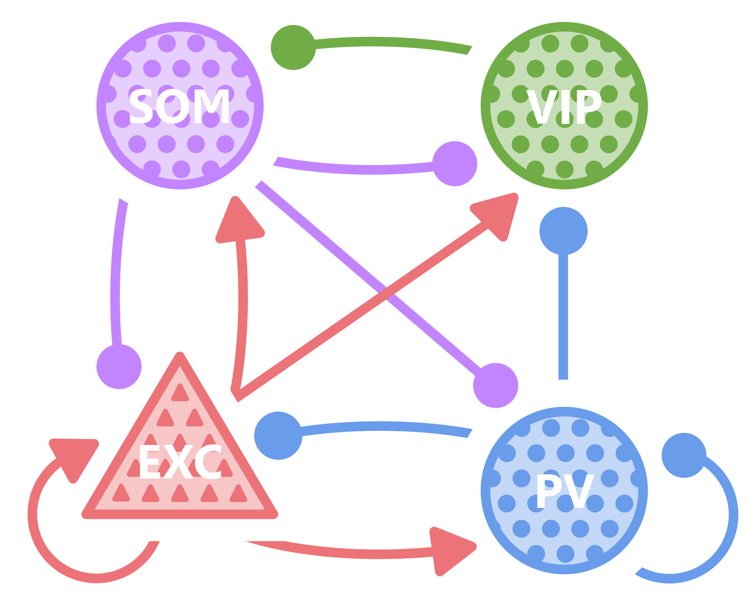
INTRODUCTION

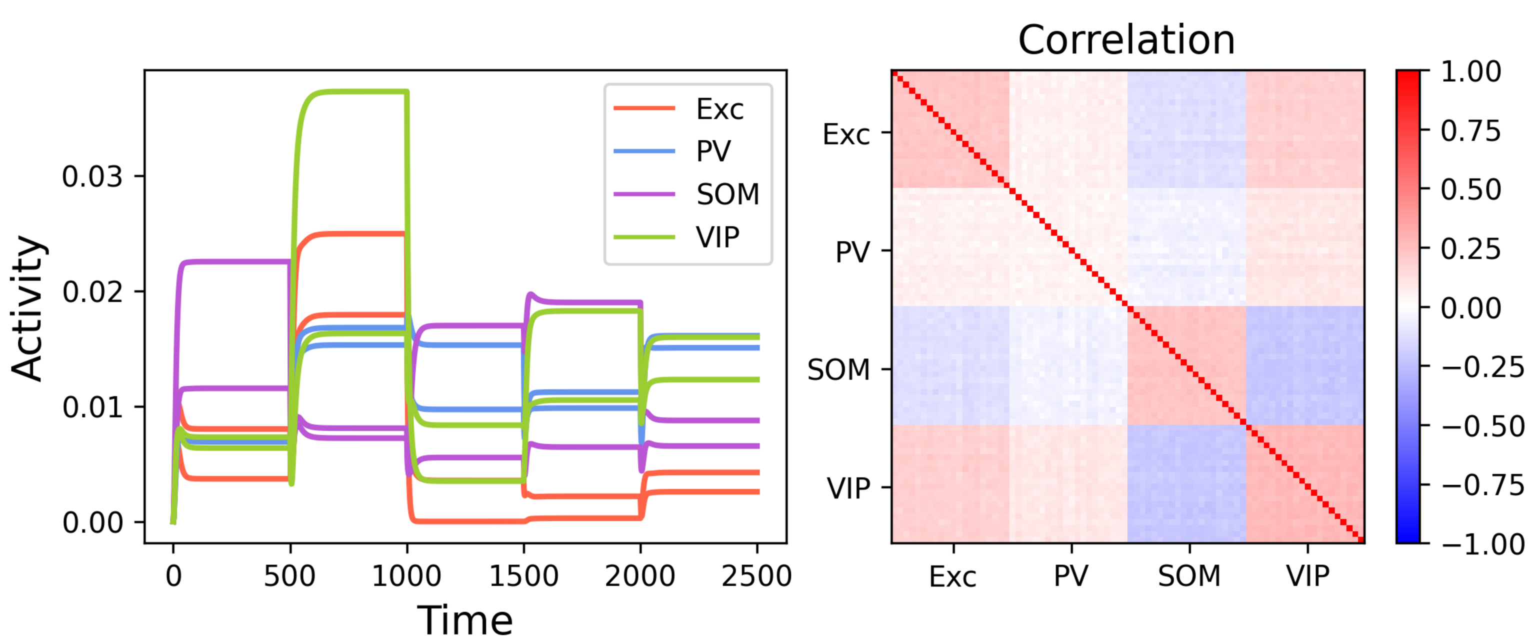
- The cerebral cortex performs the most complex operations in the mammalian brain including sensory, motor, and cognitive processes
- Neurons exhibit correlated activity which impacts brain computation
- **How do observed patterns of correlation across cortical cell types emerge from the underlying network?**
- Two-fold approach:
  - Develop expression for correlations in neural activity which is both interpretable and computationally efficient
  - Design algorithm to infer network parameters from neural activity

1. SIMULATING NEURAL ACTIVITY



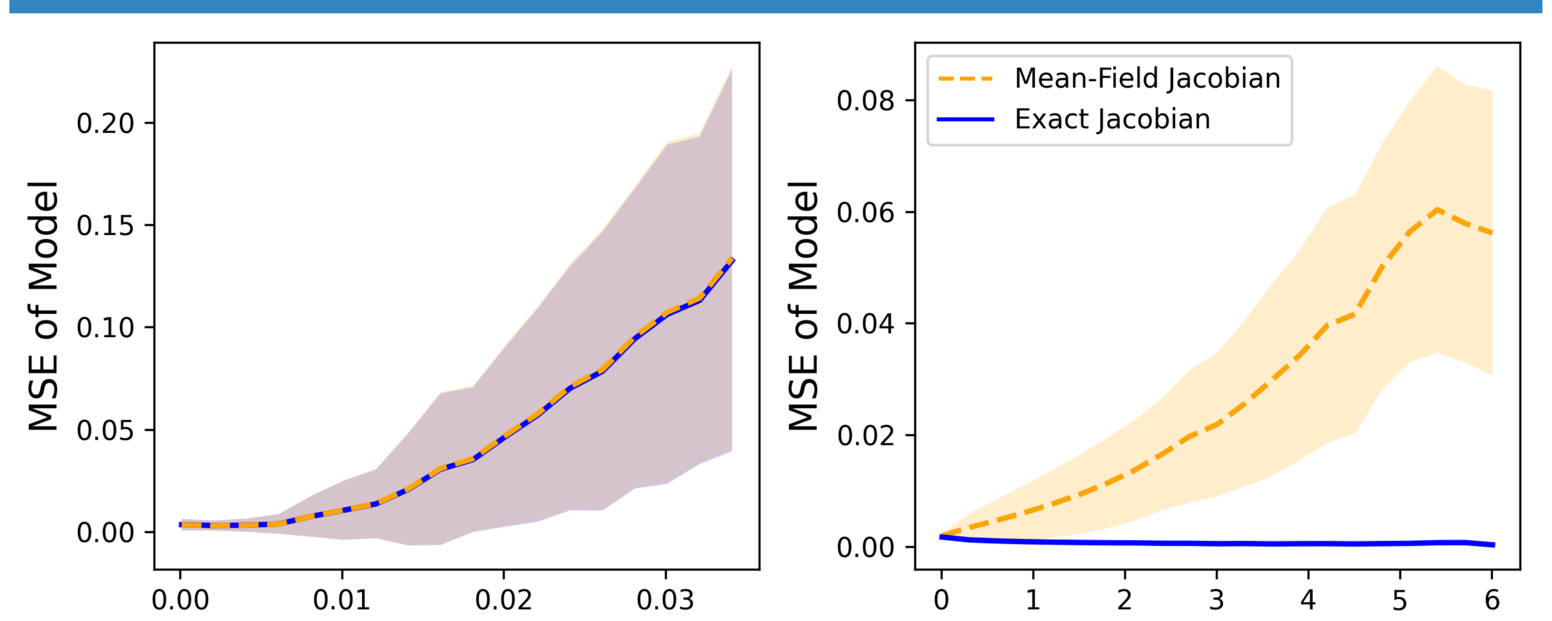
A. Schematic of neural network model. Illustrates the synaptic connections between neurons in the cortex. Includes one excitatory cell type and three inhibitory cell types:

- Parvalbumin
- Vasoactive intestinal peptide
- Somatostatin

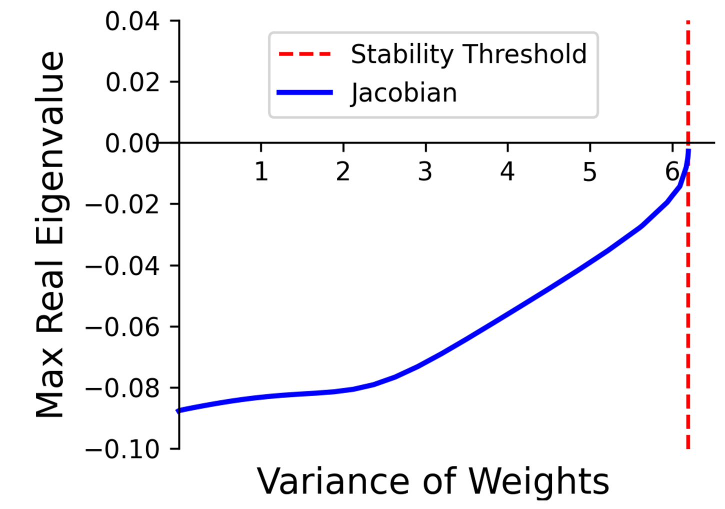


B. Example of correlated neural dynamics. Left: Neural activity converges to distinct steady states in response to five small changes in network input. Right: Correlations in neural activity between cell types.

2. ANALYZING STEADY STATE BEHAVIOR



A. Approximation of steady state dynamics is possible under specific conditions. Left: Linear approximation of network dynamics is accurate with low input variance. Right: Mean-field approximation is accurate with low variance in network weights within populations.



B. Increasing weight variance drives network from stability to instability. Max real eigenvalue of the Jacobian matrix rapidly approaches zero, coinciding with stability threshold.

3. MODELING CORRELATIONS

Voltage Dynamics Equation:

(1) $\tau \frac{d\mathbf{v}}{dt} = -\mathbf{v} + \mathbf{W}\phi(\mathbf{v}) + \mathbf{b}h$

τ = time constant
$\mathbf{v} \in \mathbb{R}^n$ = voltages
$\mathbf{W} \in \mathbb{R}^{n\times n}$ = synaptic weights
$\mathbf{b} \in \mathbb{R}^n$ = input weights
h = input

Linear Approximation of Steady State Voltage Dynamics:

(2) $0 = -\delta\mathbf{v} + \mathbf{W}\phi'(\mathbf{v}^*)\delta\mathbf{v} + \mathbf{b}\delta h$

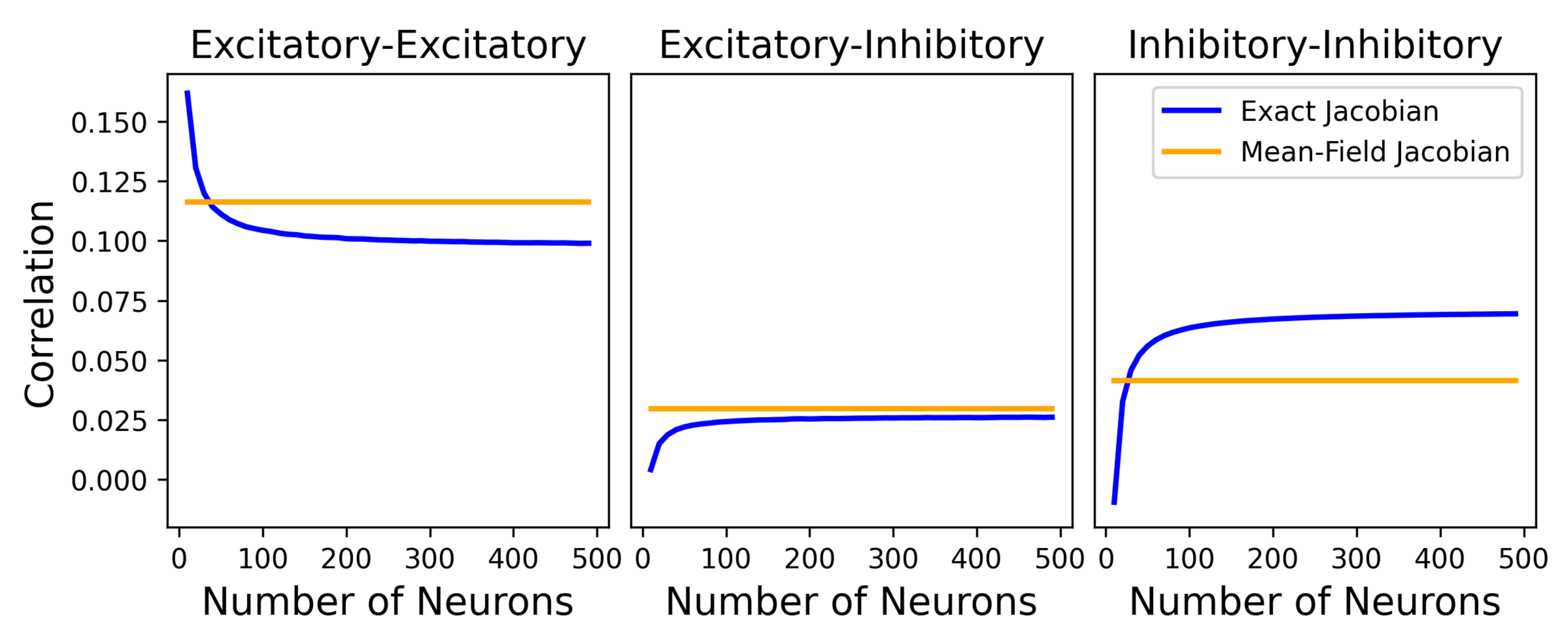
$\mathbf{v}^* \in \mathbb{R}^n$ = steady state voltages

(3) $\delta\mathbf{v} = (-\mathbf{J})^{-1}\mathbf{b}\delta h$

$\mathbf{J} \in \mathbb{R}^{n\times n}$ = Jacobian $= -\mathbf{I} + \mathbf{W}\phi'(\mathbf{v}^*)$

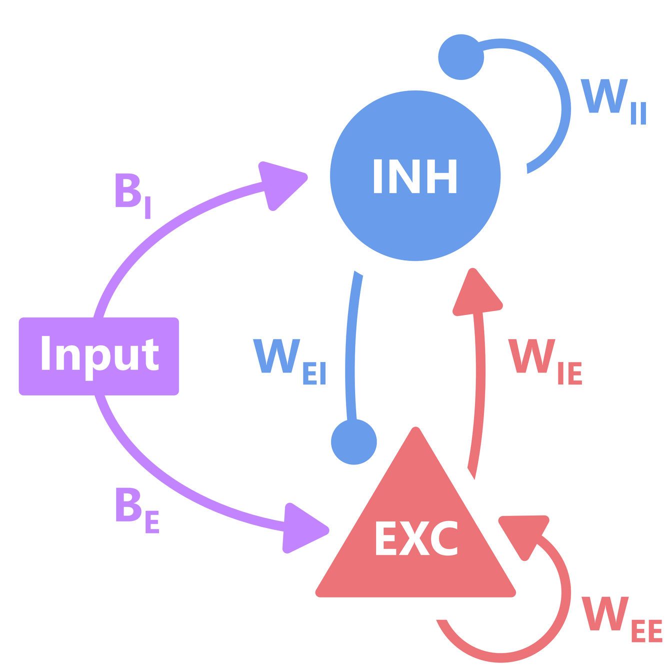
Simplification of Inverse of Block Matrix:

(4) $$\begin{bmatrix}\mathbf{A} & \mathbf{B}\\ \mathbf{C} & \mathbf{D}\end{bmatrix}^{-1} = \begin{bmatrix}(\mathbf{A}-\mathbf{B}\mathbf{D}^{-1}\mathbf{C})^{-1} & 0\\ 0 & (\mathbf{D}-\mathbf{C}\mathbf{A}^{-1}\mathbf{B})^{-1}\end{bmatrix}\begin{bmatrix}\mathbf{I} & -\mathbf{B}\mathbf{D}^{-1}\\ -\mathbf{C}\mathbf{A}^{-1} & \mathbf{I}\end{bmatrix}$$



A. Explicit equations can approximate correlation. Mean-field approximation can estimate exact correlations for large populations and is computed using an explicit expression for the inverse.

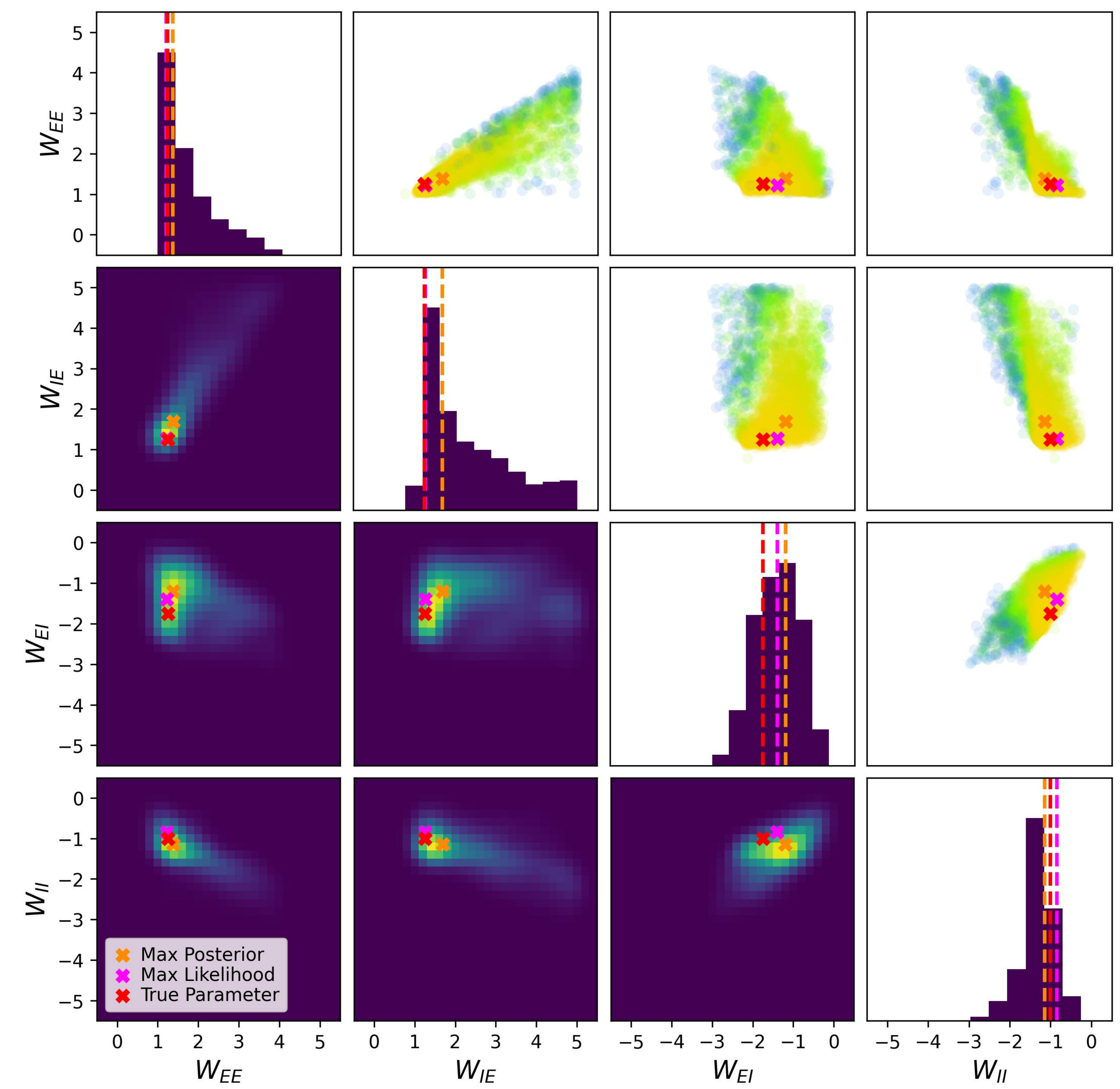
4. INFERRING PARAMETERS



A. Schematic of simplified network model. Includes only one excitatory and inhibitory neuron each with a shared weighted input.

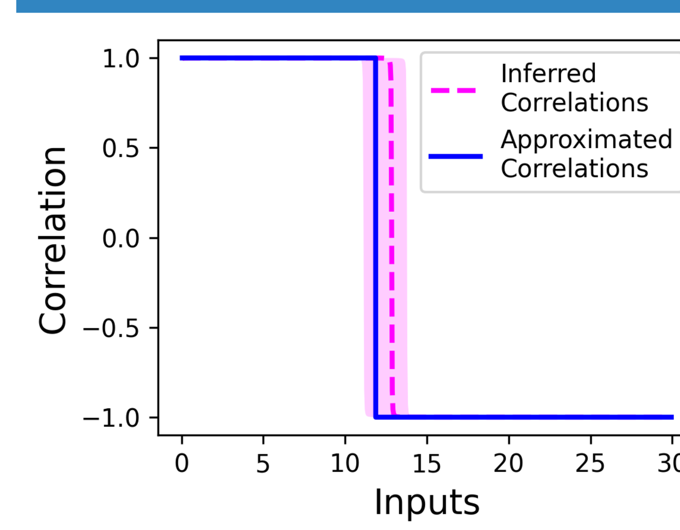
Adapted Metropolis-Hastings:

Inputs: $\bar{\boldsymbol{\theta}} = \{\bar{\mathbf{W}}, \bar{\mathbf{b}}\}$, $\bar{\rho}$ = noise
Run dynamics $\bar{\mathbf{v}}^* = \mathrm{D}(\bar{\boldsymbol{\theta}}, \bar{h})$
Add noise $\mathrm{v}^{*\prime} \sim \mathcal{N}(\bar{\mathbf{v}}^*, \bar{\rho})$, $h' \sim \mathcal{N}(\bar{h}, \bar{\rho})$
for K iterations **do**
Initialize random $\boldsymbol{\theta}_0, h_0, \rho_0$
$\boldsymbol{\theta}_c = \boldsymbol{\theta}_0, h_c = h_0, \rho_c = \rho_0$
for $n = 1 \dots N$ **do**
Propose $\boldsymbol{\theta}_n \sim \mathcal{N}(\boldsymbol{\theta}_c, \sigma)$, $h_n \sim \mathcal{N}(h_c, \sigma)$
$\rho_n = \bar{\rho} + (\rho_0 - \bar{\rho})e^{-bn}$
Run dynamics $\mathbf{v}_n^* = \mathrm{D}(\boldsymbol{\theta}_n, h_n)$
$P(\mathrm{acc}) = \frac{P(\mathbf{v}^{*\prime}, h' \mid \mathbf{v}_n^*, h_n, \rho_n)P(\boldsymbol{\theta}_n, h_n, \rho_n)}{P(\mathbf{v}^{*\prime}, h' \mid \mathbf{v}_c^*, h_c, \rho_c)P(\boldsymbol{\theta}_c, h_c, \rho_c)}$
if $P(\mathrm{acc}) > \mathrm{rand}(0,1)$
$\boldsymbol{\theta}_c = \boldsymbol{\theta}_n$, $h_c = h_n$



B. Metropolis-Hasting algorithm accurately estimates network parameters. Barplots: Marginal distributions of the inferred posterior. Heatmaps: Pairwise inferred gaussian KDE posterior distribution. Scatterplots: Pairwise posterior samples colored by likelihood.

5. CORRELATIONS OF INFERRED NETWORK



A. Inferred parameters reproduce correlations derived by theoretical model. Correlation in excitatory and inhibitory activity remains consistent between inferred and ground truth parameters.

DISCUSSION

- Dialogue between experimental and theoretical research:
  - Inference algorithm extracts network structure from data
  - Correlation model used to develop theories on how network structure influences correlations in activity between cell types
  - Theories are tested and validated by experimentalists
- Future directions:
  - Expand our methods to account for multiple inhibitory cell types
  - Use gradient descent to more efficiently explore parameter space

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