Estimating the Topology of Neural Networks from Distributed Observations

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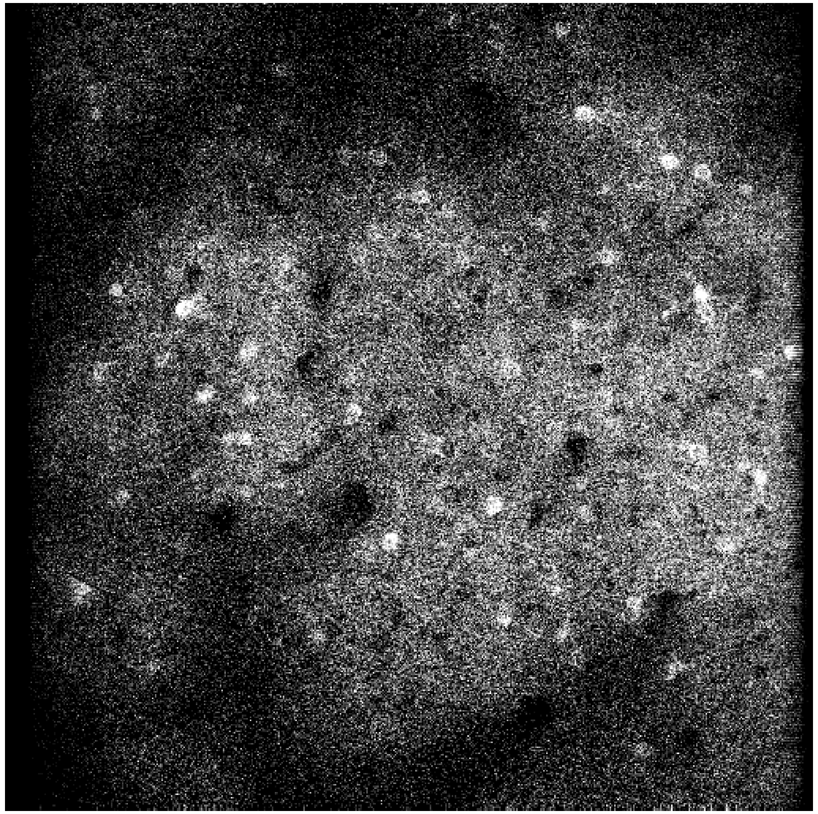
Connectivity within the Brain

- *Structural connectivity* describes the physical connections between different neurons.
  - Diffusion tensor imaging
  - Tractography from magnetic resonance imaging

- *Functional connectivity* refers to statistical dependencies between different units in the brain.
  - Functional MRI (fMRI)
  - Electroencephalography (EEG)
  - Magnetoencephalography (MEG)
  - Multielectrode array (MEA)

- *Effective connectivity* describes the causal relationships between neurons.
  - Structural equation modelling
  - Dynamics causal modelling
  - Granger causality

Calcium imaging: functional imaging of neural activity



- Can monitor activity of 100s-1000s of neurons simultaneously, at single cell resolution.
- Can image *in vivo* in behaving animals.
- Can image same cell populations over multiple months.

[1] Dataset available online: http://neurofinder.codeneuro.org/. Accessed 01/07/2017.

NetRate Algorithm for Network Topology Inference

- NetRate is an algorithm proposed by Gomez-Rodriguez, used to infer the edges of a static, directed network [2].

- The spreading model is the susceptible-infected one.

- Each edge from node *j* to *i* is assigned the conditional likelihood $f\left(t_i \middle| t_j, \alpha_{j,i}\right)$, of node i to get infected at time t_i, given node j was infected at time t_j, and the edge weight $\alpha_{j,i}$.

- The parameters $\alpha_{j,i}$ represent the transmission rates associated with edges.

[2] Manuel Gomez Rodriguez, David Balduzzi, and Bernhard Schölkopf. Uncovering the Temporal Dynamics of Diffusion Networks. Proceedings of the 28th International Conference on Machine Learning, May 2011.

NetRate Algorithm for Network Topology Inference

- The algorithm assumes access to multiple independent cascades of information.

- Each cascade is generated by randomly selecting a source node, and allowing information to spread according to the likelihoods $f(t_i|t_j, \alpha_{j,i})$.

- Each cascade contains the infection times of all the network nodes.

- NetRate aims to infer the transmission edges $\alpha_{j,i}$, by maximizing the likelihood of the observed cascades.

NetRate Algorithm for Network Topology Inference

Likelihood of a cascade

- The probability node i to be infected at time t_i given node j was infected at time t_j is $f\left(t_i \middle| t_j, \alpha_{i,j}\right)$.

- The probability that node i is not infected by node j by time t_i is given by the *survival* function:

$$S\left(t_i \middle| t_j, \alpha_{i,j}\right) = 1 - F\left(t_i \middle| t_j, \alpha_{i,j}\right)$$

- The *hazard* function is defined as the instantaneous infection rate, and given by:

$$H\left(t_i \middle| t_j, \alpha_{i,j}\right) = \frac{f\left(t_i \middle| t_j, \alpha_{i,j}\right)}{S\left(t_i \middle| t_j, \alpha_{i,j}\right)}$$

NetRate Algorithm for Network Topology Inference

Likelihood of a cascade

- The likelihood of a cascade is the probability of observing the state of the susceptible and infected nodes:

$$f(t^c; A) = \underbrace{\prod_{t_i<T} \prod_{t_m>T} S(T|t_i, \alpha_{i,m})}_{\text{Susceptible at } T} \times \underbrace{\prod_{k:t_k<t_i} S(t_i|t_k, \alpha_{k,i}) \sum_{j:t_j<t_i} H(t_i|t_j, \alpha_{j,i})}_{\text{Infected before } T}$$

- Assuming independent cascades, the NetRate algorithm aims to solve the network inference problem given by:

$$\min_{A} - \sum_{c \in C} \log f(t^c; A)$$

where:

$A \coloneqq \left\{\alpha_{j,i} > 0 \middle| i, j = 1, \dots, N, i \neq j\right\}$,

C is the set of cascades,

c is a cascade in this set,

t^c are the observed infection times in cascade c ,

T is the length of the observation window.

NetRate Algorithm for Network Topology Inference

Likelihood of a cascade

- NetRate aims to solve the network inference problem given by:

$$\min_{A} - \sum_{c \in C} \log f(t^{c}; A)$$

where:

$A \coloneqq \{\alpha_{j,i} > 0 \,|\, i, j = 1, \ldots, N, i \neq j\}$,

C is the set of cascades,

c is a cascade,

t^{c} are the observed infection times in cascade c ,

T is the length of the observation window.

- This problem is convex if the transmission likelihood has log-concave survival function and concave hazard function.

- The network inference problem is convex for the exponential, power-law and Rayleigh models.

NetRate Algorithm for Brain Topology Inference

- We have access to multiple independent cascades of information.
  - Cascades generated using constant input to Izhikevich's neuron model.
- The spreading of information within the brain follows the susceptible-infected model.
  - During a cascade, each neuron spikes at most once.
- The diffusion of information between neurons can be modelled probabilistically.
  - Proved through stability analysis of Izhikevich's dynamical system.
- The network inference problem is convex if the underlying distribution $f(t_i|t_j, \alpha_{i,j})$ follows the exponential, power-law or Rayleigh models.
  - The shape of this likelihood is derived empirically, using stability analysis of Izhikevich's dynamical system.

Temporal Dynamics of Neural Networks

Spiking Neuron Model

- Izhikevich's spiking neuron model accurately replicates the spiking behaviour of biological neurons [3]:

$$\frac{dv(t)}{dt} = 0.04v^2(t) + 5v(t) + 140 - u(t) + I$$
$$\frac{du(t)}{dt} = a\big(bv(t) - u(t)\big)$$

membrane potential ($v(t)$); membrane recovery ($u(t)$); input noise due to unobserved neurons (I)

- If $v(t) > 30mV$, then:

$$\begin{cases} v(t) \leftarrow c, \\ u(t) \leftarrow u + d \end{cases}$$

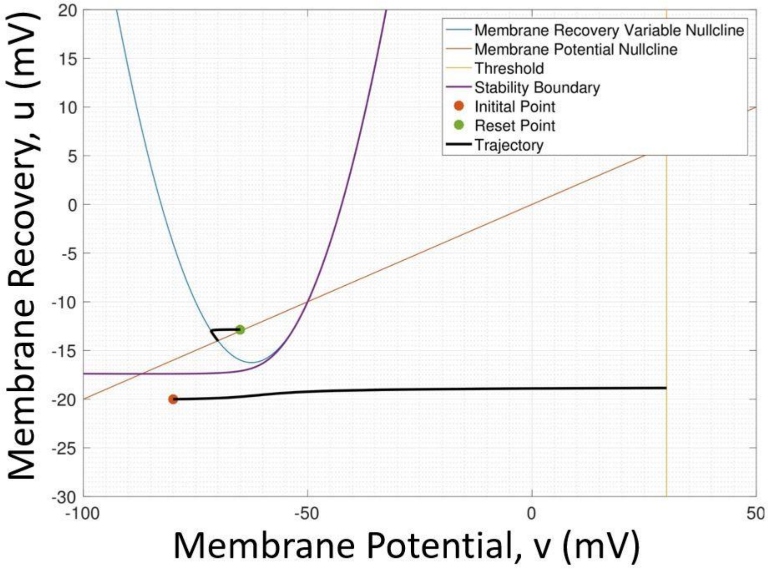
- Regular spiking behaviour is obtained by setting: $a = 0.02$, $b = 0.2$, $c = -65$, $d = 8$.

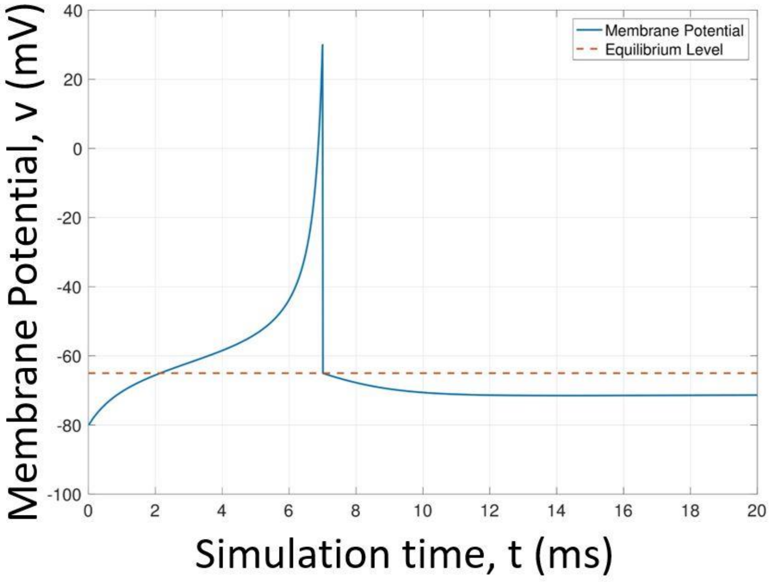
[3] Eugene M Izhikevich. Simple Model of Spiking Neurons. IEEE Transactions on Neural Networks, 14(6):1569–1572, 2003.

Temporal Dynamics of Neural Networks

Transmission Likelihood

- We identify the causes of neuron spikes through stability analysis of Izhikevich's system.
- If a neuron's initial state is unstable, its potential will diverge to infinity, equivalent to a spike.
- Initial values of membrane potential and recovery determine the time a neuron takes to spike.

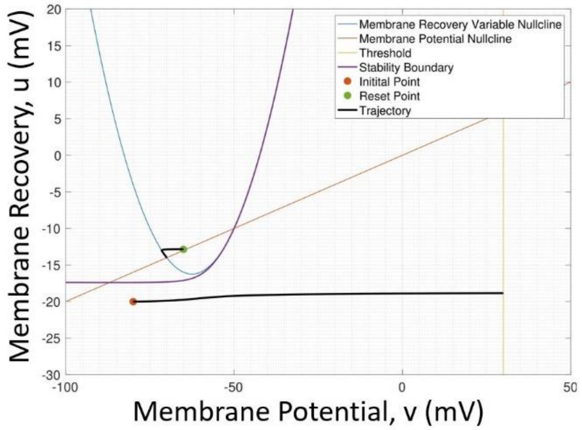


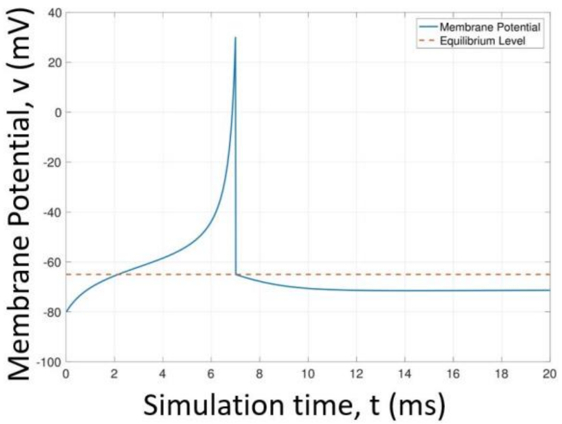


Temporal Dynamics of Neural Networks

Transmission Likelihood

- Initial values of membrane potential and recovery determine the time a neuron takes to spike.
- If $(v_{init}, u_{init}) = (-80, -20)$, the time to spike is $t \approx 7s$.
- If $(v_{init}, u_{init}) = (-40, -30)$, the time to spike is $t \approx 1s$.
- A pre-synaptic node j can drive neuron i into a different unstable state, compared to pre-synaptic neuron k, if $\alpha_{k,i} \neq \alpha_{j,i}$.
- This shows that the diffusion of information between neurons can be modelled probabilistically, according to the rates α.

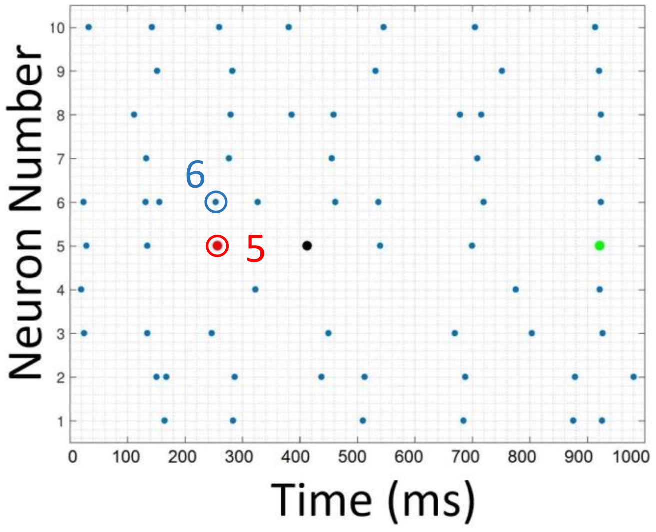


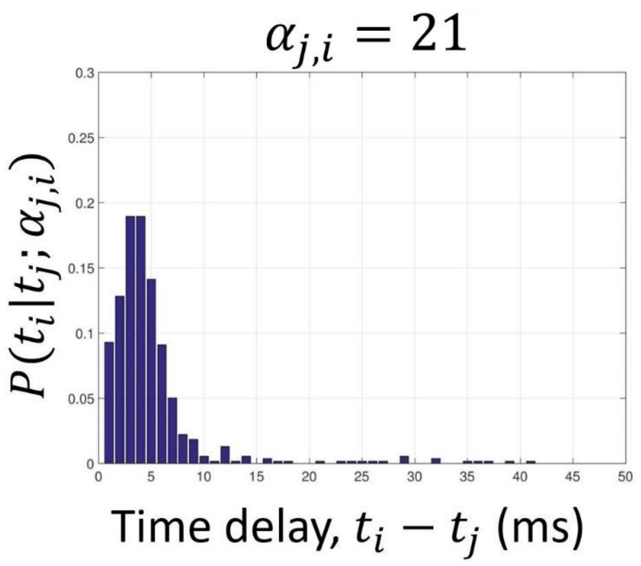


Temporal Dynamics of Neural Networks

Transmission Likelihood

- For each neuron i that spikes, we identify the pre-synaptic neuron that spikes when i became unstable.
- For example, neuron 5 fires at time $t = 257$. It enters the unstable region at time $t = 254$, the exact time when neuron 6 fires.
- The time delay between the spikes is $t_{6,5} = 3$, and the transmission rate $\alpha_{6,5} = 21$.

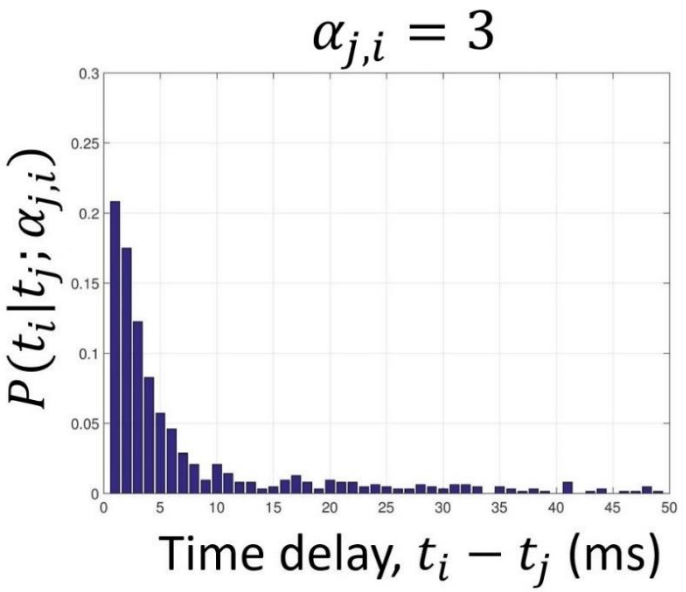


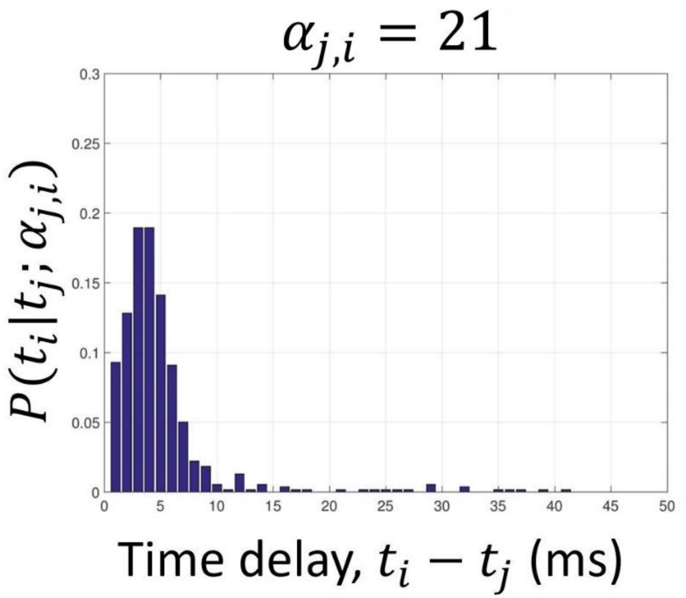


Temporal Dynamics of Neural Networks

Transmission Likelihood

- For small transmission rates, the shape of the likelihood is approximately exponential.
- For large transmission rates, the shape is approximately Rayleigh.
- We choose Rayleigh in order to accurately detect larger transmission rates.
- This proves the optimisation problem imposed by NetRate is convex.





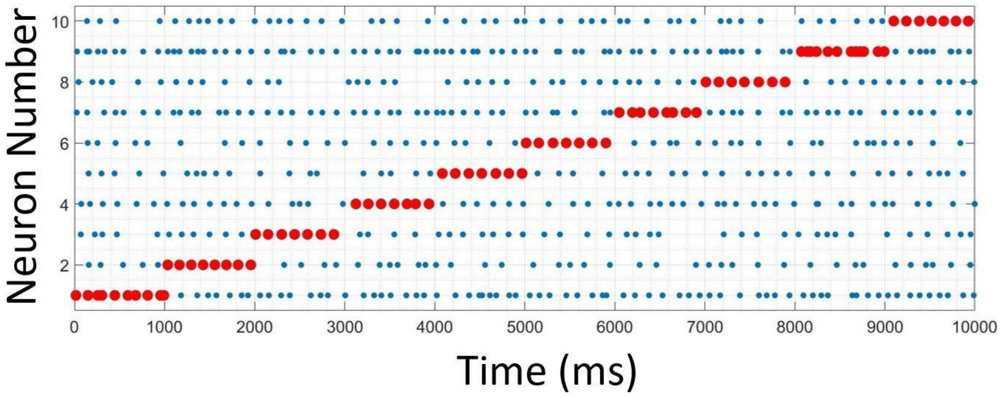
Simulations

- Generate independent cascades of information.
  - Supply excitatory spiking neurons with a constant input:

$$\frac{dv(t)}{dt} = 0.04v^2(t) + 5v(t) + 140 - u(t) + I$$

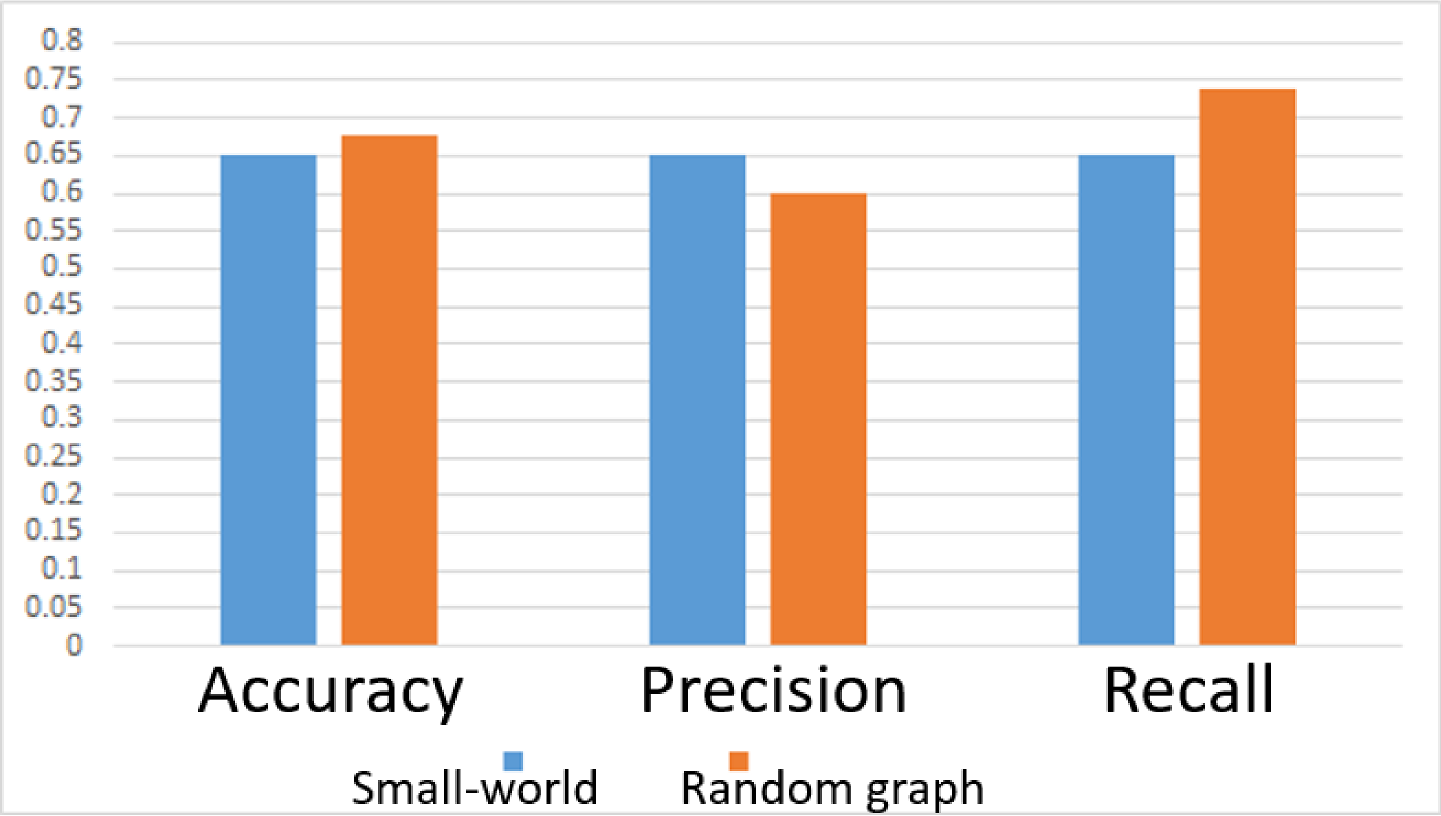
$$\frac{du(t)}{dt} = a\big(bv(t) - u(t)\big)$$

  - This makes them spike periodically, generating independent cascades of information.



- Run NetRate on small-world networks and random geometric graphs.

Simulations



Conclusion

- We proposed a novel method to infer the topologies of biological neural networks, using the NetRate algorithm.
- The spike propagation has a probabilistic nature. The shape of the pairwise transmission likelihood is found empirically.
- We showed that the optimisation problem NetRate solves for neural connectivity inference, is convex.
- Results indicate that NetRate is a suitable algorithm for neural network inference.

Future Work

- Define a weighted transmission likelihood, such that NetRate accurately infers both small and larger weights.

Thank you for listening!

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Any questions?