Constraining directed information estimation to improve pairwise neural connectivity inference

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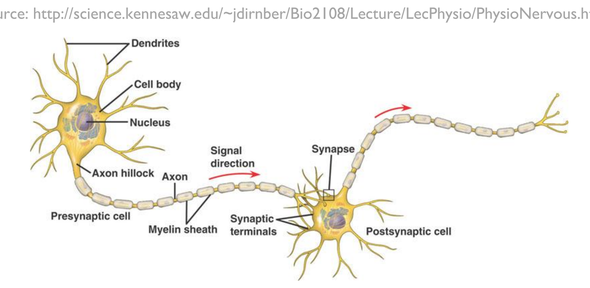
Background

- Neurons mainly communicate with each other by way of action potentials (spikes) and chemical synapses
- When recording from two neurons, we would like to use recorded data to determine whether they are connected

Source: http://science.kennesaw.edu/~jdirnber/Bio2108/Lecture/LecPhysio/PhysioNervous.html



Directed Information

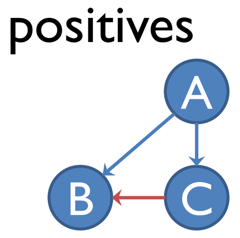
- If probability of the random process Y^n given the causal components of X^n is higher than the probability of Y^n without conditioning, then X^n can be said to cause Y^n in the Granger causality sense [1]
- Quinn et al. [2] apply this using directed information

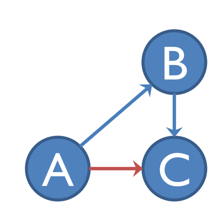
$$I(X^n \to Y^n) \triangleq H(Y^n) - \sum_{i=1}^{n} H\left(Y_i \middle| Y^{i-1}, X^i\right)$$

Y_1	Y_2	...	Y_{i-2}	Y_{i-1}	Y_i	...	Y_n
X_1	X_2	...	X_{i-2}	X_{i-1}	X_i	...	X_n

Limitations

- For pairwise connections, directed information can lead to false positives





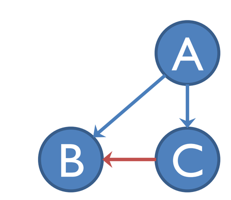
- While in [2] it is argued that these scenarios can be dealt with by considering the network, there is no guarantee that all nodes are measured

Objective

Improve the certainty of the connection between neurons using data recorded from just two neurons

Lower bound on delay

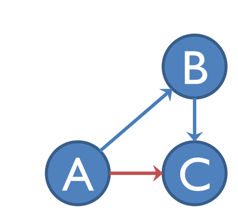
- For an action potential of one neuron to cause an action potential in another, it must actively propagate across the pre-synaptic axon, undergo neurotransmitter release and receptor bonding, and propagate through the dendrites to the post-synaptic soma
  - These steps take time, implying a delay
- Experimenter has knowledge of spacing of electrodes as well as general properties of these neurons
  - Given electrode separation and maximum speed, a minimum delay D can be estimated
- Including samples with delay less than D can lead to false positives for connectivity



Y_1	Y_2		...		Y_{i-2}	Y_{i-1}	Y_i	...	Y_n
X_1	X_2	...	X_{i-D}	X_{i-D+1}	...	X_{i-1}	X_i	...	X_n

Upper bound on delay

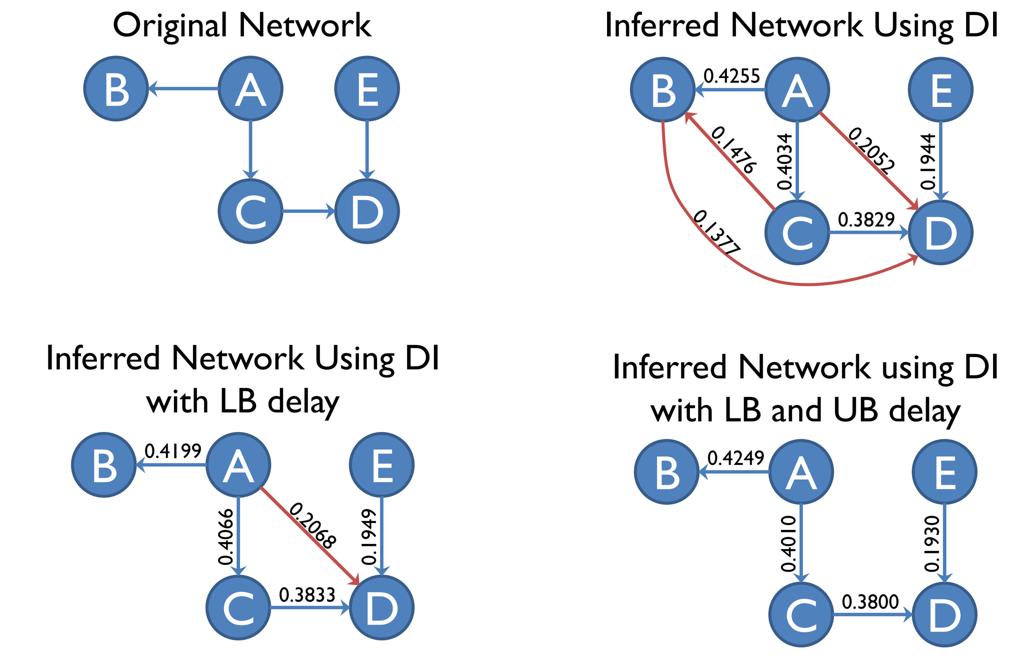
- Similar reasoning can be applied to find an upper bound on the maximum delay that a pre-synaptic action potential can have in causing a post-synaptic spike
  - Synaptic receptors remain open for a finite window of time, which depends on the type of receptor
  - Signals from the dendrites get passively filtered as they propagate to the soma, smearing them in time
  - Uncertainty in the delay due to unavoidable error in speed and distance estimates
- The more precise the window, the more useful the stronger this method will be at removing the correlations



Y_1	Y_2			...			Y_{i-2}	Y_{i-1}	Y_i	...	Y_n
X_1	...	X_{i-D-M}	$X_{i-D-M+1}$	...	X_{i-D}	X_{i-D+1}	...	X_{i-1}	X_i	...	X_n

Simulations

- Built a simple neuron using the NEURON simulation environment to capture realistic signal propagation
- Made connections to create network in which each neuron has random background firing



Conclusions

- By incorporating information known to the experimenter, we can better infer neural connectivity
- By using conservative estimates for the minimum causal delay, in the worst case scenario, it will make similar inferences as the original method
- This can be extended to any application of directed information for causality inference, where a causal response can only occur within a certain window after an event and responses outside of this window cannot be due to the monitored event

References

1. S. Kim, D. Putrino, S. Ghosh, and E. N. Brown, "A Granger causality measure for point process models of ensemble neural spiking activity," PLoS Computational Biology, vol. 7, no. 3, pp. e1001110, Mar. 2011.
2. C. Quinn, T. P. Coleman, N. Kiyavash, and N. G. Hatsopoulos, "Estimating the directed information to infer causal relationships in ensemble neural spike train recordings," Journal of Computational Neuroscience, January 2011.