Inference of topology and the nature of synapses in neuronal networks

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Abstract

In this work, we show that a recently proposed informational quantity, the causal mutual information, employed with an appropriate methodology, can be used not only to correctly infer the direction of the underlying physical synapses, but also to identify their excitatory or inhibitory nature, considering easy to handle and measure bivariate time series. We also demonstrate that our methodology can be used to correctly infer directionality of synapses even in the presence of dynamic and observational Gaussian noise, and is also successful in providing the effective directionality of inter-modular connectivity, when only mean fields can be measured.

Introduction

One of the most challenging problems in neuronal networks is the inference of its topology, that is, the determination of the underlying synaptic connectivity by indirect means, based on functional measurements of time-series of the membrane potential.

Inference based on functional measures requires a threshold analysis that establishes a link between the measurement and the physical connection. Rubido et al. [1] showed that a threshold can be calculated whenever a functional measure between nodes (CC or MI) in a network is dissimilar. Higher functional values correspond to a pair of adjacent nodes, lower functional values to non-adjacent nodes. Therefore, this threshold technique provide an inferred network that matched exactly with the real network.

In this work, we use the recently defined causal mutual information (CaMI) [2] calculated using an appropriate methodology to infer the direction of chemical synapses in complex neuronal networks without any mistake, by only considering easy to handle and to measure bivariate time-series.

Neural Network

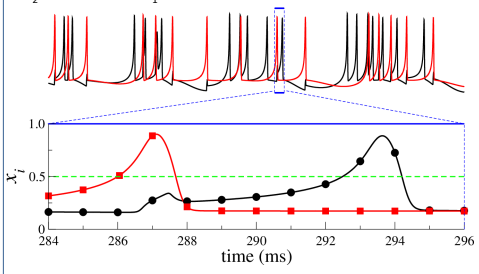
We consider the random neuronal network and the neuronal network of the nematode worm C. elegans whose structure was completely mapped at a cellular level [3,4]. The node dynamics in the network is expressed by the Hidmarsh-Rose (HR) neuron model [5] coupled by chemical synapses

$$\dot{p}_i = q_i - a p_i^3 + b p_i^2 - n_i + I_{\text{ext}} + g_c(V_{\text{syn}} - p_i) \sum_{j=1}^{N} \varepsilon_{ij} \Gamma(p_j),$$

where N is the neurons number, and gc is the chemical coupling strength. The chemical synapse function is modelled by the sigmoidal function. To do our analysis, we normalise p_i through the equation

$$x_i = \frac{p_i^{\max} - p_i}{p_i^{\max} - p_i^{\min}},$$

Figure 1. Normalized membrane potential of two chemical coupled HR neurons with connection from x_2 (red line) to x_1 (black line).

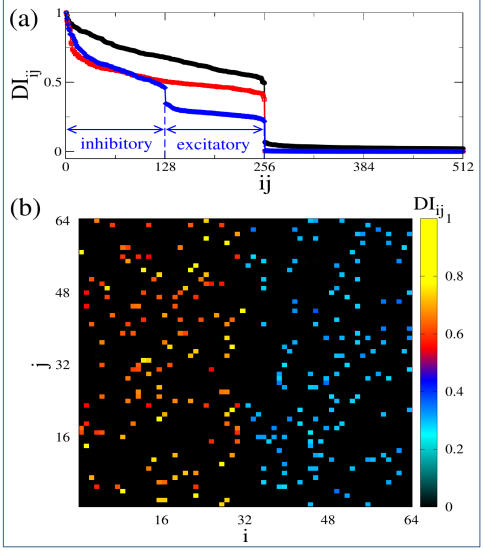


n	x_1^n	s_1^n	$S_1^{L=2}(n)$	x_2^n	s_2^n	$S_2^{L=4}(n)$
285	0.163043	0	00	0.374431	0	0110
286	0.161350	0	00	0.500448	1	1100
287	0.274266	0	00	0.886694	1	1000

$$\text{CaMI}_{X_i \to X_j} = \sum_{S_i, S_j} P(S_i^L, S_j^{2L}) \log \frac{P(S_i^L, S_j^{2L})}{P(S_i^L) P(S_j^{2L})},$$

$$\text{DI}_{X_i \to X_j} = \text{CaMI}_{X_i \to X_j} - \text{CaMI}_{X_j \to X_i}.$$

Figure 2. (a) Normalised directional index, ranked from larger to smaller values, for a random neuronal network with 64 neurons. We consider 3 cases for the connectivity: 256 excitatory synapses (black line), 256 inhibitory synapses (red line), and 128 excitatory and 128 inhibitory synapses (blue line). (b) Matrix of the normalised directional index of latter case..

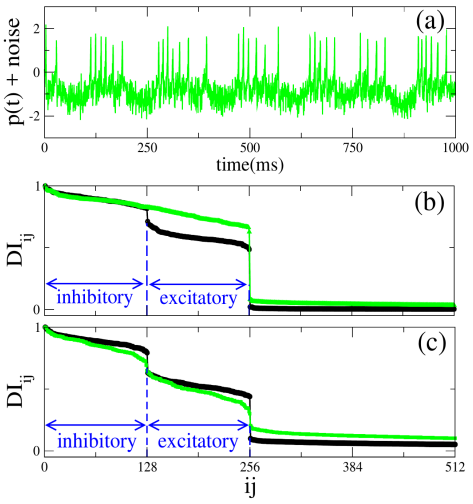


Noise Robustness

The additive noise is related to the imprecision of the equipment responsible for capturing the electrical signals in the neural membrane, so in our simulations we add to the values os p(t) a Gaussian noise with zero mean and standard deviation SD.

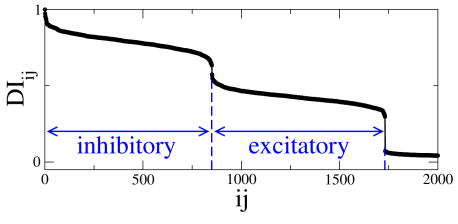
The dynamic noise can be related to several sources, such as synaptic noise and ion conductance noise. We add a Gaussian noise with zero mean and standard deviation SD In the action potential equation.

Figure 3. (a) Membrane potential with additive noise SD=0.35. (b) DI for aditive noise with SD=0.1 (black line) and SD=0.35 (green line). (c) DI for dynamic noise with SD=3 (black line) and SD=4 (green line).



C. elegans Network

We consider in our study the connectome of the large somatic nervous system [4] that consists of 277 neurons. To test our inference approach, we consider approximately 50% of excitatory and 50% of inhibitory synapses in the C. elegans network with 1731 directed connections.



Conclusions

We propose a successful methodology based on CaMI to infer, characterise and investigate the transmission of information in neuronal networks. Through the CaMI, we show not only how to infer the existence of synapses, but also to identify the nature of the synapse.

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