BMC Neuroscience

Poster presentation

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Information theory based methods to estimate the functional connectivity in dissociated neuronal networks

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from Eighteenth Annual Computational Neuroscience Meeting: CNS*2009
Berlin, Germany. 18–23 July 2009

Published: 13 July 2009

BMC Neuroscience 2009, **10**(Suppl 1):P109 doi:10.1186/1471-2202-10-S1-P109

This abstract is available from: http://www.biomedcentral.com/1471-2202/10/S1/P109

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Introduction

Large random networks of *in vitro* cortical neurons coupled to Micro Electrode Arrays (MEAs) can be used as a model for studying the network mechanisms of information coding, learning and memory [1]. To better investigate the neuronal dynamics of these complex systems, one must quantify the couplings among pairs of neurons based upon electrophysiological measurements (functional connectivity).

Methods

We estimated the functional connectivity of highly connected neuronal networks by means of cross correlation (CC), joint entropy (JE), mutual information (MI), and transfer entropy (TE) [2]. Since MI is symmetrical, we built an MI function delaying the peak trains in order to detect directional flow of information. JE is based on the cross inter spike intervals and it has been applied for the first time in this context. The methods performances were evaluated by ROCs (Receiver Operating Characteristic) and by an *ad hoc* method named PPC (Positive Precision Curve), on a neuronal network model made up of excitatory and inhibitory (20%) neurons.

Results

On simulated networks, TE showed the best performances while JE might provide an adequate alternative (Figure 1A). However, on experimental data recorded by MEAs, CC showed a good agreement with TE (Figure 1B). MI, instead, showed the worst performances both on simulated data and experimental recordings. Connectivity maps (Figure 1C) can be obtained by the identification of the highest connectivity methods values.

Discussion

PPCs allow to evaluate the absolute number of True Positives (TP) and False Positives (FP) and provide further information regarding their identification and about how to maximize the methods performances. The PPCs (Figure 1A) evaluated on the simulated models are entirely negative due to the complexity of the analyzed system. On real data, we estimated the overlap level (Figure 1B) among the connectivity methods discovering a high level of agreement between TE and CC on identifying some common FPs. It could be interpreted as the capability of such methods to detect some indirect connections.

References

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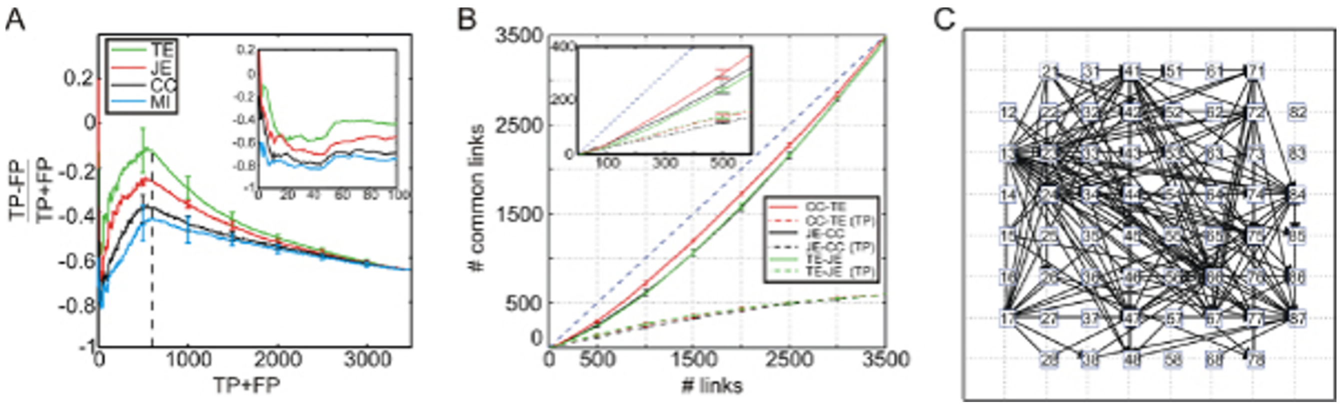

Figure 1
(A) PPCs relative to the simulated models. (B) Overlap curves from experimental data (dashed curves correspond to TPs commonly identified). (C) A connectivity map obtained by TE (200 links) on experimental data.

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