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# **ACCEPTED MANUSCRIPT**

# Two step Transfer Entropy- an estimator of delayed directional couplings between multivariate EEG time series

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#### Abstract

Quantifying delayed directional couplings between electroencephalographic (EEG) time series requires an efficient method of causal network inference. This is especially due to the limited knowledge about the underlying dynamics of the brain activity. Recent methods based on information theoretic measures such as Transfer Entropy (TE) made significant progress on this issue by providing a model-free framework for causality detection. However, TE estimation from observed data is not a trivial task, especially when the number of variables is large that is the case in a highly complex system like human brain. Here we propose a computationally efficient procedure for TE estimation based on using sets of the *Most Informative Variables* that effectively contribute to resolving the uncertainty of the destination. In the first step of this method, some conditioning sets are determined through a nonlinear state space reconstruction; then in the second step, optimal estimation of TE is done based on these sets. Validation of the proposed method using synthetic data and neurophysiological signals demonstrates computational efficiency in quantifying delayed directional couplings compared with the common TE analysis.

**Keywords:** Information Theory, Effective Connectivity, Causality, Transfer Entropy, Convergent Cross Mapping, Electroencephalography

## Introduction

Investigating the dynamics of the underlying processes of human brain activity using complex network analysis and graph-theoretical approaches has attracted a growing attention in recent years. These techniques are essentially based on the quantification of information flow among neuronal ensembles and result in the construction of a graph of effective connections (Moon et al., 2015). From a theoretical point of view, when performing large-scale analysis using EEG time series, the nodes of the graph represent the brain regions around each electrode. The coupling between particular neuronal ensembles activated during any brain function, may be illustrated by a directed link that indicates the information flow from the driver to the response region. Moreover, information transfer between different regions involves time delays due to the propagation of action potentials along axons as well as synaptic transmissions (Wibral et al., 2013). Therefore, the coupling direction, delay and strength are three characteristics of the links of the resulting graph, which must be specified using an appropriate measure of coupling (Vakorin et al., 2011).

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