Journal of Neuroscience Methods 268 (2016) 87–97

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Non-parametric directionality analysis – Extension for removal of a single common predictor and application to time series

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HIGHLIGHTS

- We describe non-parametric estimates of conditional directionality between signals.
- Scalar metrics decompose the conditional product moment correlation by direction.
- Additional functions decompose the partial coherence estimate by direction.
- Method is applied to simulated (cortical neuron) and real (hippocampal LFP) data.
- Framework can be applied to time series and spike train data.

ARTICLE INFO

Article history:
Received 16 December 2015
Received in revised form 18 March 2016
Accepted 4 May 2016
Available online 7 May 2016

Keywords:
Directionality
Partial coherence
Non-parametric
Time series
Point process
Conditional independence
Granger causality

ABSTRACT

Background: The ability to infer network structure from multivariate neuronal signals is central to computational neuroscience. Directed network analyses typically use parametric approaches based on auto-regressive (AR) models, where networks are constructed from estimates of AR model parameters. However, the validity of using low order AR models for neurophysiological signals has been questioned. A recent article introduced a non-parametric approach to estimate directionality in bivariate data, non-parametric approaches are free from concerns over model validity.
New method: We extend the non-parametric framework to include measures of directed conditional independence, using scalar measures that decompose the overall partial correlation coefficient summatively by direction, and a set of functions that decompose the partial coherence summatively by direction. A time domain partial correlation function allows both time and frequency views of the data to be constructed. The conditional independence estimates are conditioned on a single predictor.
Results: The framework is applied to simulated cortical neuron networks and mixtures of Gaussian time series data with known interactions. It is applied to experimental data consisting of local field potential recordings from bilateral hippocampus in anaesthetised rats.
Comparison with existing method(s): The framework offers a non-parametric approach to estimation of directed interactions in multivariate neuronal recordings, and increased flexibility in dealing with both spike train and time series data.
Conclusions: The framework offers a novel alternative non-parametric approach to estimate directed interactions in multivariate neuronal recordings, and is applicable to spike train and time series data.

1. Introduction

Directed network analyses are widely used in neuroscience to infer network structure in multivariate neural recordings (Rubinov and Sporns, 2010). The majority of approaches are parametric, which rely on estimating the parameters of a model to describe the patten of interactions between the observed signals, typically using auto-regressive (AR) models (Granger, 1969; Geweke, 1982). Once the AR parameters have been estimated different metrics relating to directionality can be constructed directly as a function of the model parameters (Baccala and Sameshima, 2001; Kaminski et al., 2001; Chen et al., 2006; Schelter et al., 2006; Chicharro, 2012). A number of concerns have been raised regarding the validity of AR models to accurately capture the complex structure present

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http://dx.doi.org/10.1016/j.jneumeth.2016.05.008
0165-0270/

in multivariate neural and other time series typically encountered in scientific problems (Gersch, 1972; Thomson and Chave, 1991; Lindsay and Rosenberg, 2011). A number of alternative non-parametric approaches have been considered to describe directed interactions in neurophysiological signals (Gersch, 1972; Eichler et al., 2003; Lindsay and Rosenberg, 2011; Dhamala, 2008a,b). A recent article introduced a non-parametric framework for directionality analysis of bivariate data (Halliday, 2015), with application to single unit spike train data.

The concept of conditional independence is a powerful one that is widely used in partial regression models where the effects of variables that are believed to influence the correlation between dependent variables are removed to provide a more accurate description of any dependency (e.g. Ezekiel and Fox, 1958). The use of conditional causality measures to distinguish between direct and indirect influences has been considered in parametric approaches to directionality. Granger (1969) considers two and three variable models, leading in the three variable model case to a partial cross spectrum from which causal and feedback relationships between two variables conditioned on a third can be derived. An alternative parametric approach using information theoretic measures (Geweke, 1982) has also been extended to include conditioning variables (Pierce, 1982; Geweke, 1984). Related approaches are considered in Chen et al. (2006) and Guo et al. (2008).

This paper presents a novel extension to the non-parametric approach in Halliday (2015) for multivariate data by presenting a framework for analysis of three random processes. We also investigate applicability of the framework to both time series data and spike train data. One advantage of considering time series data is that measures derived from residual and conditional variance metrics can readily be calibrated against known (simulated) data. We undertake such a comparison to establish the accuracy and usefulness of our multivariate extension. The approach is further validated through application to experimental data consisting of local field potential recordings from bilateral hippocampus in anaesthetised rat. Our results demonstrate the flexibility of the non-parametric approach in dealing with both spike train and time series data. Our novel approach should therefore have broad applicability across a wide range of electrophysiological data.

The paper is arranged as follows. Section 2 presents the methods including sub-sections on algorithms and significance testing. Section 3 describes results from application of the conditional non-parametric framework to simulated cortical neuron networks, to artificial mixtures of Gaussian time-series used to verify quantitative aspects of the framework and to the experimental data. Conclusions and discussion are in Section 4.

2. Methods

Our framework assumes that random processes have wide-sense (weak) stationarity (Brillinger, 1975; Priestley, 1981). The approach can be applied to time series data and point-process data. Point process data are represented using differential increments which count the number of spikes in a small interval, which we assume to be the sampling interval Δt (Rosenberg et al., 1989; Conway et al., 1993). Point processes are also assumed to be orderly, i.e. only one spike can occur in each sampling interval (Conway et al., 1993). In the derivation below (x, y, z) refer to three random processes which can be either time series or point process differential increments, or mixtures of the two data types. We use the term multivariate in the manuscript, since we are considering the analysis of three simultaneous random processes. However, only a single predictor is used, the possibility of extending the analysis to multiple predictors is considered in the discussion.

2.1. Theory

For bivariate random processes (x, y) a scalar measure of overall dependence is given by the squared correlation coefficient (Pierce, 1979; Halliday, 2015). This is defined in terms of ordinary and residual variances as

$$R^2_{yx} = \frac{\sigma^2_y - \sigma^2_{y|x}}{\sigma^2_y} \tag{1}$$

The conditioned variance, $\sigma^2_{y|x}$ can be equated to the variance of the error process after a linear regression of y on x. Eq. (1) can be interpreted as the fraction of the variance in y that can be accounted for by the regressor x. It is a symmetrical measure which does not provide any indication of directionality of interaction.

To account for any common effect that process z may have on both x and y a partial correlation coefficient can be used

$$R^2_{yx|z} = \frac{\sigma^2_{y|z} - \sigma^2_{y|x,z}}{\sigma^2_{y|z}} \tag{2}$$

In this case both processes x and y are conditioned on the third process z. Partial regression is widely used in situations where it is believed that the predictor, z, can account for some or all of the original association between x and y. The objective is to distinguish a genuine correlation, $R^2_{yx|z}$, from an apparent or induced correlation, R^2_{yx}. Throughout this paper we use linear models and consider linear interactions.

The relationship between the scalar R^2_{yx} and the coherence function, $|R_{yx}(\lambda)|^2$ was used as the starting point for the derivation of non-parametric directionality measures in Halliday (2015). The frequency domain equivalent of the partial regression coefficient, Eq. (2), is the partial coherence function

$$|R_{yx|z}(\lambda)|^2 = \frac{|f_{yx|z}(\lambda)|^2}{f_{xx|z}(\lambda) f_{yy|z}(\lambda)} \tag{3}$$

where $f_{yx|z}(\lambda)$ is the partial cross power spectral density (or partial cross-spectrum) between processes x and y with predictor z. The two partial auto-spectra are $f_{xx|z}(\lambda)$ and $f_{yy|z}(\lambda)$. Partial coherence estimates have proved useful in identifying direct interactions from common inputs in functional connectivity studies of neural circuits (Rosenberg et al., 1998; Eichler et al., 2003; Salvador et al., 2005; Medkour et al., 2009).

The link between the partial coherence function in Eq. (3) and the partial correlation coefficient in Eq. (2) can be made by considering the residual variance in the partial regression model, $\sigma^2_{y|x,z}$. In the frequency domain this residual variance is the residual spectrum $f_{yy|x,z}(\lambda)$. Using the same derivation as the bivariate framework (Halliday, 2015) we can derive the result

$$\left|R_{yx|z}(\lambda)\right|^2 = \frac{f_{yy|z}(\lambda) - f_{yy|x,z}(\lambda)}{f_{yy|z}(\lambda)} \tag{4}$$

We have used the partial gain function (Halliday et al., 1995), $f_{yx|z}(\lambda)/f_{xx|z}(\lambda)$, in this derivation. Thus, as in the bivariate case, there is a close correspondence between the partial coherence function in Eq. (4) and the partial regression coefficient in Eq. (2). The partial coherence function decomposes the R^2 value by frequency, thus $R^2_{yx|z}$ can be recovered by integrating the partial coherence

$$R^2_{yx|z} = \frac{1}{2\pi} \int_{-\pi}^{+\pi} \left|R_{yx|z}(\lambda)\right|^2 d\lambda \tag{5}$$

where the partial coherence is defined over the normalised angluar frequency range $[-\pi, +\pi]$.

Application of the minimum mean square error (MMSE) pre-whitening step (Eldar and Oppenheim, 2003) is next applied to