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How to detect the Granger-causal flow direction in the presence of additive noise?

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ABSTRACT

Granger-causality metrics have become increasingly popular tools to identify directed interactions between brain areas. However, it is known that additive noise can strongly affect Granger-causality metrics, which can lead to spurious conclusions about neuronal interactions. To solve this problem, previous studies have proposed the detection of Granger-causal directionality, i.e. the dominant Granger-causal flow, using either the slope of the coherency (Phase Slope Index; PSI), or by comparing Granger-causality values between original and time-reversed signals (reversed Granger testing). We show that for ensembles of vector autoregressive (VAR) models encompassing bidirectionally coupled sources, these alternative methods do not correctly measure Granger-causal directionality for a substantial fraction of VAR models, even in the absence of noise. We then demonstrate that uncorrelated noise has fundamentally different effects on directed connectivity metrics than linearly mixed noise, where the latter may result as a consequence of electric volume conduction. Uncorrelated noise only weakly affects the detection of Granger-causal directionality, whereas linearly mixed noise causes a large fraction of false positives for standard Granger-causality metrics and PSI, but not for reversed Granger testing. We further show that we can reliably identify cases where linearly mixed noise causes a large fraction of false positives by examining the magnitude of the instantaneous influence coefficient in a structural VAR model. By rejecting cases with strong instantaneous influence, we obtain an improved detection of Granger-causal flow between neuronal sources in the presence of additive noise. These techniques are applicable to real data, which we demonstrate using actual area V1 and area V4 LFP data, recorded from the awake monkey performing a visual attention task.

The Wiener–Granger definition of causality allows inference of causal relationships between interacting stochastic sources. Causality analysis methods have been applied in many fields, including physics, econometrics, geology, ecology, genetics, physiology and neuroscience (Barnett et al., 2009; Bernasconi and Konig, 1999; Bressler and Seth, 2011; Brovelli et al., 2004; Ding et al., 2006; Geweke, 1982; Granger, 1969; Gregoriou et al., 2009; Hiemstra and Jones, 1994; Hu and Nenov, 2004; Kaufmann and Stern, 1997; Lozano et al., 2009; Marinazzo et al., 2008; Nolte et al., 2008; Rosenblum and Pikovsky, 2001; Salazar et al., 2012; Schreiber, 2000; Smirnov and Mokhov, 2009; Staniek and Lehnertz, 2008; Sugihara et al., 2012). Standard Granger-causality metrics are typically based on linear vector autoregressive (VAR) modeling, with Granger-causality $f_{i \to j}$ defined by examining x_i's effect on the residual errors in forecasting $x_j(t)$ (Geweke, 1982; Granger, 1969, Eqs. (4)–(5)). In the neurosciences, Granger-causality metrics have become increasingly popular tools to identify functional, frequency-specific directed influences between brain areas (e.g. Bernasconi and Konig, 1999; Bressler and Seth, 2011; Brovelli et al., 2004; Ding et al., 2006; Friston et al., 2014). Two recent studies have shown interesting applications of Granger causality to characterize functional interactions in the visual system. Bastos et al. (2014) and van Kerkoerle et al. (2014) have shown that gamma frequencies contribute to a feedforward flow of information, whereas alpha and beta frequencies contribute to a flow of information in the feedback direction. Interestingly, Bastos et al. (2014) succeeded to reconstruct the visual hierarchy based on anatomical tracing studies on the mere basis of examining the asymmetry of Granger-causality spectra, and showed that this cortical hierarchy was task-dependent.

Granger-causality metrics were originally developed for systems whose measurements are not corrupted by additive noise. It has been shown that they can be strongly affected by both uncorrelated and linearly mixed additive noise (Albo et al., 2004; Friston et al., 2014;

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Haufe et al., 2012, 2013; Nalatore et al., 2007; Newbold, 1978; Nolte et al., 2008; Seth et al., 2013; Sommerlade et al., 2012). Nolte et al. (2008) showed that adding a linear mixture of noise sources (correlated noise) often leads to a misidentification of causal driver and recipient when using the standard Granger-causality metrics proposed by Granger (1969). This is an important issue in the neurosciences, as electric currents spread instantaneously from single brain or noise sources to multiple sensors ('volume conduction'), posing a major problem especially for scalp EEG (Electro-encephalography), MEG (Magneto-encephalography), and intracranial LFP (Local Field Potential) signals (Nolte et al., 2004; Nunez and Srinivasan, 2006; Stam et al., 2007; Vinck et al., 2011). This problem can, as far as the estimation of symmetric, undirected connectivity (like coherence, phase locking value) metrics is concerned, be adequately addressed by using metrics that are based on the imaginary component of the cross-spectral density (Nolte et al., 2004; Stam et al., 2007; Vinck et al., 2011). In this paper, we ask whether directed connectivity measures like Granger-causality can be protected against linearly mixed noise as well.

Recently, two directed connectivity measures were introduced to address the volume conduction problem. Nolte et al. (2008) proposed to detect Granger-causal directionality by examining whether fluctuations of one signal precede fluctuations of another signal in time — i.e. temporal precedence — using a measure called phase slope index (PSI). Haufe et al. (2012, 2013) proposed to protect Granger-causality metrics against linearly mixed noise by comparing Granger-causality values with those for time-reversed signals (Haufe et al., 2013), henceforth referred to as RGT (*reversed Granger testing*). In terms of the true positives vs false positives mix, PSI was found to exhibit a slightly better performance than RGT and a much better performance than standard Granger-causality metrics (Haufe et al., 2012, 2013; Nolte et al., 2008).

While initial results using these alternative directed connectivity metrics have been promising (Haufe et al., 2013; Nolte et al., 2008), there are several critical questions that need to be addressed. Firstly, it is unknown under which conditions PSI and RGT are in fact valid measures of Granger-causal directionality, as previous work evaluated their use only for unidirectional, but not bidirectional VAR models (Haufe et al., 2013; Nolte et al., 2008) (Case of no additive noise section). This question is critical because interactions between cortical areas are typically bidirectional rather than unidirectional. Secondly, it remains unclear to what extent directed connectivity measures are affected by uncorrelated noise, which occurs for example for spatially distant spike trains, current source densities and bipolarly referenced LFPs (Mitzdorf, 1985) (Case of uncorrelated noise section). Haufe et al. (2013) and Nolte et al. (2008) only considered the effect of linearly mixed noise (which is prominent for scalp EEG and MEG) but not uncorrelated noise. It is thus unknown whether standard Granger-causality metrics can be safely used in the regime of uncorrelated noise. Thirdly, it remains unclear whether PSI and RGT are indeed robust to linearly mixed noise, and how their overall performances compare, since to date they have been evaluated only for finite-length data traces and unidirectional VAR models. This is problematic, because small fractions of false positives may arise because of a lack of statistical power (finite data traces) and the use of unidirectional VAR models. The performances of PSI and RGT should therefore also be evaluated in the asymptotic sampling regime (i.e., infinitely long data traces) and for the bidirectional VAR models (Case of linearly mixed noise section). Here, we employ algorithms to compute the various directed connectivity metrics analytically given the VAR models of signal and noise sources. Surprisingly, we find that PSI, like standard Granger-causality metrics, does not constrain the false positive rate at acceptable levels. In contrast, RGT yields a much smaller fraction of false positives and a much better overall performance than standard Granger and PSI, although it still shows failures in a significant fraction of test cases. This paper also aims to advance the theoretical analyses of PSI and RGT; in particular, we use theoretical analysis to identify regimes in which RGT always fails or succeeds.

We find that further performance gains are achievable beyond those obtained by RGT, by indirectly measuring the amount of linearly mixed noise impinging on two measurement sensors. The idea of this approach is quite simple but effective: We can examine the degree to which there is instantaneous (i.e., zero-lag) feedback between time series by using a structural VAR model that contains an explicit instantaneous transfer coefficient. This allows us to reject cases where the instantaneous transfer is too large compared with the transfer at other lags. In the Criterion on instantaneous influence section we show that failures of Granger-causality metrics due to linearly mixed noise can be reliably predicted and removed by examining the magnitude of the instantaneous prediction coefficient in a structural VAR model. This provides a means to reduce the false positive rate and to improve the overall performance of the analysis in terms of the true and false positive mix.

We apply these techniques to actual LFP data obtained from areas V1 and V4 in the awake monkey performing a visual attention task.

Introduction of Granger analysis techniques and VAR model with additive noise

In this section, we define the basic VAR model, the VAR model with additive noise included, the various directed connectivity metrics, and performance measures for the different metrics.

The bivariate VAR model and a measure of linear Granger feedback

In this paper, we will be concerned with a bivariate signal $\mathbf{x}(t)$ described by a bivariate VAR model of order M

$$\mathbf{x}(t) = \sum_{\tau=1}^{M} \mathbf{A}(\tau)\mathbf{x}(t-\tau) + \mathbf{U}(t), \tag{1}$$

where *innovation* $\mathbf{U}(t)$ — the remaining error after incorporating the predictions from past values of $\mathbf{x}(t)$ — has a covariance matrix

$$\sum \equiv \mathrm{Cov}\{\mathbf{U}(t), \mathbf{U}(t)\}. \tag{2}$$

We refer to x_1 and x_2 as the *signal sources*. The matrices $\mathbf{A}(\tau)$ hold the real-valued VAR coefficients. Also $\mathbf{x}(t)$ can be represented by the restricted AR model

$$\mathbf{x}(t) = \sum_{\tau=1}^{M} \mathbf{F}(\tau)\mathbf{x}(t-\tau) + \mathbf{V}(t) \tag{3}$$

with diagonal coefficient matrix $\mathbf{F}(\tau)$ and $\mathbf{\Omega} \equiv \mathrm{Cov}\{\mathbf{V}(t), \mathbf{V}(t)\}$. The standard measure of Granger-causal flow is defined by the log-ratio of the variances of the innovation errors (Granger, 1969)

$$f_{j\to i} \equiv \ln\left(\frac{\Omega_{ii}}{\Sigma_{ii}}\right), i \neq j. \tag{4}$$

The feedback metric $f_{j \to i}$ measures the degree to which past values of $x_j(t)$ improve the prediction of future values of $x_i(t)$ relative to what can be derived from past values of $x_i(t)$. We define x_1 to be *Granger-causally dominant* over x_2 if the *Granger-causal directionality* measure

$$g \equiv f_{1\to 2} - f_{2\to 1} > 0. \tag{5}$$

In this paper, we study the simplified problem of detecting $\mathrm{sgn}(g)$, where $\mathrm{sgn}(g)$ is the sign function, from noisy data, as in Nolte et al. (2008); we are not concerned with the problem of estimating $f_{2\to 1}$ and $f_{1\to 2}$ separately. The problem is stated as providing a measure of $\mathrm{sgn}(g)$ that optimizes performance in terms of the false and true