



## Computational Neuroscience

# Assessing the strength of directed influences among neural signals: An approach to noisy data



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## HIGHLIGHTS

- Inference of Granger causality in noisy signals.
- Analytical calculations explaining false positive conclusions in the presence of noise.
- Derivation of statistics that enable reliable inference of Granger causality from noisy signals.
- Application to sleep stage in mice EEG data.

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## ABSTRACT

**Background:** Measurements in the neurosciences are afflicted with observational noise. Granger-causality inference typically does not take this effect into account. We demonstrate that this leads to false positives conclusions and spurious causalities.

**New method:** State space modelling provides a convenient framework to obtain reliable estimates for Granger-causality. Despite its previous application in several studies, the analytical derivation of the statistics for parameter estimation in the state space model was missing. This prevented a rigorous evaluation of the results.

**Results:** In this manuscript we derive the statistics for parameter estimation in the state space model. We demonstrate in an extensive simulation study that our novel approach outperforms standard approaches and avoids false positive conclusions about Granger-causality.

**Comparison with existing methods:** In comparison with the naive application of Granger-causality inference, we demonstrate the superiority of our novel approach. The wide-spread applicability of our procedure provides a statistical framework for future studies. The application to mice electroencephalogram data demonstrates the immediate applicability of our approach.

**Conclusions:** The analytical derivation of the statistics presented in this manuscript enables a rigorous evaluation of the results of Granger causal network inference. It is noteworthy that the statistics can be readily applied to various measures for Granger causality and other approaches that are based on vector autoregressive models.

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## 1. Introduction

Complex systems are relevant in different branches of physics, economics, sociology, biology or the neurosciences. They can be investigated either by explicit first principle modelling of the dynamics, the so-called *direct approach*, or by inferring the system based on observed data, i.e. the *inverse approach*. The first requires profound *a priori* knowledge about the investigated system while the second relies on measurements of the system.

Within the framework of data-based modelling, various techniques have been developed. For many years, the methodological developments and concepts evolved independently in the different disciplines. In the past decade however, the transfer of knowledge across the borders of the different research fields has increased substantially, for example when methods dealing with non-linear stochastic systems have been introduced (Schelter et al., 2006).

Networks of interacting nodes, each with its own dynamics, are a key mathematical tool for the description of complex systems (Strogatz, 2001). Depending on the particular application, the dynamics of the individual nodes, their coupling structure or their collective behaviour all determine the dynamics of the system. In the neurosciences, for instance, detecting interactions between signals, i.e. the coupling structure among nodes, is of particular interest. Understanding brain networks promises to disclose the biological basis underlying natural behaviour or certain diseases (e.g. Hesse et al., 2003; Tass et al., 1998; Pitzalis et al., 1998; Keyl et al., 2000; Nollo et al., 2005; Bowers and Murray, 2004). Several techniques have been proposed so far to infer the network structure of complex systems from observed signals. These include but are not limited to transfer entropy (Schreiber, 2000; Staniek and Lehnertz, 2008), recurrences in state space (Arnhold et al., 1999; Chicharro and Andrzejak, 2009; Romano et al., 2007), mutual information (Pompe et al., 1998; Paluš and Stefanovska, 2003; Paluš and Vejmelka, 2007; Vejmelka and Paluš, 2008; Frenzel and Pompe, 2007), phase dynamics (Rosenblum and Pikovsky, 2001; Rosenblum et al., 2002), coherence (Halliday and Rosenberg, 2000; Dahlhaus, 2000; Nolte et al., 2008), the Fokker Planck formalism (Prussek and Lehnertz, 2008; Bahraminasab et al., 2009), or autoregressive modelling (Dahlhaus and Eichler, 2003; Schack et al., 1995; Eichler, 2000; Korzeniewska et al., 1997; Kamiński et al., 1997; Kamiński and Blinowska, 1991; Arnold et al., 1998).

When investigating interactions among processes, cross-spectral analysis is often chosen (Brockwell and Davis, 1998). If the number of processes exceeds two, the question arises, whether interactions are direct or indirect. To address this challenge, the concept of partialisation is used (Dahlhaus, 2000; Brillinger, 1981). Partialisation aims at revealing *direct* connections by subtracting influences of third processes (Schad et al., 2009).

Since (partial) cross-spectra are Hermitian, it is not possible to infer the direction of an influence from coherences. Additional information of the complex valued cross-spectra can be revealed by analysing their phases. The phase spectra can be used to draw conclusions about the direction of an influence. However, these conclusions are hampered if, for instance, filters are present. Since filters are present in many applications, a straight forward interpretation of the phase spectra is usually not possible. Other approaches to investigate the direction of an influence use the concept of *causality*. Many methods (e.g. Hesse et al., 2003; Geweke, 1982, 1984; Chen and Wasterlain, 2006; Dhamala et al., 2008; Baccalá and Sameshima, 2001; Sameshima and Baccalá, 1999; Eichler, 2006; Kamiński and Blinowska, 1991) are based on Granger's definition of causality (Granger, 1969). Briefly, this definition states that a process  $x_1$  is causal for another process  $x_2$ , if  $x_1$  is useful for the prediction of the future of  $x_2$ . Linear Granger-causality is typically modelled by means of vector autoregressive processes, which are estimated via multivariate Yule–Walker equations or similar approaches (Lütkepohl, 1993).

The estimators for the vector autoregressive models do not account for observational noise, which afflicts almost any observed signal. There are different reasons for an inaccurate measurement, such as the precision of the measurement device or influences from the environment. This inevitably leads to a misestimation of the parameters; typically parameters are underestimated (Brockwell and Davis, 1998). We emphasise that in particular an over-estimation of certain parameters has a severe impact on Granger-causality analysis. As also discussed in Newbold (1978), Nalatore et al. (2007), and Nolte et al. (2008), we argue that this leads to spurious causalities independently of the specific measure for Granger-causality used, providing a more detailed view on the relation between parameter values and the severity of the misestimation for various signal to noise ratios. This explains in particular how under- as well as over-estimation of parameters leads to spurious interactions. Based on analytical calculations we reveal the cause of these spurious causalities. To this aim, we discuss a vector autoregressive process of order 2, to simplify the notation. We then investigate in details the consequences of the misestimation. We will also show that increasing the order of the fitted process yields an improved estimator. However, this is not sufficient to avoid false positive conclusions in the presence of observational noise (Timmer, 1998). Therefore, in this manuscript, state space modelling is used to explicitly include observational noise in the model. The idea of state space modelling for improving measures quantifying Granger-causality has been introduced in Winterhalder et al. (2005). This triggered further research that discussed the matter in more detail (Nalatore et al., 2007) and also an application to neurophysiological data (Nalatore et al., 2009). The corresponding statistics to assess the statistical significance of these Granger-causality measures, however, has not been thoroughly investigated. Typically Monte-Carlo based procedures, numerical approximations or bootstrap based approaches are employed to approximate the statistics for these measures. In this manuscript we assume that the system under investigation can be approximated by a linear system. Based on this assumption, we derive an analytical statistics for Granger-causality based measures.

Throughout, we demonstrate our results for a specific measure for Granger-causality, the so-called renormalised partial directed coherence (rPDC) (Schelter et al., 2009). It is a generalisation of partial directed coherence, which was introduced to quantify Granger causal influences (Baccalá and Sameshima, 2001) in the neurosciences (Sameshima and Baccalá, 1999; Nicolelis and Fanselow, 2002). The advantage of renormalised partial directed coherence is that it allows us to interpret the results also in terms of the strengths of interactions and it enables a rigorous comparison of the results. We emphasise though that the results apply to any Granger-causality measure that is based on vector autoregressive processes. The results are presented in a way that they can readily be generalised.

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