The effect of latent confounding processes on the estimation of the strength of causal influences in chain-type networks

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Abstract
Reliable recognition of casual interactions between processes is an issue particularly prevalent in the Neurosciences. When the structure of a network is not a priori known it is almost impossible to observe and measure all components of a system, and missing certain components could potentially lead to the inference of spurious interactions. The aim of this study is to demonstrate the effect of missing components of a network on the inferred strength of a spurious interaction. Our novel method uses vector autoregressive modelling and renormalised partial directed coherence to show how and why the inferred strength of causal interactions between processes changes when components in a network are missed. In cases where a latent confounder is influencing a network and consequently a spurious interaction appears, it is not possible to rely on estimates of the strength of this link as strength estimation methods are influenced by the noise of the latent confounder. Our novel approach demonstrates precisely how a latent confounder can affect the strength measure using analysis of vector autoregressive models. While it is possible to measure the strength of directed causal influences between processes the estimation of strength can be confounded if not all components of a system have been observed during measurement.

Introduction

Reliable recognition of causal interactions between processes is a multi- faceted problem found in a wide variety of research areas, however, one area in which it is particularly prevalent is that of the Neurosciences. One particular area of interest is the investigation of the network of causal influences between regions of the brain, as unlocking this valuable network can give in- sight into the connectivity of the brain and hence those pathologies which target it. There have been many and varied studies which analyse electroencephalography (EEG), magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI) data to investigate and infer the interdependencies, causal and otherwise, between brain regions (Rubinov and Sporns, 2010; Karamzadeh et al., 2013; Schelter et al., 2006; Dahlhaus et al., 1997; Eichler, 2005; Schreiber, 2000; Smirnov and Bezruchko, 2003; Sommerlade et al., 2012; Schad et al., 2009; Ramb et al., 2013).

In this case to speak of causality is to speak of Granger causality, in which causes must always precede their effects in time and all relevant processes must be taken into account for an accurate depiction of the network. Granger causality between processes can be simulated using vector autoregressive (VAR) models in which past values of a process influence with some weight, the present value of another process (Granger, 1969). A recent advancement in the field of inference of Granger causal influences between processes is that of the de- velopment of renormalised partial directed coherence (rPDC), which allows the measurement of the strength of causal interactions between processes from time series measurements in the frequency domain (Schelter et al., 2009). This method is free from the limitations of its predecessor, partial directed coherence (Baccalá and Sameshima, 2001), as it allows for the direct comparison of the strength of causal interactions directly from time series. That is to say, PDC is limited because it measures the strength of a causal influence from one process to another relative to another source signal. Furthermore, when more processes are causally linked to the source this artificially decreases the PDC value of these connections. This means that it does not allow for direct comparisons of the strength of interactions between processes or across frequencies.

The rPDC value indicating the strength of a causal influence from one process to another is derived in part from the coefficient of weight of the under- lying VAR model, which is estimated from the measured time series. The rPDC estimates of the strength of each link in a given network are directly comparable between processes and across frequencies.

In first introducing his idea of causality, latterly known as Granger causality, Granger (1969) stated that the concept relies upon the observation of all relevant processes. When the structure of a network is not a priori known this is not always possible. This leads to the creation of latent confounders, processes which are relevant to the network in that they influence, or are influenced by observed processes but are not observed or explicitly accounted for in the network structure. Latent confounders causally influence observed processes, but they themselves remain hidden, creating spurious causal influences between visible nodes,

confounding our understanding of the true structure of the underlying network (Eichler, 2005). Precisely how a latent confounder can affect a network is explored in (Ramb et al., 2013), and network reconstruction methods are explored in (Elsegai et al., 2015).
We will demonstrate how the average rPDC value of a spurious link, created as a result of a latent confounder is affected by the permutation of weights of the underlying networks links. Hence showing that the order of weightings in a chain type graph can have a substantial effect on the perceived strength of a spurious connection from the first to the final process in a chain when the intermediary processes are unobserved.

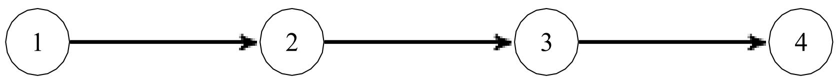


Figure 1: An example of a network with a chain-like structure

Method

Granger causality is rooted in the notion that causes will always precede their effects in time, the concept was first formulated in the area of econometrics (Granger, 1969), and was suggested as a means to investigate causal connections between variables. The concept of Granger causality is closely linked to (vector) autoregressive models which are used to represent time delayed, causal relationships between variables.
Vector autoregressive processes are stochastic, multivariate models in which past values of a process influence current values of itself or another process with a specified time delay. A vector autoregressive process of order p, VAR[p], is represented thusly,

$$X(t) = \sum_{r=1}^{p} a(r)\ X(t-r) + \ \varepsilon(t) \qquad (1)$$

with p coefficient matrices a(r), $r = 1, \ldots, p$ each with dimension $n \times n$. In which $E(t)$ is Gaussian distributed white noise and Σ is the covariance matrix of the noise, $E(t) \sim N\ (0, \Sigma)$. Here $X(t)$ is a value or vector of values describing the state of one or more evolving variables at a single point in time t. The dimension of the vector is dictated by the dimension of the system, or the number of time evolving variables accounted for in the model, denoted by dimension n.
Graphical models are used as a convenient means to visualise causal influ- ences between processes, a graph is a representation of a set of two sets, one of vertices and one of edges. In which vertices represent processes and directed edges represent directed causal influences between them, sometimes known as links. The weights on the graphs in this work indicate the coefficient of the strength of the influence from one process to another, as specified in the VAR model as entries in the a(r) matrix of coefficient in equation (1). The words "graph" and "network" are used interchangeably

in this work. Nodes and edges in graphs can take on many configurations, one of which is known as a chain. This configuration occurs when one node influences the next node in a sequence and so on, with no additional influences, an example of a 4 node chain is shown in figure 1 (Ramb et al., 2013). Chain networks are utilised to demonstrate the effect latent confounders can have on estimates of connection strength in its simplest form. More complex graphs are used towards the end of the paper, showing that the effect demonstrated is present in any network in which a chain exists.

Many methods of identifying causal interactions between time series involve fitting vector autoregressive models. Further steps are then taken to calculate strength of interaction and noise.

Fitting a VAR process would not typically result in a covariance matrix of the noise process equalling the identity matrix, but the covariance matrix can be adjusted to meet this requirement. This necessarily results in an adjustment of the matrices of coefficients A, which is discussed in the following. Typically a VAR process can be written as,

$$X(t) = A\,X(t-1) + \varepsilon(t), \qquad \varepsilon(t) \sim \mathcal{N}(0, \Sigma), \tag{2}$$

where Σ is the covariance matrix of the noise. Taking into account the above mentioned adjustments to the A matrix of coefficients of causal interactions and the $\varepsilon(t)$ matrix of the noise of the processes needed to account for a change of the variance of the process. Thus, the VAR model can be rewritten as,

$$X(t) = \tilde{A}\,X(t-1) + \eta(t), \qquad \eta(t) \sim \mathcal{N}(0, \mathbb{I}). \tag{3}$$

with,

$$\tilde{A} = \Sigma^{-\frac{1}{2}} A\, \Sigma^{\frac{1}{2}}, \tag{4}$$

$$\eta(t) = \Sigma^{-\frac{1}{2}} \varepsilon(t). \tag{5}$$

The limitation described in this work arises as a result of initially fitting a VAR model to time series data and setting the variance of the VAR model to 1. For demonstrative purposes in order to identify causal interactions between time series, renormalised partial directed coherence is used in this paper. A multivariate technique developed in Schelter et al. (2006), it is used here to measure the strength of Granger causal influences in the frequency domain.

The Fourier transform,

$$A(\omega) = I - \sum_{r=1}^{p} a(r) e^{i\omega r}, \tag{6}$$

of the coefficients of the VAR process, a(r) are split into real and imaginary parts

$$Z_{kj}(\omega) = \begin{pmatrix} Re(A_{kj}(\omega)) \\ Im(A_{kj}(\omega)) \end{pmatrix}. \tag{7}$$

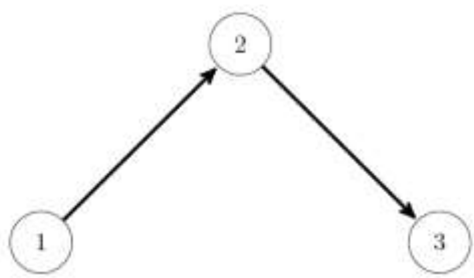
The corresponding estimator $\hat{Z}_{kj}(\omega)$, is asymptotically distributed with mean $Z_{kj}(\omega)$ and covariance matrix,

$$\frac{V_{kj}(\omega)}{N} = \sum_{l,m=1}^{p} R_{jj}^{-1}(l,m)\Sigma_{kk} \times \frac{1}{N}\begin{bmatrix} \cos(l\omega)\cos(m\omega) & \cos(l\omega)\sin(m\omega) \\ \sin(l\omega)\cos(m\omega) & \sin(l\omega)\sin(m\omega) \end{bmatrix}, \tag{8}$$

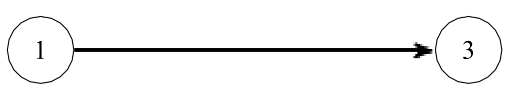
where N is the number of data points in the time series and R^{-1} is the inverse of the covariance matrix of the VAR process. The renormalised partial directed coherence is then,

$$\lambda_{kj}(\omega) = Z_{kj}(\omega)' \, V_{kj}^{-1}(\omega) \, Z_{kj}(\omega). \tag{9}$$

If $\lambda_{ij}(\omega)=0$, then the existence of an interaction from process j onto process i is rejected, where all the processes are taken into account. $\chi^2_{2,1-\alpha}/N$ is the α-significance level for $\lambda_{ij}(\omega)$ (Sommerlade et al., 2012), and $\chi^2_{2,1-\alpha}$ denotes the quartile 1-α of the χ^2-distribution with two degrees of freedom.



(a) 3 dimensional chain structure network.



(b) 2 dimensional network showing influence be- tween nodes 1 and 3 when node 2 is unobserved.

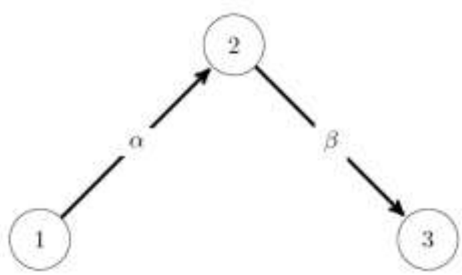
Figure 2: 3 dimensional chain graph and the spurious interaction that arises between nodes 1 and 3 as a result of unobserving node 2.

Granger stated that his interpretation of causality relied upon the inclusion in the model of all relevant processes, hence all processes or nodes present in the network. When the structure of the network is not a priori known, it is not always possible for all processes or nodes in the network to be observed, thus leading to the creation of latent confounders. The consequence of this is that hidden processes can be causally influenced and in turn causally influence other processes without being explicitly seen. This can lead to spurious or false causal interactions arising been observed nodes, an example is shown in figure 2. Here, a 3 dimensional network with a chain structure is simulated, and the second intermediary node is unobserved. As a result of this, in the 2 dimensional sub network a spurious interaction exists between nodes 1 and 3 which does not exist in the underlying network.

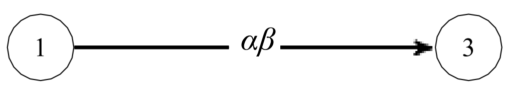
Simulations

Three dimensional chain networks

To demonstrate how the rPDC value of a spurious link created by a latent confounder is affected by the permutation of weights of the underlying network links we simulate a 3 node network arranged in a chain structure, in which node

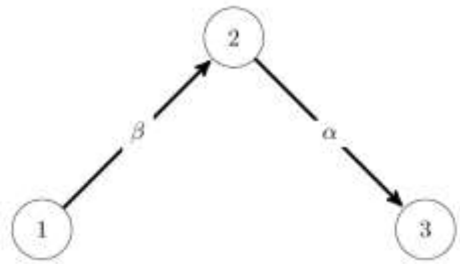


(a) 3 dimensional chain structure network with weighted edges α on the first link in the chain and β on the second link.

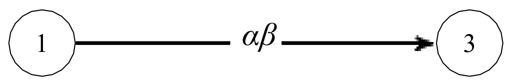


(b) 2 dimensional network showing influence be- tween nodes 1 and 3 when node 2 is unobserved in- cluding weighting $\alpha\beta$ derived from the VAR model.

Figure 3: 3 dimensional chain graph and the spurious interaction that arises between nodes 1 and 3 as a result of unobserving node 2, including weighting derived from the VAR model underlying the network.



(a) 3 dimensional chain structure network with weighted edges β on the first link in the chain and α on the second link, the reverse of figure 3(a).



(b) 2 dimensional network showing influence be- tween nodes 1 and 3 when node 2 is unobserved in- cluding weighting $\alpha\beta$ derived from the VAR model.

Figure 4: 3 dimensional chain graph and the spurious interaction that arises between nodes 1 and 3 as a result of unobserving node 2, including weighting derived from the VAR model underlying to network, the reverse weightings to those in figure 3(a).

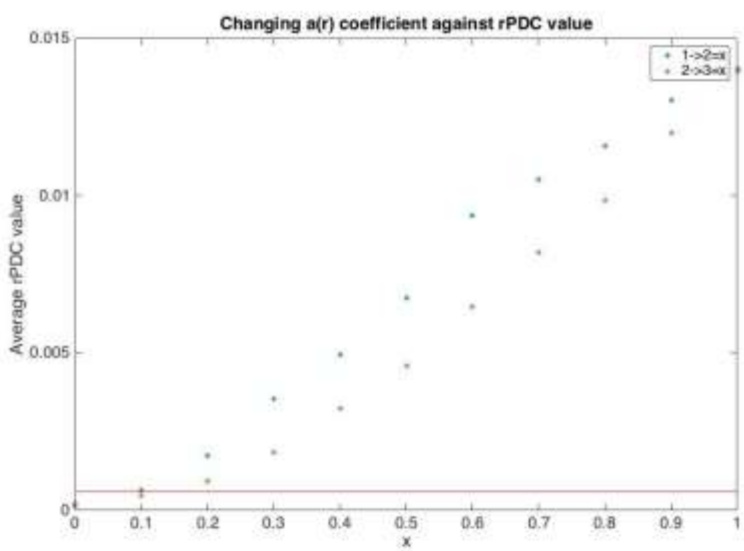


Figure 5: A graph showing the difference in average rPDC values of a spurious link between nodes 1 and 3 of the oberved 2 dimensional network, as x changes between 0.1 and 1 in steps of 0.1 for the graphs in figure 3 and figure 4, where the changing weight x is the weight of the first or second link in the 3 dimensional graph. In both graphs the weight of the spurious link is $\alpha\beta$ but the resulting average rPDC values of this link are different for many values of x. The solid red line shows the critical value at 5% significance level.

1 influences node 2 with some weight and node 2 influence node 3 with some other weight. The intermediary nodes in the chain are then unobserved - not explicitly accounted for in connectivity analysis with the intention of simulating a situation in which the node was not observed in the first instance - leaving only the first and final nodes. In this case the intermediary node is node 2 and to unobserve it leaves only nodes 1 and 3 in the network. Unobserving node 2 constitutes a latent confounder in the network, and consequently a spurious causal influence from node 1 to node 3 appears. This occurs as a direct result of not all the relevant processes being taken into account, a condition upon which Granger causality is founded. Measuring the average rPDC value of this spurious interaction it can be shown that the permutation of the weights, or the order in which the same combination of weights appear on the causal influences in the underlying network can affect the average rPDC value of the spurious interaction from the first node to the last node in the chain, in this case from node 1 to node 3.

Such an example can be demonstrated using a chain configuration of causal influence in a 3 node network, where node 1 influences node 2 with strength α and node 2 influences node 3 with strength β. If the true interaction structure of the underlying network can be visualised as in figure 3(a), then if node 2 - as the intermediary node - is not observed in the measurement of the network, e.g., only nodes 1 and 3 are observed in the network analysis, a causal influence appears from node 1 to node 3 with strength $\alpha\beta$ as shown in figure 3(b). This weighting can be derived analytically by consulting the VAR model from which the graph is derived,

$$X_1(t) = \varepsilon_1(t) \tag{10}$$

$$X_2(t) = \alpha X_1(t-1) + \varepsilon_1(t) \tag{11}$$

$$X_3(t) = \beta X_2(t-1) + \varepsilon_3(t). \tag{12}$$

Substituting $X_2(t)$ into the equation for $X_3(t)$ and multiplying out gives a revised VAR model for nodes 1 and 3,

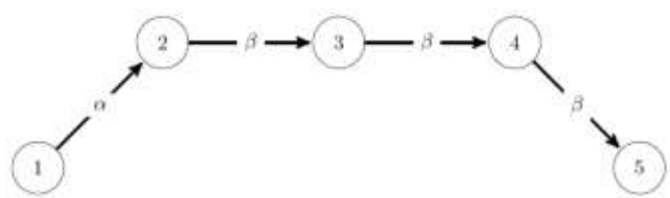
$$X_1(t) = \varepsilon_1(t) \tag{13}$$

$$X_3(t) = \alpha\beta\, X_1(t-2) + \tilde{\varepsilon}_3(t). \tag{14}$$

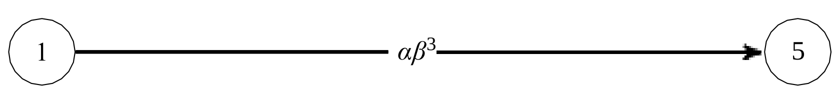
This work investigates how different permutations of weights α and β for each of the chain links affects the average rPDC values for the spurious link from node 1 to node 3, where node 2 is not observed in a 3 dimensional net- work. Firstly, we set $\alpha = 1$ and set $\beta = x$ where x varies from 0.1 to 1 in steps of 0.1, and measure the average rPDC values indicating the strength of the spurious interaction between nodes 1 and 3 when node 2 is not observed. The values of α and β were then switched, as indicated in figure 4, so that the causal influence from node 1 to node 2 has strength x, again varying between 0.1 and 1 in steps of 0.1, and the causal influence from node 2 to node 3 is set to 1. Again we measure the strength of the spurious interaction from node 1 to node 3 when node 2 is not observed by measuring the average rPDC value of the link. In both of these configurations of the α and β weighted links, the spurious link between nodes 1 and 3 has weight $\alpha\beta$ in the VAR model. However, in each of the two simulations the average rPDC values of the spurious links from nodes 1 and 3 differ despite the same "x" weighting values, as shown in figure 5, because of the different treatment of the covariance noise terms (c.f. eq (4), (5) versus (8)). In the case of a chain-type network the order in which weights occur on the causal network influences affects the rPDC value of the spurious link from node 1 to node 3. This is because of the contribution of the final link to the noise of the final process in the chain, in a 3 dimensional network, for when α comes first as is figure 3 the 2 dimensional VAR model is,

$$X_1(t) = \varepsilon_1(t) \tag{15}$$

$$X_3(t) = \alpha\beta X_1(t-2) + \beta\varepsilon_2(t-1) + \varepsilon_3(t). \tag{16}$$



(a) 5 dimensional, chain network.



(a) 2 dimensional sub network, with intermediary nodes 2,3 and 4 unobserved.

Figure 6: An example of a larger chain network with 5 nodes; nodes 2,3 and 4 are observed this time yielding 3 latent confounders as opposed to 1. Weighting derived from VAR model.

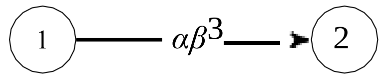


Figure 7: A 2 dimensional network with the weighting $\alpha\beta^3$, with no latent confounders.

showing a noise contribution from node 2, as a latent confounder, with weighting β, when the link weightings are switched the as in figure 4 the noise weighting from node 2 becomes α.

$$X_1(t) = \varepsilon_1(t), \tag{17}$$

$$X_3(t) = \alpha\beta X_1(t-2) + \alpha\varepsilon_2(t-1) + \varepsilon_3(t). \tag{18}$$

Where the noise contribution is greater, i.e., is consistently 1 the average rPDC value for the spurious link from node 1 to node 3 is under estimated, compare with a noise contribution varying between 0.1 and 1.

Five dimensional chain networks

Expanding on this point, a larger chain simulation with VAR model,

$$X_1(t) = \varepsilon_1(t),$$
$$X_2(t) = \beta X_1(t-1) + \varepsilon_2(t),$$
$$X_3(t) = \beta X_2(t-1) + \varepsilon_3(t),$$
$$X_4(t) = \beta X_3(t-1) + \varepsilon_4(t),$$
$$X_5(t) = \beta X_4(t-1) + \varepsilon_5(t).$$

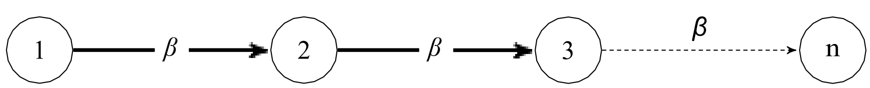


Figure 8: A chain network with n nodes and $n-1$ causal links each with weight β.

with one strongly weighted connection followed by three subsequent weakly weighted connections. The intermediary nodes 2, 3 and 4 are unobserved and the average rPDC value of the spurious link from node 1 to node 5 has half the value of a simple 2 dimensional network with a causal link of the same weighting as the spurious interactions in the 5 dimensional network.

Treating nodes 2, 3 and 4 latent confounders, leaving only nodes 1 and 5,

$$X_1(t) = \varepsilon_1(t),$$
$$X_5(t) = \alpha\beta^3 X_1(t-4) + \beta^3\varepsilon_2(t-3) + \beta^2\varepsilon_3(t-2) + \beta\varepsilon_4(t-1) + \varepsilon_5(t),$$

in which α = 1 and β = 0.8 and treating nodes 2, 3, and 4 as latent confounders the average rPDC value of the spurious link from node 1 to node 5 is 0.0042, with the spurious connection having weight $\alpha\beta^3$ = 0.5120. When a graph is created with two nodes and a causal influence from node 1 to node 2 with weight $\alpha\beta^3$ = 0.5120, as in figure 7, the average rPDC value of this link is 0.0084, doubling the strength of the interaction despite having the same weights, due to the influence of additional noise of the latent confounders on the final process in the chain.

N dimensional chain networks

Immediate generalisation of these results leads to the VAR process, for the final nodes in a chain in which all intermediary nodes are unobserved,

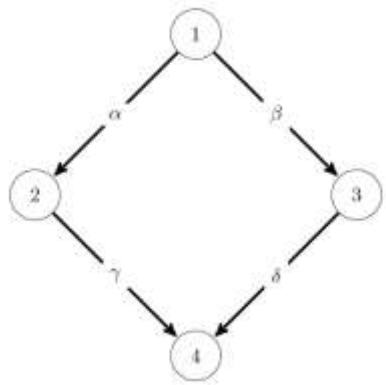
$$X_n(t) = \beta^{n-1} X_1\big(t-(n-1)\big) + \sum_{r=0}^{n-2} \beta^r\, \varepsilon_{n-r}(t-r),$$

in which n is the number of nodes in the chain network, and where each of the $n-1$ causal influences between the nodes has weight β, as shown in fig- ure 8. From this generalisation it can be shown that the effect of a single latent confounder in a chain of n nodes is diminished by those latent confounders which it influences further down the chain, the weighting becomes weaker as the signal is propagated through the processes. This is because the constraints of stationarity of the process mean that the weighting, β must always be less than or equal to 1, meaning that the more latent confounders contributing to the noise of process $Xn(t)$ the smaller the contribution as the effect is multi- plicative, e.g, the larger r the smaller its effect on the rPDC estimation of the spurious connection. However the smaller r is the larger the noise contribution and as the delayed terms are additive adding more latent confounders will in- crease the delayed noise terms. Although, as n becomes very large the effect of those delayed noise terms with large r will become negligible, meaning that there will be some finite size effect for smaller n. One could speculate that as all the noise contributions from the latent confounders are delayed, this could be a potential method of separating the effect of genuinely causal interactions and that of latent confounders, employing autoregressive moving average processes.

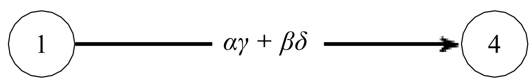
Diamond-shaped network configuration

Finally we consider a VAR [1] model, visualised using 4 dimensional graph in which the nodes and edges are arranged in a diamond-like pattern, where node 1 causally influences nodes 2 and 3 and nodes 2 and 3 both causally influence node 4, as shown in figure 9. Each edge has weight α, β, γ and δ respectively, as denoted in the same figure. Unobserving nodes 2 and 3 leave 1 spurious connection from node 1 to node 4 with weight $\alpha\gamma + \beta\delta$ as shown in figure 9.

We proceed, as before, by measuring the strength of the spurious interaction from node 1 to node 4 using rPDC, using different configurations of weights on the 4 links. Supposing each causal influence can have one of two weights; 1 or x,



(a) 4 dimensional graph with diamond like structure.



(b) 4 dimensional graph with diamond like structure, with nodes 2 and 3 unobserved leaving a spurious link from node 1 to node 4.

Figure 9: A 4 dimensional VAR[1] process, visualised as a graph in which node 1 influences node 4 indirectly via nodes 2 and 3 with weights, α, β, γ and δ. When nodes 2 and 3 are unobserved a spurious link appears from node 1 to node 4 with weight $\alpha\gamma + \beta\delta$.

and each of the weights must be used twice, there are 4 permutations of weights that can occur. These are that x can occur on the upper two links, the lower two links or on opposing diagonals of the diamond structure. In alphabetical order of the weights α, β, γ and δ these are; '*xx*11', '11*xx*', '*x*11*x*' and '1*xx*1'.

The average rPDC value of the spurious interaction from nodes 1 to 4, for weight x changing between 0 and 1 and for each configuration of weights is shown in figure 10. By this graph it is possible to see that while it is possible to distinguish, from the average rPDC value, those cases in which the x weights both sit on either the upper or lower links in the graph, i.e., the '*xx*11' and '11*xx*' weight configurations. It is impossible to distinguish those cases in which the x weighted links are on diagonally opposing links, configurations '*x*11*x*' and '1*xx*1'. This is because the weighted contributions of the latent confounders to the delayed noise term are the same in both cases.

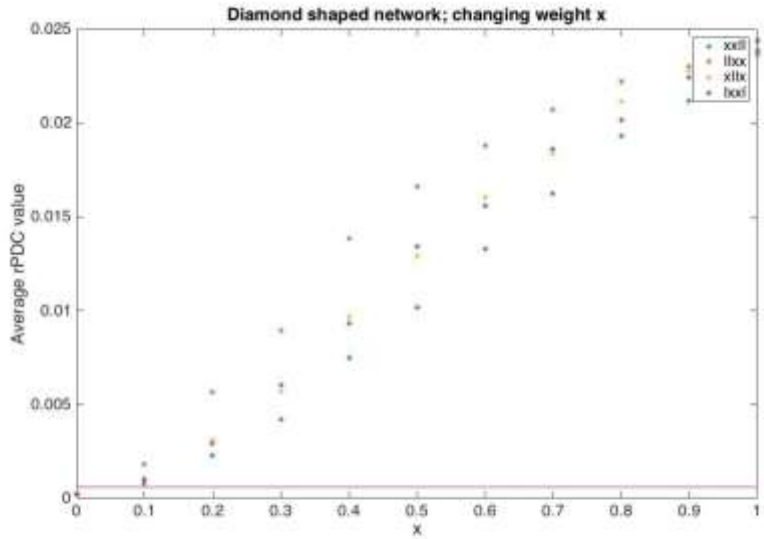


Figure 10: A graph to show the how the average rPDC strength of the spurious interaction from node 1 to node 4 is affected by a changing weight x which different configurations or x and 1 weighted nodes. The solid red line shows the critical value at 5% significance level.

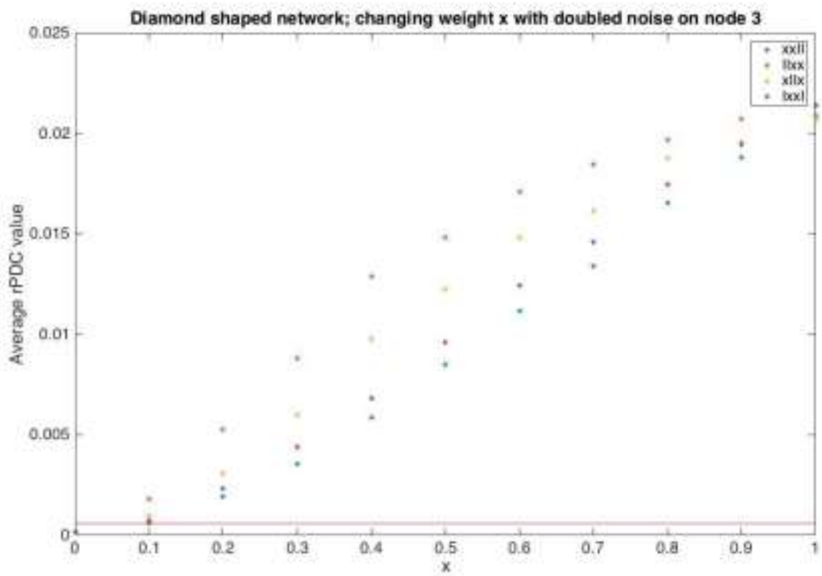


Figure 11: A graph to show how the rPDC values shown is graph 10 change when the in- stantaneous noise at node 3 is doubled. The solid red line shows the critical value at 5% significance level. the delayed noise term are the same in both cases.

However when the instantaneous noise at node 3 is doubled the same mea- surements yield figure 11, which shows the cases in which the *x* weighted links are diagonally opposing are now distinguishable from each other, where previ- ously they were indistinguishable. This is due to the alteration of the delayed noise term from node 3, thereby yielding a clear difference in the amount of noise in each case which is clearly visible in the different rPDC values.

Discussion and Conclusion

In conclusion, the permutation of weightings of the causal influences in a chain network has an effect on the measured strength of a spurious link between the first and final node in the chain, where the intermediary nodes are treated as latent confounders. This is because the weightings of certain latent confounders are included in the noise term of observed processes, which has been shown analytically.

The strength of spurious links was measured using renormalised partial di- rected coherence. The effect of latent confounders on measured rPDC, causal link strength and the normalisation of the covariance matrix of the noise of the fitted VAR model, has been shown analytically in section 2. This is due to the setting of the variance of the VAR model to one and the necessary mathematical adjustments to the matrix of coefficients of delayed, causal influences and the noise of the VAR model.

A spurious link is created from the first to the final node in a chain when intermediary nodes are treated as latent confounders. Regardless of the permutation of the weights on the links in the chain, as long as they are the same combination, the spurious, observed link from the first to the final node will analytically have the same weight in the underlying VAR model.

We have shown by generalising system for *n* nodes that the effect of the latent confounders can be captured in the delayed noise of the VAR model, and that these delayed noise effect are subject to a finite size effect. Finally we have shown that altering the contributions of the noise of a latent confounder can yield a difference in the perceived strength of a spurious, observed interaction. Finally concluding that while it is possible to measure the strength of directed causal influences between processes, the estimation strength can be confounded if not all components of a system have been observed.

A natural limitation of the method lies in the fact that VAR modeling is restricted to linear processes, therefore this method as applies non-linear processes is not addressed in this manuscript. On the other hand, the effect demonstrated in this manuscript is true for any order of VAR model as the estimation of the VAR coefficients is independent of the order of the model. Therefore the effect shown is this work is not restricted by the order of the VAR model.

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