Vector Autoregressive Models With Measurement Errors for Testing Granger Causality

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Abstract

This paper develops a method for estimating parameters of a vector au-2 toregression (VAR) observed in white noise. The estimation method assumes the noise variance matrix is known and does not require any iterative process. This study provides consistent estimators and the asymptotic distribution of 5 the parameters required for conducting tests of Granger causality. Methods in the existing statistical literature cannot be used for testing Granger causality, since under the null hypothesis the model becomes unidentifiable. Measure-8 ment error effects on parameter estimates were evaluated by using computag tional simulations. The results suggest that the proposed approach produces 10 empirical false positive rates close to the adopted nominal level (even for small 11 samples) and has a satisfactory performance around the null hypothesis. The 12 applicability and usefulness of the proposed approach are illustrated using a 13 functional magnetic resonance imaging dataset. 14

Key Words: Asymptotic property, errors-in-variables model, Granger causality, multivariate time series.

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1 INTRODUCTION

¹⁹ Multivariate time series modeling is an important component for the quantitative ²⁰ assessment of relationships between variables in many applied areas. This issue is ²¹ essential in financial applications, for example, enabling optimal portfolio allocation, ²² setting trading strategies over sectors of the market, or exchanging rates (Sims, 1980; Ni and Sun, 2003). In addition, the vector autoregressive model (VAR) is widely used
in many fields such as economics (Granger, 1969), geophysics (Liu and Rodríguez,
2005), bioinformatics (Fujita et al., 2007a) and neuroscience (Goebel et al., 2003).

The main reasons for the attractiveness of the VAR model in applied areas are 26 its simplicity and relation with the concept of Granger causality (Granger, 1969). 27 Granger causality has become a prominent concept in connectivity networks model-28 ing, because it provides inferences about the direction of information flow between 29 different time series. Several studies in biological systems emphasize the importance 30 of identification and description of gene regulator networks (Gottesman, 1984; Ka-31 toh, 2007), mainly in the study of tumors or structural diseases. Mukhopadhyay 32 and Chatterjee (2007); Fujita et al. (2007a,b) introduced the utilization of VAR-33 based models to study these issues by applying these models to gene expression 34 datasets. In Neuroscience, the *functional integration* theories highlight that brain 35 functions heavily depend on neural connectivity networks (Cohen and Tong, 2001). 36 Several neuroimaging studies (Goebel et al., 2003; Sato et al., 2006; Abler et al., 37 2006) suggested that VAR models and Granger causality are suitable to identify 38 the information flow between neural structures. Nevertheless, it is well known that 39 most biological measurements are subject to error, since the precision of acquisition 40 equipments is never absolute. Actually, this limitation is present in most studies 41 involving experimental data, such as chemistry, physics, biometrics, etc. 42

Although technically incorrect, the most common procedure is simply to ignore 43 the measurement errors, i.e.: to assume that the variables of interest are the observed 44 ones. It is important to highlight that this assumption has serious implications. The 45 conventional VAR model, in this case, would not identify correctly the relationships 46 between the variables of interest (latent variables). It happens because the model 47 white noise will not be independent which leads to misestimations of the model 48 parameters. The usual assumption is acceptable when the errors are negligible. 49 However, it is known that due to acquisition processes limitations, the measure-50 ment errors in biology (e.g.: gene expressions or neuro signals) are not negligible in 51 most cases. Thus, the utilization of conventional VAR models may result in biased 52 parameter estimation and as a consequence, unreliable Granger causality detection. 53 In the following, we define the usual VAR model (for a more detailed description, 54 see for instance, Lütkepohl, 2005). Let $\boldsymbol{z}_t = (z_{1t}, \ldots, z_{pt})^{\top}$ denotes a $(p \times 1)$ vector 55 of time series variables. The usual VAR(r) model has the form 56

$$z_t = a + B_1 z_{t-1} + \ldots + B_r z_{t-r} + q_t, \ t = 1, \cdots, n$$
 (1)

where *n* is the sample size, B_j for j = 1, ..., r are $(p \times p)$ coefficient matrices and q_t is a $(p \times 1)$ unobservable zero mean white noise vector process with covariance matrix Σ . For convenience, we consider that $z_l = 0$ for all $l \leq 0$. We are assuming throughout this paper that model (1) satisfies the stability condition defined in Lütkepohl (2005) on page 12. Therefore, under stationarity conditions, the mean and the autocovariance function are given, respectively, by

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$$\boldsymbol{\gamma}(h) = E[(\boldsymbol{z}_t - \boldsymbol{\mu}_{\boldsymbol{z}})(\boldsymbol{z}_{t-h} - \boldsymbol{\mu}_{\boldsymbol{z}})^{\top}] = \sum_{i=1}^r \boldsymbol{B}_j \boldsymbol{\gamma}(h-j), \text{ for } h = 1, 2, 3,$$

 $E(\boldsymbol{z}_t) = \boldsymbol{\mu}_{\boldsymbol{z}} = \left(\boldsymbol{I}_p - \sum_{j=1}^r \boldsymbol{B}_j\right)^{-1} \boldsymbol{a},$

64 and

$$\boldsymbol{\gamma}(0) = \sum_{j=1}^{r} \boldsymbol{B}_{j} \boldsymbol{\gamma}(-j) + \boldsymbol{\Sigma}$$

where I_p denotes the $p \times p$ identity matrix and $\gamma(-j) = \gamma(j)^{\top}$.

 $_{66}$ Model (1) can be written in short as

$$\boldsymbol{z}_t = \boldsymbol{a} + \boldsymbol{B} \boldsymbol{z}_{t-1}^* + \boldsymbol{q}_t, \ t = 1, \cdots, n$$
(2)

⁶⁷ where $\boldsymbol{B} = (\boldsymbol{B}_1 \ \boldsymbol{B}_2 \ \dots \ \boldsymbol{B}_r)$ is a $p \times pr$ matrix and $\boldsymbol{z}_{t-1}^* = (\boldsymbol{z}_{t-1}^\top, \boldsymbol{z}_{t-2}^\top, \dots, \boldsymbol{z}_{t-r}^\top)^\top$.

⁶⁸ Therefore, if the white noise has Normal distribution, the conditional Maximum ⁶⁹ Likelihood (ML) estimators of \boldsymbol{a} , \boldsymbol{B} and $\boldsymbol{\Sigma}$ are equal to the ordinary least squares ⁷⁰ estimators. They are given, respectively, by

$$\widehat{\boldsymbol{a}}_{ML} = \bar{\boldsymbol{z}}_t - \widehat{\boldsymbol{B}}_{ML} \bar{\boldsymbol{z}^*}_{t-1}, \quad \widehat{\boldsymbol{B}}_{ML} = (\boldsymbol{S}_{\boldsymbol{z}_{t-1}^*}^{-1} \boldsymbol{S}_{\boldsymbol{z}_{t-1}^* \boldsymbol{z}_t})^\top \quad \text{and} \quad \widehat{\boldsymbol{\Sigma}}_{ML} = n^{-1} \sum_{i=1}^n \widehat{\boldsymbol{q}}_i \widehat{\boldsymbol{q}}_i^\top \quad (3)$$

⁷¹ where $\bar{\boldsymbol{z}^{*}}_{t-1} = n^{-1} \sum_{i=1}^{n} \boldsymbol{z}_{i-1}^{*}, \ \bar{\boldsymbol{z}}_{t} = n^{-1} \sum_{i=1}^{n} \boldsymbol{z}_{i}, \ \hat{\boldsymbol{q}}_{i} = \boldsymbol{z}_{i} - \hat{\boldsymbol{a}}_{ML} - \hat{\boldsymbol{B}}_{ML} \boldsymbol{z}_{i-1}^{*}, \ \boldsymbol{S}_{\boldsymbol{z}_{t-1}^{*}} = n^{-1} \sum_{i=1}^{n} (\boldsymbol{z}_{i-1}^{*} - \bar{\boldsymbol{z}^{*}}_{t-1}) \boldsymbol{z}_{i-1}^{*\top} \text{ and } \boldsymbol{S}_{\boldsymbol{z}_{t-1}^{*}\boldsymbol{z}_{t}} = n^{-1} \sum_{i=1}^{n} (\boldsymbol{z}_{i-1}^{*} - \bar{\boldsymbol{z}^{*}}_{t-1}) \boldsymbol{z}_{i}^{\top}.$

The consistency of those conditional ML estimators is assured under the stationary conditions (see Lütkepohl, 2005, for further details). The consistency is shown
using the fact that

$$\bar{\boldsymbol{z}}_t \xrightarrow{\mathcal{P}} \boldsymbol{\mu}_{\boldsymbol{z}}, \quad \bar{\boldsymbol{z}^*}_{t-1} \xrightarrow{\mathcal{P}} \boldsymbol{\mu}_{\boldsymbol{z}^*} = \mathbf{1}_r \otimes \boldsymbol{\mu}_{\boldsymbol{z}}, \quad \boldsymbol{S}_{\boldsymbol{z}^*_{t-1}} \xrightarrow{\mathcal{P}} \boldsymbol{\Gamma}_r(0) \quad \text{and} \quad \boldsymbol{S}_{\boldsymbol{z}^*_{t-1}\boldsymbol{z}_t} \xrightarrow{\mathcal{P}} \boldsymbol{\Gamma}_r(0) \boldsymbol{B}^{\top}$$

⁷⁶ where " $\xrightarrow{\mathcal{P}}$ " denotes convergence in probability when the sample size increases, \otimes ⁷⁷ denotes the Kronecker product, $\mathbf{1}_r$ is a *r*-dimensional column vector of ones, and The covariance function of \boldsymbol{z}^*_{t-1} is given by

$$\Gamma_{r}(h) = E[(\boldsymbol{z}_{t-1}^{*} - \boldsymbol{\mu}_{\boldsymbol{z}^{*}})(\boldsymbol{z}_{t-h-1}^{*} - \boldsymbol{\mu}_{\boldsymbol{z}^{*}})^{\top}]$$

$$= \begin{bmatrix} \boldsymbol{\gamma}(h) \quad \boldsymbol{\gamma}(h+1) \quad \dots \quad \boldsymbol{\gamma}(h+r-1) \\ \boldsymbol{\gamma}(h-1) \quad \boldsymbol{\gamma}(h) \quad \dots \quad \boldsymbol{\gamma}(h+r-2) \\ \vdots \quad \vdots \quad \ddots \quad \vdots \\ \boldsymbol{\gamma}(h-r+1) \quad \boldsymbol{\gamma}(h-r+2) \quad \dots \quad \boldsymbol{\gamma}(h) \end{bmatrix}$$

As described previously, VAR modeling is commonly applied for detecting Granger 79 causality relationships. The basic idea of Granger causality is the evaluation of 80 temporal information founded on the assumption that the cause always precedes 81 its effect (Granger, 1969). Let x_t and y_t be two time series. From the statistical 82 perspective, x_t is said to Granger-cause y_t if the prediction error of y_t , conditioning 83 on the past values of both series, is less than considering solely the past values of y_t . 84 In other words, the past values of x_t contains relevant information to improve the 85 predictions of y_t . Note that Granger causality concept is not equivalent to classical 86 Aristotelian causality, since the former is based solely on prediction errors. However, 87 due to its simplicity, it is more tractable in scientific experiments and may suggest 88 possible causal relationships. 89

One possible approach of using VAR models for Granger causality detection is 90 by performing statistical tests on B_i 's coefficients. Considering y_t equation, if there 91 is at least one coefficient multiplying the past values of x_t which is not equal to zero, 92 then x_t is said to Granger-cause y_t . Thus, this procedure involves the estimation of 93 B_i , their respective covariance matrices, and the application of hypothesis testing. 94 In general, many physical, biological and chemical variables have the measure-95 ment process subject to noise effects and it is very common to analyze them by 96 using models assuming that these measurement errors are negligible. It may bring 97 up undesirable features as biased estimates as well as their standard errors and, 98 as a consequence, dangerously false confidence intervals and unreliable hypotheses 99 testing. Thus, it is necessary to consider the measurement error in the modeling of 100 these type of data. 101

In this paper, we study a VAR model with main concern on including measurement errors. Let z_t be the true (latent) variable that is not directly observed, instead a substitute variable Z_t is observed. The relation between the latent and observed variables is given by the following additive structure

$$\boldsymbol{Z}_t = \boldsymbol{z}_t + \boldsymbol{e}_t, \ t = 1, \cdots, n \tag{4}$$

where $\mathbf{Z}_t = (Z_{1t}, Z_{2t}, \cdots, Z_{pt})^{\top}$ is the observed vector and $\mathbf{e}_t = (e_{1t}, e_{2t}, \cdots, e_{pt})^{\top}$ 106 is the measurement error vector with mean zero and variance-covariance matrix Σ_e . 10 In most cases, if the usual conditional ML estimator is adopted for the observations 108 subject to errors, i.e., replacing z_t with Z_t in equation (1), the estimator of **B** will 109 not be consistent (as can be seen in (6)). Therefore, measurement error equation 110 (4) should be included in the estimation procedure. Nevertheless, model (1) with 111 equation (4) is not identifiable, since the covariance matrices of q_t and e_t are con-112 founded when B = 0. It is easy to see that in the univariate AR(1), note that when 113 r = p = 1 and b = 0 we have: $Z_i = a + q_i + e_i$ with $E(Z_i) = a, \gamma(0) = \sigma^2 + \sigma_e^2$ and 114 $\gamma(h) = 0$ for all $h \neq 0$. It is impossible to estimate σ^2 and σ_e^2 separately by observing 115 only Z_1, \ldots, Z_n . This problem can be avoided by using previous knowledge about 116 the variance of e_t . 117

This paper is organized as follows. Section 2 proposes consistent estimators for 118 the VAR model with measurement errors and also presents the asymptotic distri-119 bution of the estimator of the elements of B. In Section 3, simulation studies are 120 undertaken to investigate some aspects of the proposed estimators (rejection rates 121 for a test of hypothesis, biases and mean square errors) also it is verified the impact 122 by erroneously considering the usual model. We applied the models in a functional 123 magnetic resonance imaging dataset in Section 4 and we finish the paper with con-124 clusions and remarks in Section 5. 125

2 VAR WITH MEASUREMENT ERRORS

In the presence of measurement errors, the conventional ML estimation of VAR 127 models produces biased estimators and they may lead to wrong statistical infer-128 ences (see Fuller, 1987, in which it is found a discussion over errors-in-variables in 129 regression models). And ersson (2005) warns for the problems in testing Granger 130 causality by using a VAR model when the variables are subject to measurement 131 errors. However, the author does not propose any approach to overcome such prob-132 lems. There are some studies to treat time series observed in white noise in the 133 literature, those studies use Kalman filtering methodology and an Expectation and 134 Maximization algorithm that requires intensive iterative procedures, (e.g., Geweke, 135 1977; Aigner et al., 1984). Maravall and Aigner (1977) have provided a careful ex-136 position of the identifiability of some time series models with errors in variables. 137 Beck (1990) describes approaches based on state space modeling and Kalman fil-138

tering and demonstrates the usefulness of these tools in dynamic models. Kellstedt
et al. (1996) show the efficiency gains adopting errors-in-variables models, and the
precision of Kalman filter estimates in the face of autocorrelation. These measurement techniques have been applied to a variety of substantive problems, including
dynamic representation, social problems (such as racial inequality), monetary policy
and public entrepreneurship (Williams and McGinnis, 1992).

These state space models can be attractive alternatives to conventional VAR 145 modeling. However, in practice, the implementation of the estimators are not de-146 scribed in analytical form, but by interactive algorithms or numerical optimization 147 solutions. In addition, the derivation of the asymptotic distribution of those esti-148 mators may be complex. In Shumway and Stoffer (2000), the section on state space 149 methods shows an alternative procedure for how to estimate B, Σ and Σ_e under 150 model (1) with error equations (4), using the EM algorithm. Hannan et al. (2003)151 proposed another iterative procedure to estimate these parameters. Nevertheless, as 152 the main goal of this paper is to test Granger causality and the effect of the autore-153 gressive coefficientes, e.g., the coefficient that relates $z_{t,j} \to z_{t,j+r}$, these approaches 154 cannot be used, since the model becomes unidentifiable under the hypothesis B = 0. 155 In this study, we provide simple and closed forms for the estimators when Σ_e is 156

¹⁵⁷ known, which allows the direct derivation of their respective asymptotic properties. ¹⁵⁸ Since the main concern of several practical applications is Granger causality testing, ¹⁵⁹ this information is essential to data analysis. In this section, the main concern is the ¹⁶⁰ parameter estimation and its asymptotic properties. Theorem 1 states consistent ¹⁶¹ estimators for the model parameters and Theorem 2 establishes the asymptotic ¹⁶² distribution for the estimator of $vec(B^{\top})$ given in Theorem 1, where vec(C) is an ¹⁶³ operator that heaps the columns of the matrix C.

The methodology presented in this section is based on correcting the asymptotic 164 bias of conventional ML estimator caused by the measurement error effect. The 165 outcome is a consistent estimator with good asymptotic properties such as normality. 166 The estimators and the asymptotic covariance matrix for the proposed estimator 167 of $\operatorname{vec}(B^{\top})$ are computed easily and no iterative procedure is required. We must 168 remark that those estimators are not the conditional ML estimators nor the ML 169 estimators taking into account the measurement errors which are very complicated 170 to reach by maximizing the likelihood, even under normality of the errors. 171

Theorem 1. If $e_t \sim \mathcal{N}(0, \Sigma_e)$ with Σ_e known. Then, the parameters of model (1)

under measurement errors as in (4) have consistent estimators given by

$$\widehat{\boldsymbol{a}} = \overline{\boldsymbol{Z}}_t - \widehat{\boldsymbol{B}}\overline{\boldsymbol{Z}}_{t-1}^*, \quad \widehat{\boldsymbol{B}} = \left[(\boldsymbol{S}_{\boldsymbol{Z}_{t-1}^*} - \boldsymbol{I}_r \otimes \boldsymbol{\Sigma}_e)^{-1} \boldsymbol{S}_{\boldsymbol{Z}_{t-1}^*} \boldsymbol{Z}_t \right]^\top$$
(5)

174 and

$$\widehat{\boldsymbol{\Sigma}} = n^{-1} \sum_{i=1}^{n} (\boldsymbol{Z}_{i} - \widehat{\boldsymbol{a}} - \widehat{\boldsymbol{B}} \boldsymbol{Z}_{i-1}^{*}) (\boldsymbol{Z}_{i} - \widehat{\boldsymbol{a}} - \widehat{\boldsymbol{B}} \boldsymbol{Z}_{i-1}^{*})^{\top} - \boldsymbol{\Sigma}_{e} - \widehat{\boldsymbol{B}} (\boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e}) \widehat{\boldsymbol{B}}^{\top}$$

where $\bar{Z}_{t-1}^{*} = n^{-1} \sum_{i} Z_{i-1}^{*}, \ \bar{Z}_{t} = n^{-1} \sum_{i} Z_{i}, \ S_{Z_{t-1}^{*}} = n^{-1} \sum_{i} (Z_{i-1}^{*} - \bar{Z}_{t-1}^{*}) Z_{i-1}^{*\top}$ and $S_{Z_{t-1}^{*}Z_{t}} = n^{-1} \sum_{i} (Z_{i-1}^{*} - \bar{Z}_{t-1}^{*}) Z_{i}^{\top}.$

The proof of Theorem 1 can be found in Appendix A.1. Notice that, if $\Sigma_e = \mathbf{0}_{p \times p}$, that is, when there is no measurement error, then the estimators of Theorem 1 become the conditional ML estimators presented in (3). Also, it can be seen that the conditional ML estimator of **B** from model (1), without considering errors (4), is given by

$$\widehat{\boldsymbol{B}}_{ML} = \left[\boldsymbol{S}_{\boldsymbol{Z}_{t-1}^*}^{-1} \boldsymbol{S}_{\boldsymbol{Z}_{t-1}^* \boldsymbol{Z}_t}
ight]^{ op},$$

¹⁸² which is not consistent, since

$$\widehat{\boldsymbol{B}}_{ML} \xrightarrow{\mathcal{P}} \boldsymbol{B}[\boldsymbol{I}_{pr} + (\boldsymbol{I}_r \otimes \boldsymbol{\Sigma}_e)\boldsymbol{\Gamma}_r(0)^{-1}]^{-1}.$$
(6)

The main steps to demonstrate (6) is given in Appendix A.1, in which is sufficient to compute the limit of $S_{Z_{t-1}^*}$ and $S_{Z_{t-1}^*Z_t}$. The quantity $S_{Z_{t-1}^*}$ has two sources of variations, one that refers to the unobservable variable z_{t-1}^* and another one that refers to the measurement error.

If the measurement error is huge and the sample size is not large enough, the quantity $(\mathbf{S}_{\mathbf{Z}_{t-1}^*} - \mathbf{I}_r \otimes \boldsymbol{\Sigma}_e)$ may not be positive definite and the estimator $\hat{\mathbf{B}}$, presented in (5), will be inadmissible. If the quantity $(\mathbf{S}_{\mathbf{Z}_{t-1}^*} - \mathbf{I}_r \otimes \boldsymbol{\Sigma}_e)$ has at least one eigenvalue close to zero the estimator $\hat{\mathbf{B}}$, presented in (5), will be unstable (because the computation of a matrix inverse requires all eigenvalues to be different from zero). If the matrix $\boldsymbol{\Sigma}_e$ is well specified, one way to avoid such inadmissibility and instability is increasing the sample size.

In many practical applications, there is some interest on testing some elements of the matrix \boldsymbol{B} (e.g., the so called Granger causality test). However, the exact distribution of $\operatorname{vec}(\hat{\boldsymbol{B}}^{\top})$ is difficult to compute. Thus, one can use its asymptotic distribution to build confidence regions and hypothesis testing as an approximation when the sample size is finite. The Theorem below gives us the asymptotic distribution of $\operatorname{vec}(\hat{\boldsymbol{B}}^{\top})$. Theorem 2. If $e_t \sim \mathcal{N}(\mathbf{0}, \Sigma_e)$ with Σ_e known and $E(q_{ij_1}q_{ij_2}q_{ij_3}q_{ij_4}) < \infty$ for all $j_1, j_2, j_3, j_4 \in \{1, \dots, p\}$, where q_{ij} is the j^{th} element of \mathbf{q}_i . Then, the asymptotic distribution of $vec(\widehat{\mathbf{B}}^{\top})$ obtained in Theorem 1 is given by

$$\sqrt{n}(\operatorname{vec}(\widehat{B}^{\top}) - \operatorname{vec}(B^{\top})) \xrightarrow{D} \mathcal{N}(\mathbf{0}, \Phi),$$
(7)

where the $p^2r \times p^2r$ matrix $\mathbf{\Phi}$ is given by

$$\boldsymbol{\Phi} = \boldsymbol{\Sigma}_{\vartheta} \otimes \boldsymbol{\Gamma}_r(0)^{-1} + (\boldsymbol{I}_p \otimes \boldsymbol{\Gamma}_r(0)^{-1}) \boldsymbol{A}_r(\boldsymbol{I}_p \otimes \boldsymbol{\Gamma}_r(0)^{-1})$$

203 where

$$\begin{aligned} \boldsymbol{A}_{r} &= \boldsymbol{\Sigma}_{\vartheta} \otimes (\boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e}) + \boldsymbol{B}^{\top} \otimes [\boldsymbol{\Sigma}_{e} \boldsymbol{B}(\boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e})] + \\ &- \sum_{h=1}^{r} \left\{ (\boldsymbol{B}_{h} \boldsymbol{\Sigma}_{e}) \otimes \boldsymbol{\Gamma}_{r}(h) + (\boldsymbol{\Sigma}_{e} \boldsymbol{B}_{h}^{\top}) \otimes \boldsymbol{\Gamma}_{r}(-h) \right\} + \\ &+ \sum_{h=1-r}^{r-1} [\boldsymbol{B}(\boldsymbol{J}_{-h} \otimes \boldsymbol{\Sigma}_{e}) \boldsymbol{B}^{\top}] \otimes \boldsymbol{\Gamma}_{r}(h). \end{aligned}$$

and $\Sigma_{\vartheta} = \Sigma + \Sigma_e + B(I_r \otimes \Sigma_e)B^{\top}$, where J_l is a $(r \times r)$ matrix of zeros with one's in the $|l|^{th}$ diagonal above (below) the main diagonal if l > 0 (l < 0) and J_0 is a $(r \times r)$ matrix of zeros.

The proof of Theorem 2 can be seen in Appendix A.2. For all r and $\Sigma_e = 0$ we have $\Phi = \Sigma \otimes \Gamma_r(0)^{-1}$, as given in Lütkepohl (2005). The Normal distribution assumption for the measurement error is required to compute the expectation of polynomial functions (until forth degrees) of the elements of e_t .

The assumption of known measurement error variance is usually considered in 211 many fields; such as, astrophysics (Akritas and Bershady, 1996; Kelly, 2007; Kelly 212 et al., 2008), epidemiology (Kulathinal et al., 2002; Patriota et al., 2009), analytical 213 chemistry (Cheng and Riu, 2006), among others. However, in real datasets this 214 measurement error variance is, in general, estimated. If $\widehat{\Sigma}_e$ is a consistent estimator 215 for Σ_e , then we have usually that $\widehat{\Sigma}_e = \Sigma_e + O_p(m^{-1/2})$, where m is the sample 216 size used in the previous experiment, and $O_p(m^{-1/2})$ means limited in probability 217 even multiplying by $m^{1/2}$. Then, provided that $\lim n/m = 0$, all asymptotic even multiplying by m^{-r} . Then, provided that $\lim_{n\to\infty} m n/m = 0$, $\lim_{n\to\infty} n/m = \infty$, results derived in this section remain valid. However, note that if $\lim_{n\to\infty} n/m = \infty$, 218 219 then it is not possible to compute the asymptotic distribution for vec(\widehat{B}^{\top}), since its 220 covariance matrix will diverge. We remark that, although if $\lim_{n \to \infty} n/m \in (0, \infty)$ 221 the asymptotic distribution derived in this paper will not be valid, our results can 222 also be used here with some caution. Our simulation studies (see Section 3) show 223

that the rejection rates under the null hypothesis are controlled even when Σ_e is replaced by an estimator built by using a previous sample (m) proportional to the sample size (n).

In some cases, the partitioner can just specify the covariance matrix Σ_e rather than estimating it through previous experiments. In such cases, a misspecification in this covariance matrix may occur. For the sake of simplicity, suppose that Σ_e is the true covariance matrix and the misspecified one is $\Sigma_e^{(mis)} = \delta \Sigma_e$. Let $\hat{B}^{(mis)}$ be the estimator of B built by using the misspecified covariance matrix $\Sigma_e^{(mis)}$ instead of Σ_e . Then, using the results of the Appendix, we have that

$$\widehat{\boldsymbol{B}}^{(mis)} \xrightarrow{\mathcal{P}} \boldsymbol{B} \big[\boldsymbol{I}_{pr} + (1-\delta) (\boldsymbol{I}_r \otimes \boldsymbol{\Sigma}_e) \boldsymbol{\Gamma}_r(0)^{-1} \big]^{-1},$$

i.e., the estimator $\widehat{B}^{(mis)}$ is not consistent for **B**. However, if $0 < \delta < 2$ the matrix 233 $\left[I_{pr}+(1-\delta)(I_r\otimes\Sigma_e)\Gamma_r(0)^{-1}\right]^{-1}$ will have eigenvalues closer to 1, in absolute value, 234 than the ones of $[I_{pr} + (I_r \otimes \Sigma_e)\Gamma_r(0)^{-1}]^{-1}$ (notice that, if λ_C is the eigenvalue of 235 C, then $1 + \gamma \lambda_C$ is the eigenvalue of $I + \gamma C$). In this sense, the estimator $\widehat{B}^{(mis)}$ 236 will have lesser asymptotic bias than \widehat{B}_{ML} , for $0 < \delta < 2$. In other words, even if 237 we underestimate the true matrix Σ_e or if we overestimate by up to two times, the 238 multiplicative term of the asymptotic bias will be closer to the identity matrix than 239 the one produced by the naive estimator (i.e., considering that $\Sigma_e = 0$). 240

Notice that, if r = 1 we have the VAR(1) model and the asymptotic covariance simplifies to

$$\boldsymbol{\Phi} = \boldsymbol{\Sigma}_{\boldsymbol{\vartheta}} \otimes \boldsymbol{\gamma}(0)^{-1} + (\boldsymbol{I}_p \otimes \boldsymbol{\gamma}(0)^{-1}) \boldsymbol{A}_1(\boldsymbol{I}_p \otimes \boldsymbol{\gamma}(0)^{-1})$$

243 where

$$\boldsymbol{A}_1 = \boldsymbol{\Sigma}_{\vartheta} \otimes \boldsymbol{\Sigma}_e + \boldsymbol{B}^\top \otimes (\boldsymbol{\Sigma}_e \boldsymbol{B} \boldsymbol{\Sigma}_e) - [(\boldsymbol{B} \boldsymbol{\Sigma}_e) \otimes (\boldsymbol{\gamma}(0) \boldsymbol{B}^\top) + (\boldsymbol{\Sigma}_e \boldsymbol{B}^\top) \otimes (\boldsymbol{B} \boldsymbol{\gamma}(0))].$$

The i^{th} element of $\operatorname{vec}(\widehat{B}^{\top})$, is asymptotically normally distributed with standard error given by the square root of i^{th} diagonal element of Φ . Thus, we can obtain hypothesis tests on the individual coefficients, or more general form of contrasts

$$H_0: \mathbf{C} \operatorname{vec}(\mathbf{B}^{\top}) = \mathbf{d}$$
 Versus $H_1: \mathbf{C} \operatorname{vec}(\mathbf{B}^{\top}) \neq \mathbf{d}$,

which involve coefficients across different equations of the VAR model. Thus, Granger causality testing can be carried out by adequately specifying this contrasts matrix. An illustrative example is the case of series x_t and y_t , in which we are interested in evaluating the Granger causality from x_t to y_t in an r-order VAR model. The matrix C has r rows, one for each coefficient related to the past values of x_t in the y_t equation. Considering that each column of C refers to each VAR coefficient, the contrast matrix is specified by simply setting 1 to the cell at the respective column and row for the x_t coefficients in y_t equation. This may be tested using the Wald-type statistic conveniently expressed as

$$n(\boldsymbol{C}\operatorname{vec}(\widehat{\boldsymbol{B}}^{\top}) - \boldsymbol{d})^{\top} \left[\boldsymbol{C} \boldsymbol{\Phi} \boldsymbol{C}^{\top} \right]^{-1} (\boldsymbol{C}\operatorname{vec}(\widehat{\boldsymbol{B}}^{\top}) - \boldsymbol{d})$$
(8)

Under the null hypothesis, (8) has a $\chi^2(c)$ distribution in the limit, where $c = rank(\mathbf{C})$ gives the number of linear restrictions.

The previous procedure can also be developed to include the intercept by applying the delta method (Lehmann and Casella, 1998) in the asymptotic distribution of $(\bar{Z}_t^{\top}, \bar{Z}_{t-1}^{*\top}, \operatorname{vec}(\widehat{B}^{\top})^{\top})$, since $\widehat{a} = \bar{Z}_t - (I \otimes \bar{Z}_{t-1}^{*\top})\operatorname{vec}(\widehat{B}^{\top})$. Although, this asymptotic distribution is important to test hypotheses regarding the model intercept, it is outside the main scope of this article and does not have any impact on the Granger causality.

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3 SIMULATION RESULTS

In this section, some simulation studies were conducted in order to evaluate the adequacy of the asymptotic distribution of $\operatorname{vec}(\widehat{B}^{\top})$ for small and moderate samples sizes. Computations were performed using the software R (www.r-project.org).

For each setup of parameters and sample sizes, it was considered 15,000 Monte Carlo samples generated from a VAR(1) model with measurement errors, given by

$$\begin{pmatrix} z_{1,t} \\ z_{2,t} \end{pmatrix} = \begin{pmatrix} a_1 \\ a_2 \end{pmatrix} + \begin{bmatrix} b_{11} & b_{12} \\ b_{21} & b_{22} \end{bmatrix} \begin{pmatrix} z_{1,t-1} \\ z_{2,t-1} \end{pmatrix} + \begin{pmatrix} q_{1t} \\ q_{2t} \end{pmatrix},$$
(9)

$$\begin{pmatrix} Z_{1,t} \\ Z_{2,t} \end{pmatrix} = \begin{pmatrix} z_{1,t} \\ z_{2,t} \end{pmatrix} + \begin{pmatrix} e_{1t} \\ e_{2t} \end{pmatrix}.$$
 (10)

In all samples, the following setup of parameters was considered: $a_1 = a_2 = 1$, $b_{11} = b_{22} = 0.5$,

$$\boldsymbol{\Sigma} = \left[\begin{array}{cc} 10 & 5\\ 5 & 5 \end{array} \right],$$

where the vector parameters values of (b_{12}, b_{21}) were the values of the set $\{(b_{12}, b_{21}); b_{12} \in S\}$ and $b_{21} \in S\}$, where $S = \{-0.4, -0.2, 0.0, 0.2, 0.4\}$, the variance of the measurement error e_t was $\Sigma_e = 2I_2$, and the sample sizes n = 50, 100, 250, 500. As in actual datasets Σ_e is usually estimated, we simulated m = 0.6n identically and independent random variables from a Normal distribution with mean zero and variance two. Then, we estimate $\widehat{\Sigma}_e = \widehat{\sigma}_e^2 I_2$, where $\widehat{\sigma}_e^2$ is the sample variance computed from this random variables.

The rejection rates of the hypothesis H_0 : $b_{12} = b_{21} = 0$ (i.e., $z_{2,t-1}$ does not 279 help to explain $z_{1,t}$ and $z_{1,t-1}$ does not help to explain $z_{2,t}$) are shown in Table 1, in 280 which the test sizes are the rejection rates under the null hypothesis (that appears 281 in bold). Wald-type statistic (8) is used at 5% nominal level. From this table we 282 conclude that the test sizes from the proposed model are closer to the nominal level 283 (5%), as compared to the usual approach for all sample sizes. Furthermore, when 284 n increases the test sizes for the usual model also increase and, consequently, they 285 do not converge to the adopted nominal level. This is an expected behavior because 286 the usual approach produces biased estimates and standard errors. Table 1 depicts 287 the power of the test in each methodology, which shows a good performance of the 288 proposed approach. Nevertheless, it is not possible to compare the power between 289 the two methods because they have different empirical test sizes. 290

[[Table 1]]

In addition, the results shown in Table 1 are similar for other values of the parameters a and B, if the same proportionality of Σ and Σ_e is set as defined above. But, other simulations suggest that the larger the measurement error, the larger the sample size required to have a good asymptotic approximation for Waldtype statistic (8).

Further, simulation studies were also conducted for testing the hypothesis H_0 : $b_{12} = 0$ at 5% nominal level. In this study, we consider $b_{21} = 0.2$. Other simulations were built considering other values for b_{21} , however, the results are close to each other and, for this reason, they were omitted. As can be seen, Tables 1 and 2 present similar behaviors, i.e., the proposed model has always empirical size test closer to the nominal level than the usual one.

[[Table 2]]

In Tables 1 and 2, the usual approach seems to be most powerful than the proposed approach when $b_{21} = 0.2$ and $b_{21} = 0.4$. However, as aforementioned, they cannot be compared directly, just because the real nominal level used to compute that powers are not the same. Thus, a descriptive measure was defined in order to analyze both methodologies around the null hypothesis. Let $a_n(\alpha)$ be the probability of the error type I using the true distribution of (8) when the sample size is n and

 α is the adopting nominal level based on its asymptotic distribution. For instance, 308 in Table 2 $\widehat{a_{100}}(0.05) = 0.0541$ for the proposed approach and $\widehat{a_{100}}(0.05) = 0.0851$ 309 for the usual one (i.e., $\widehat{a_n}(\alpha)$ is the test size for a given n and α). An expected 310 behavior for good statistics is $a_n(\alpha) \xrightarrow{n \to \infty} \alpha$ which means that the quantiles of the 311 true distribution of (8) will be close to the quantiles of the asymptotic distribution, 312 $\chi^2(c)$, when the sample size is sufficiently large. Thus, the relation $a_n(\alpha)/\alpha$ measures 313 how far is the α -quantile of the asymptotic distribution from the true distribution 314 of (8) for each n. Therefore, a corrected power may be defined by 315

$$P_n^{(c)}(\alpha) = \frac{P_n(a_n(\alpha))}{(a_n(\alpha)/\alpha)}$$

where $P_n(a(\alpha))$ is the power using the true probability of the error type I, namely $a_n(\alpha)$. The main idea is penalizing the power by the ratio between $a_n(\alpha)$ and α . Note that, the power under the null hypothesis has to be the nominal level and the comparison of powers from different statistics must be done adopting the same nominal level. Under the null hypothesis, we have that

$$P_{1n}^{(c)}(\alpha) = P_{2n}^{(c)}(\alpha) = \alpha,$$

since under the null hypothesis $P_n(a_n(\alpha)) = a_n(\alpha)$. Hence, the corrected powers 321 $P_{1n}^{(c)}$ and $P_{2n}^{(c)}$ are comparable. Moreover, under an alternative hypothesis and when 322 n increases, an expected behavior of $P_n^{(c)}(\alpha)$ is to converge towards one. Although, 323 this corrected power is not a monotonic function of the sample size nor of the 324 nominal level, we believe that it can be used as a descriptive measure to evidence 325 how unsuitable is the usual model when compared with the proposed one outside the 326 null hypothesis. Furthermore, the proposed corrected power varies between 0 and 327 infinity. Figure 1 shows the corrected power for both approaches, the null hypothesis 328 was $H_0: b_{12} = 0$. The full line refers to the proposed approach and the dashed line 329 refers to the usual one. The panels (a.1), (b.1), (c.1) and (d.1) refer to the corrected 330 power when the alternative hypothesis are $b_{12} = -0.4$, $b_{12} = -0.2$, $b_{12} = 0.2$ and 331 $b_{12} = 0.4$, respectively at $\alpha = 0.01$. The panels (a.2), (b.2), (c.2) and (d.2) refer 332 to the corrected power when the alternative hypothesis are $b_{12} = -0.4$, $b_{12} = -0.2$, 333 $b_{12} = 0.2$ and $b_{12} = 0.4$, respectively at $\alpha = 0.05$. The panels (a.3), (b.3), (c.3) and 334 (d.3) refer to the corrected power when the alternative hypothesis are $b_{12} = -0.4$, 335 $b_{12} = -0.2, b_{12} = 0.2$ and $b_{12} = 0.4$, respectively at $\alpha = 0.10$. We observe in all 336 graphs that, the usual approach has the worst performance (going to zero when 337 the sample size increases) while the proposed one have an expected behavior for

a good statistic (going to one when the sample size increases). In general, the corrected power under the usual methodology goes to zero because the distance between $a_n(\alpha)$ and α increases much faster than the uncorrected power, $P_n(a_n(\alpha))$, when *n* increases. This behavior is still true for other setups of parameters.

[[Figure 1]]

[[Table 3]]

Table 3 shows that the biases of the estimators of b_{ij} (i, j = 1, 2) from the proposed model are almost always smaller (in absolute value) than the value supplied by the usual model (except only for the parameter b_{21} when n = 50). Moreover, the larger the sample size, the smaller the bias and MSE under the proposed model (this does not happen for the usual approach). For this specific table, the true parameters are $b_{21} = 0.2$ and $b_{12} = -0.4$, all other parameters were chosen as previously described.

Table 4 presents the rejection rates for testing univariate hypotheses. In this table, the model was generated by considering p = 4, $a_1 = a_2 = a_3 = a_4 = 1$, $b_{11} = 0.9$, $b_{22} = 0.6$, $b_{33} = 0.4$, $b_{44} = 0.5$, $b_{41} = 0.5$, $b_{14} = -0.3$, $b_{12} = b_{13} = b_{21} =$ $b_{23} = b_{24} = b_{31} = b_{32} = b_{34} = b_{42} = b_{43} = 0$. The measurement error variance was 0.60 and the variance of q_t was

$$\boldsymbol{\Sigma} = \begin{pmatrix} 0.80 & 0.20 & 0.20 & 0.05 \\ 0.20 & 0.80 & 0.05 & -0.05 \\ 0.20 & 0.05 & 1.00 & 0.10 \\ 0.05 & -0.05 & 0.10 & 0.90 \end{pmatrix}$$

Notice that, these parameters and hypothesis tests were chosen to mimic our application (see next section for further details). We test the univariate hypotheses in each Monte Carlo simulation, say H_0 : $b_{12} = 0$, H_0 : $b_{13} = 0$, H_0 : $b_{21} = 0$, H_0 : $b_{23} = 0$, H_0 : $b_{24} = 0$, H_0 : $b_{31} = 0$, H_0 : $b_{32} = 0$, H_0 : $b_{42} = 0$ and H_0 : $b_{43} = 0$ by using the usual and proposed approaches. The measurement error variance was estimated through replications (m = 0.6n). Here, n = 100, 200, 400 in which for the real data n = m = 200.

[[Table 4]]

Notice that, for the proposed model the test sizes are, in average, closer to 5% than the usual one. Next section presents a comparison between of the results of Table 4 and the application.

4 APPLICATION

As previously described, the models including measurement errors have great rel-366 evance in applied sciences, since equipment imprecisions are inherent to data ac-36 quisition. Actually, the usual models are commonly applied ignoring these errors. 368 Nowadays, the scientific community started to pay enough attention to the fact 369 that these procedures may lead to spurious results. In this section, we illustrate the 370 concepts introduced in the present study with an application embedded in Neuro-371 science research, with the utilization of VAR modeling for the characterization of 372 brain networks. 373

The dataset explored in this application is proceeding from a functional mag-374 netic resonance imaging (fMRI) experiment. Basically, fMRI acquisition is based on 375 monitoring the BOLD signal (blood oxygenation level dependent) at several brain 376 regions through time. One of the main advantages of fMRI over other imaging tech-377 niques is its non-invasive protocol and relative high spatial resolution. The BOLD 378 signal is related to oxygen consumption and blood flow, being considered as an in-379 direct measure of local neural activity (Logothetis et al. (2001)). Regarding this 380 property, BOLD signal is used to quantify and locate the brain activity in humans. 381 In this study, the BOLD signals at four brain regions from a subject in a resting 382 state (eyes closed) experiment were considered. The data was collected in a Siemens 383 3Tesla MR system (TR=1800ms, TA=900ms, TE=30ms). The selected brain re-384 gions were: left primary motor cortex (left M1), right primary motor cortex (right 385 M1), supplementary motor area (SMA) and right cerebellum. For this volunteer, 386 these regions were previously mapped by using a fingertap motor experiment. The 387 anatomical location of these areas are shown in Figure 2. These regions are fre-388 quently involved in active and planned right hand fingertapping, and their role is 389 already established in motor execution. However, we aim to evaluate the default 390 connectivity network between these areas, which can be depicted by the informa-391 tion flow during a resting state run, which may be identified using VAR models and 392 Granger causality concept. 393

A well described limitation inherent to all fMRI acquisition is the high level of scanner noise. Thus, the signals observed mirror not only the physiological variations but also includes measurement errors. For this specific dataset, it was estimated that the error composed approximately 57.10% of the observed time series standard deviation. This estimate was obtained by considering the squared root of the median variance of BOLD time series from extracranial voxels (i.e., we used 2,354 auxiliar time series of length 200), with baseline signal (mean) greater than 75. Voxels with baseline below this threshold are too far from tissue (image corners) and have minimal variance, which may lead to an underestimate of noise level. For simplicity, each observed series were normalized to have mean zero and variance one. The measurement error was considered to be serially uncorrelated, independent of the latent variables and with a standard deviation estimated at 0.571.

⁴⁰⁶ The model considered for the latent variable is given by

$$\boldsymbol{z}_t = \boldsymbol{a} + \boldsymbol{B}_1 \boldsymbol{z}_{t-1} + \boldsymbol{q}_t, \ t = 1, \cdots, n$$
(11)

where n = 200 is the time series length, $\mathbf{z}_t = (z_{1t}, z_{2t}, z_{3t}, z_{4t})^{\top}$ with z_{1t} : Left M1 signal, z_{2t} : SMA signal, z_{3t} : Right M1 signal and z_{4t} : Right cerebellum signal; \mathbf{B}_1 is the (4×4) autoregressive coefficients matrix

$$\boldsymbol{B}_{1} = \begin{pmatrix} b_{11} & b_{12} & b_{13} & b_{14} \\ b_{21} & b_{22} & b_{23} & b_{24} \\ b_{31} & b_{32} & b_{33} & b_{34} \\ b_{41} & b_{42} & b_{43} & b_{44} \end{pmatrix},$$
(12)

and q_t is an (4×1) unobservable zero mean white noise vector. The observed variables are given by

$$\boldsymbol{Z}_t = \boldsymbol{z}_t + \boldsymbol{e}_t, \ t = 1, \cdots, n \tag{13}$$

where $\mathbf{Z}_t = (Z_{1t}, Z_{2t}, Z_{3t}, Z_{4t})^{\top}$ and $\mathbf{e}_t = (e_{1t}, e_{2t}, e_{3t}, e_{4t})^{\top}$ is the measurement error vector with $\operatorname{Var}(\mathbf{e}_t) = 0.571^2 \mathbf{I}_4$.

The time series plots corresponding to the respective observed BOLD signal at each brain region are represented in Figure 3. Since we are interested in identifying the links of connectivity networks using Granger causality, the statistical inferences are related to the parameters b_{ij} (i, j = 1, 2, 3, 4). If $b_{ij} \neq 0$, then there is a information flow from brain area j to area i (Baccala and Sameshima (2001)). The coefficient estimates, standard errors and p-values $(H_0: b_{ij} = 0 \text{ vs } H_1: b_{ij} \neq 0)$ for both usual and proposed approaches are shown in Tables 5 and 6, respectively.

> [[Figure 2]] [[Figure 3]] [[Figure 4]] [[Figure 5]] [[Table 5]] [[Table 6]]

$$\widehat{\boldsymbol{\Sigma}} = \begin{pmatrix} 0.81 & 0.16 & 0.18 & 0.04 \\ 0.16 & 0.76 & 0.05 & -0.05 \\ 0.18 & 0.05 & 0.95 & 0.09 \\ 0.04 & -0.05 & 0.09 & 0.87 \end{pmatrix}$$

The results described in Tables 5 and 6 suggest the existence of bidirectional 422 information flow between Left M1 and Cerebellum. However, the application of 423 usual approach indicates also that Left M1 sends information to SMA and Right 424 M1, and that the latter sends to SMA. For both usual and proposed approaches, 425 the diagrams of the networks at the significance level of 5% are shown in Figure 4. 426 As highlighted by the simulations results, the utilization of usual VAR estimation, 427 ignoring the measurement errors, may result in wrong test nominal sizes. In this 428 context, it is important to mention that the main differences between the usual 429 and proposal results were on standard deviation estimates. Further, the proposal 430 estimates are almost twice the values resulting from usual approach. The theory and 431 simulations suggest the existence of biases in the latter. Consequently, the p-values 432 from the usual method tend to be underestimated, resulting in high rejection rates. 433 Note that these connections may possibly exist, but since the nominal level of the 434 test is "incorrect", the type I error is not under control. In addition, note that some 435 coefficients were considerably underestimated, for example b_{11} , b_{22} and b_{33} . See, 436 the qq-plots represented in Figure 5, which suggest that the probability density of 437 residuals $Z_t - Z_t$ are reasonably approximated by the Normal distribution. 438

In what follows we compare the results of Tables 5 and 6 with Table 4. Note 439 that, for the real data, at a 5% nominal level, the proposed approach does not detect 440 difference from zero for the following coefficients b_{12} , b_{13} , b_{21} , b_{23} , b_{24} , b_{31} , b_{32} , b_{34} , 441 b_{42} and b_{43} . In contrast, the usual approach does not detect such differences only for 442 the coefficients b_{12} , b_{13} , b_{24} , b_{32} , b_{34} , b_{42} and b_{43} . That is, the results agree for these 443 coefficientes, however for b_{21} (Left M1 \rightarrow SMA, p-value for the usual and proposed 444 methods are 0.008 and 0.332, respectively), b_{23} (Right M1 \rightarrow SMA, p-value for 445 the usual and proposed methods are 0.002 and 0.053, respectively), b_{31} (Left M1 446 \rightarrow Right M1, p-value for the usual and proposed methods are 0.030 and 0.073, 447 respectively) they do not coincide. Futhermore, the hypothesis $b_{21} = 0$ presents the 448 greatest difference between the p-values, which keeps different conclusions even if 449 we set a 10% nominal level. While, for the hypotheses $b_{23} = 0$ and $b_{31} = 0$ the 450 conclusions become the same at a 10% nominal level. Thus, looking at the results 451

of Table 4 we can find a possible explanation for this fact. Notice that, for the 452 usual approach and n = 200, the empirical false positive rates under the hypothesis 453 $b_{21} = 0$ is 7.55% (the proposed approach is 4.75%); under the hypothesis $b_{23} = 0$ is 454 5.72% (the proposed approach is 4.75%) and under the hypothesis $b_{31} = 0$ is 5.73% 455 (the proposed approach is 5.25%). As can be seen, the usual method is rejecting 456 more than the proposed one for the hypothesis $b_{21} = 0$, whereas for the hypotheses 457 $b_{23} = 0$ and $b_{32} = 0$ the usual method is still rejecting more than the proposed one, 458 but a little less pronouced. The same behavior can be seen in the application. 459

Some studies (Biswal et al (1995)) suggest the existence of functional networks 460 between motor areas even in resting state condition. These studies are based on 461 correlation analysis between the BOLD signal at different brain sites. First, it is 462 important to note that Granger causality is conceptually different from correlation, 463 which is symmetric (it does not provide the direction of information flow), evaluated 464 in a pairwise fashion (and not in the full multivariate sense) and it does not take 465 into account temporal information. In fact, correlation analysis is more closely 466 related to instantaneous Granger Causality concept, which can be useful to quantify 467 simultaneity between time series but it is unsuitable in the context of information 468 flow detection. Second, the usual correlation analysis does not consider the presence 469 of measurement errors, which may also affect the statistical significance of the results. 470 The nature of functional networks in resting state is still unclear and is the subject 471 of several studies (Long et al. (2008)). Nevertheless, we have demonstrated in this 472 study that the inclusion of measurement errors can considerably influence the final 473 results. Thus, the development of novel approaches dealing with this artifact is 474 necessary. 475

In summary, since the proposal and usual results differ, we conclude that the presence of measurement error cannot be ignored. An adequate treatment for this artifact is essential for the adequate description and modeling of brain networks. It is surprising that this important limitation received proper attention only recently. We believe that a preliminary analysis of this problem points toward the demand for the development of new estimation procedures regarding scanner noise characterization, physiological noise and computational implementation.

5 CONCLUSION

This paper has introduced a new approach to model multivariate times series when 484 measurement errors are present. The simulation studies indicate that the proposed 485 approach provides coherent results (test size close to the nominal level even for 486 small samples, power increasing with the sample size under alternative hypotheses, 487 biases and mean square errors decreasing when the sample size increases) under 488 small and moderate measurement error. Such features seem no to be shared by the 489 conventional maximum likelihood estimators which present a much inferior perfor-490 mance. Furthermore, the proposal is easily attained and iterative procedures are 491 not required. The theory, simulations and application showed that the presence of 492 measurement error cannot be neglected and a proper model has to be considered 493 for an adequate description and modeling of brain networks. We expect to report 494 extensions of the proposed model (for elliptical errors, heteroscedasticity situations, 495 also trying to incorporate the variability of the measurement error variance esti-496 mation in the asymptotics), a residual study and more simulation studies for large 497 measurement errors on incoming papers. 498

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A PROOF OF THEOREMS

⁵⁰⁴ A.1 Proof of Theorem 1

⁵⁰⁵ In order to prove the consistence of the estimators stated in Theorem 1, namely

$$\widehat{oldsymbol{a}} = ar{oldsymbol{Z}}_t - \widehat{oldsymbol{B}}ar{oldsymbol{Z}}^*_{t-1}, \qquad \widehat{oldsymbol{B}} = \left[(oldsymbol{S}_{oldsymbol{Z}^*_{t-1}} - oldsymbol{I}_r \otimes oldsymbol{\Sigma}_e)^{-1}oldsymbol{S}_{oldsymbol{Z}^*_{t-1}}oldsymbol{Z}_t
ight]^ op$$

506 and

$$\widehat{\boldsymbol{\Sigma}} = n^{-1} \sum_{i=1}^{n} (\boldsymbol{Z}_{i} - \widehat{\boldsymbol{a}} - \widehat{\boldsymbol{B}} \boldsymbol{Z}_{i-1}^{*}) (\boldsymbol{Z}_{i} - \widehat{\boldsymbol{a}} - \widehat{\boldsymbol{B}} \boldsymbol{Z}_{i-1}^{*})^{\top} - \boldsymbol{\Sigma}_{e} - \widehat{\boldsymbol{B}} (\boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e}) \widehat{\boldsymbol{B}}^{\top},$$

we must study the limits of the quantities $S_{Z_{t-1}^*}$, $S_{Z_{t-1}^*Z_t}$, \bar{Z}_{t-1}^* and \bar{Z}_t^* when the sample size goes to infinity. Note that $Z_{t-1}^* = z_{t-1}^* + e_{t-1}^*$, where $e_{t-1}^* =$ ⁵⁰⁹ $(\boldsymbol{e}_{t-1}^{\top},\ldots,\boldsymbol{e}_{t-r}^{\top})^{\top}$, and under the stationary conditions of a VAR(r) model we have ⁵¹⁰ that

$$\begin{split} \boldsymbol{S}_{\boldsymbol{Z}_{t-1}^{*}} &= n^{-1} \sum_{i=1}^{n} (\boldsymbol{Z}_{i-1}^{*} - \bar{\boldsymbol{Z}}_{t-1}^{*}) \boldsymbol{Z}_{i-1}^{*\top} \\ &= n^{-1} \sum_{i=1}^{n} (\boldsymbol{z}_{i-1}^{*} + \boldsymbol{e}_{i-1}^{*} - \bar{\boldsymbol{z}}_{t-1}^{*} - \bar{\boldsymbol{e}}_{t-1}^{*}) (\boldsymbol{z}_{i-1}^{*} + \boldsymbol{e}_{i-1}^{*})^{\top} \\ &= \boldsymbol{S}_{\boldsymbol{z}_{t-1}^{*}} + \boldsymbol{S}_{\boldsymbol{e}_{t-1}^{*}} + O_{p} (n^{-1/2}) \\ &= \boldsymbol{\Gamma}_{r}(0) + \boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e} + O_{p} (n^{-1/2}), \end{split}$$

where $S_{e_{t-1}^*} = n^{-1} \sum_{i=1}^n e_{i-1}^* e_{i-1}^{*\top}$, and $O_p(n^{-1/2})$ means limited in probability even multiplying by $n^{1/2}$ (it happens with the crossing product in the above expression). That is, $S_{Z_{t-1}^*} \xrightarrow{\mathcal{P}} \Gamma_r(0) + I_r \otimes \Sigma_e$. Following the same scheme, we have that

$$\begin{aligned} \boldsymbol{S}_{\boldsymbol{Z}_{t-1}^{*}\boldsymbol{Z}_{t}} &= n^{-1}\sum_{i=1}^{n}(\boldsymbol{Z}_{i-1}^{*}-\bar{\boldsymbol{Z}}_{t-1}^{*})\boldsymbol{Z}_{i}^{\top} \\ &= n^{-1}\sum_{i=1}^{n}(\boldsymbol{z}_{i-1}^{*}+\boldsymbol{e}_{i-1}^{*}-\bar{\boldsymbol{z}}_{t-1}^{*}-\bar{\boldsymbol{e}}_{t-1}^{*})(\boldsymbol{z}_{i}+\boldsymbol{e}_{i})^{\top} \\ &= \boldsymbol{S}_{\boldsymbol{z}_{t-1}^{*}\boldsymbol{z}_{t}}+O_{p}(n^{-1/2}) \\ &= \boldsymbol{\Gamma}_{r}(0)\boldsymbol{B}^{\top}+O_{p}(n^{-1/2}), \end{aligned}$$

and finally, both the quantities \bar{Z}^*_{t-1} and \bar{Z}^*_t converge in probability to μ^* . Hence,

$$(\boldsymbol{S}_{\boldsymbol{Z}_{t-1}^*} - \boldsymbol{I}_r \otimes \boldsymbol{\Sigma}_e)^{-1} \xrightarrow{\mathcal{P}} \boldsymbol{\Gamma}_r(0)^{-1} \quad \text{and} \quad \boldsymbol{S}_{\boldsymbol{Z}_{t-1}^*} \boldsymbol{Z}_t \xrightarrow{\mathcal{P}} \boldsymbol{\Gamma}_r(0) \boldsymbol{B}^\top,$$

thus, the probability convergence of \hat{a} , \hat{B} and $\hat{\Sigma}$ to a, B and Σ follow, respectively.

516 A.2 Proof of Theorem 2

The proof idea has three steps. The first step consists in showing that $\operatorname{vec}(\widehat{B}^{\top}) - \operatorname{vec}(B^{\top})$ can be written as linear combinations of a vectorial mean. The second one, we must demonstrate that this vectorial mean has an asymptotic Normal distribution. The last step must conclude that $\operatorname{vec}(\widehat{B}^{\top}) - \operatorname{vec}(B^{\top})$ also has an asymptotic Normal distribution. In order to prove Theorem 2, we need some auxiliary results, which are exposed in two propositions below.

⁵²³ **Proposition 1.** Under the model (1) and (4), the proposed estimator \widehat{B} has the ⁵²⁴ following relationship

$$vec(\widehat{\boldsymbol{B}}^{\top}) - vec(\boldsymbol{B}^{\top}) = (\boldsymbol{I}_p \otimes \boldsymbol{\Gamma}_r(0)^{-1})\overline{\boldsymbol{W}} + O_p(n^{-1}),$$

525 where

$$\bar{\boldsymbol{W}} = n^{-1} \sum_{i=1}^{n} \begin{pmatrix} \boldsymbol{W}_{1i} \\ \vdots \\ \boldsymbol{W}_{qi} \end{pmatrix} = n^{-1} \sum_{i=1}^{n} \boldsymbol{W}_{i}$$

sign with $W_i = (q_i + e_i - Be_{i-1}^*) \otimes (z_{i-1}^* - \mu^* + e_{i-1}^*) - \Psi$ and $\Psi = [I_p \otimes (I_r \otimes \Sigma_e)] vec(B^\top).$

⁵²⁷ **Proof:** Define $\boldsymbol{B}_{.k}$ as a vector $(rp \times 1)$ of coefficients associated with the k^{th} element ⁵²⁸ of the vector \boldsymbol{z}_t , that is

$$z_{kt} = a_k + \boldsymbol{B}_{.k}^{\top} \boldsymbol{z}_{t-1}^* + q_{kt}$$

Thus, we have that $\operatorname{vec}(\boldsymbol{B}^{\top}) = (\boldsymbol{B}_{.1}^{\top}, \boldsymbol{B}_{.2}^{\top}, \cdots, \boldsymbol{B}_{.p}^{\top})^{\top}$ and the estimator of Theorem 1 for it can be written as $\operatorname{vec}(\hat{\boldsymbol{B}}) = (\hat{\boldsymbol{B}}_{.1}^{\top}, \hat{\boldsymbol{B}}_{.2}^{\top}, \cdots, \hat{\boldsymbol{B}}_{.p}^{\top})^{\top}$, where $\hat{\boldsymbol{B}}_{.k} = (\boldsymbol{S}_{\boldsymbol{Z}_{t-1}^{*}} - \boldsymbol{S}_{t-1})^{T}$ $\boldsymbol{I} \otimes \boldsymbol{\Sigma}_{e})^{-1} \boldsymbol{S}_{\boldsymbol{Z}_{t-1}^{*}\boldsymbol{Z}_{kt}}$ and $\boldsymbol{S}_{\boldsymbol{Z}_{t-1}^{*}\boldsymbol{Z}_{kt}} = n^{-1} \sum_{i=1}^{n} (\boldsymbol{Z}_{i-1}^{*} - \boldsymbol{Z}_{t-1})^{T})^{T}$ for $k = 1, \dots, p$. Moreover, the model (2) may be rewritten in terms of the observed variables as

$$Z_t = a + BZ_{t-1}^* + \vartheta_t,$$

$$\vartheta_t = q_t + e_t - Be_{t-1}^*,$$
(14)

533 and for the k^{th} element of \boldsymbol{Z}_t we have

$$Z_{kt} = a_k + \boldsymbol{B}_{.k}^{\top} \boldsymbol{Z}_{t-1}^* + \vartheta_{kt},$$

$$\vartheta_{kt} = q_{kt} + e_{kt} - \boldsymbol{B}_{.k}^{\top} \boldsymbol{e}_{t-1}^*.$$
(15)

534 Then, it follows that

$$S_{Z_{t-1}^*Z_k} = n^{-1} \sum_{i=1}^n (Z_{i-1}^* - \bar{Z}_{t-1}^*) (a_k + B_{.k}^\top Z_{i-1}^* + \vartheta_{ki}) = S_{Z_{t-1}^*} B_{.k} + S_{Z_{t-1}^*\vartheta_k},$$

⁵³⁵ where $\boldsymbol{S}_{\boldsymbol{Z}_{t-1}^{*}\vartheta_{k}} = n^{-1}\sum_{i=1}^{n}(\boldsymbol{Z}_{i-1}^{*}-\bar{\boldsymbol{Z}}_{t-1}^{*})\vartheta_{ki} = n^{-1}\sum_{i=1}^{n}(\boldsymbol{z}_{i-1}^{*}-\boldsymbol{\mu}^{*}+\boldsymbol{e}_{i-1}^{*})\vartheta_{ki} + O_{p}(n^{-1})$. Hence, denoting $\boldsymbol{S}_{\boldsymbol{z}_{t-1}^{*}\vartheta_{k}} = n^{-1}\sum_{i=1}^{n}(\boldsymbol{z}_{i-1}^{*}-\boldsymbol{\mu}^{*}+\boldsymbol{e}_{i-1}^{*})\vartheta_{ki}$ we have that

$$\boldsymbol{S}_{\boldsymbol{Z}_{t-1}^{*}\boldsymbol{Z}_{k}} = (\boldsymbol{S}_{\boldsymbol{Z}_{t-1}^{*}} - \boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e}) \boldsymbol{B}_{.k} + \boldsymbol{S}_{\boldsymbol{z}_{t-1}^{*}\vartheta_{k}} - \boldsymbol{\Psi}_{k} + O_{p}(n^{-1}),$$

537 with $\Psi_k = -(I_r \otimes \Sigma_e) B_{.k}$. As a result, we have

$$\widehat{\boldsymbol{B}}_{.k} = \boldsymbol{B}_{.k} + \boldsymbol{\Gamma}_r^{-1}(0) \bar{\boldsymbol{W}}_k + O_p(n^{-1})$$

⁵³⁸ where $\bar{W}_k = n^{-1} \sum_{i=1}^n W_{ki}$ and $W_{ki} = (z_{i-1}^* - \mu^* + e_{i-1}^*) \vartheta_{ki} - \Psi_k$. Hence, it follows ⁵³⁹ that

$$\operatorname{vec}(\widehat{\boldsymbol{B}}^{\top}) - \operatorname{vec}(\boldsymbol{B}^{\top}) = (\boldsymbol{I}_p \otimes \boldsymbol{\Gamma}_r(0)^{-1})\overline{\boldsymbol{W}} + O_p(n^{-1}),$$

540 where

$$\bar{\boldsymbol{W}} = n^{-1} \sum_{i=1}^{n} \begin{pmatrix} \boldsymbol{W}_{1i} \\ \vdots \\ \boldsymbol{W}_{qi} \end{pmatrix} = n^{-1} \sum_{i=1}^{n} \boldsymbol{W}_{i}$$

with $W_i = (\boldsymbol{q}_i + \boldsymbol{e}_i - \boldsymbol{B}\boldsymbol{e}_{i-1}^*) \otimes (\boldsymbol{z}_{i-1}^* - \boldsymbol{\mu}^* + \boldsymbol{e}_{i-1}^*) - \Psi$ and $\Psi = [\boldsymbol{I}_p \otimes (\boldsymbol{I}_r \otimes \boldsymbol{\Sigma}_e)] \operatorname{vec}(\boldsymbol{B}^\top).$

Proposition 2. If $e_t \sim \mathcal{N}(\mathbf{0}, \Sigma_e)$ with Σ_e known and $E(q_{ij_1}q_{ij_2}q_{ij_3}q_{ij_4}) < \infty$ for all $j_1, j_2, j_3, j_4 \in \{1, \dots, p\}$, where q_{ij} is the j^{th} element of \mathbf{q}_i . The mean, \mathbf{W} , of Proposition 1 has an asymptotic distribution given by

$$\sqrt{n} \bar{\boldsymbol{W}} \stackrel{\mathcal{D}}{\longrightarrow} \mathcal{N}(\boldsymbol{0}, \boldsymbol{T}_r),$$

545 where

$$\begin{split} \boldsymbol{T}_{r} &= \boldsymbol{\Sigma}_{\vartheta} \otimes \boldsymbol{\Gamma}_{r}(0) + \boldsymbol{\Sigma}_{\vartheta} \otimes (\boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e}) + \boldsymbol{B}^{\top} \otimes [\boldsymbol{\Sigma}_{e} \boldsymbol{B}(\boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e})] + \\ &- \sum_{h=1}^{r} \left\{ (\boldsymbol{B}_{h} \boldsymbol{\Sigma}_{e}) \otimes \boldsymbol{\Gamma}_{r}(h) + (\boldsymbol{\Sigma}_{e} \boldsymbol{B}_{h}^{\top}) \otimes \boldsymbol{\Gamma}_{r}(-h) \right\} + \\ &+ \sum_{h=1-r}^{r-1} [\boldsymbol{B}(\boldsymbol{J}_{-h} \otimes \boldsymbol{\Sigma}_{e}) \boldsymbol{B}^{\top}] \otimes \boldsymbol{\Gamma}_{r}(h). \end{split}$$

where J_l is a $(r \times r)$ matrix of zeros with one's in the $|l|^{th}$ diagonal above (below) the main diagonal if l > 0 (l < 0) and J_0 is a $(r \times r)$ matrix of zeros.

Proof: Notice that the expectation of W_i is equal to zero for all *i*. Shumway 548 and Stoffer (2000) state a central limit theorem to a univariate M-dependent se-549 quence of random variables with mean zero. We say that a time series x_t is 550 M-dependent if the set of values $x_s, s \leq t$ is independent of the set of values 551 $x_s, s \ge t + M + 1$ (Shumway and Stoffer, 2000, on pg. 66). Then, assuming that 552 $E(q_{ij_1}q_{ij_2}q_{ij_3}q_{ij_4}) < \infty$ for all $j_1, j_2, j_3, j_4 \in \{1, \ldots, p\}$ where q_{ij} is the j^{th} element 553 of \boldsymbol{q}_i and defining $\bar{x} = n^{-1} \sum_{i=1}^n x_i$, where $x_i = \boldsymbol{\delta}^\top \boldsymbol{W}_i$ we have that $E(x_i) = 0$, 554 $\operatorname{Cov}(x_i, x_{i-h}) = \boldsymbol{\delta}^{\top} \operatorname{Cov}(\boldsymbol{W}_i, \boldsymbol{W}_{i-h}^{\top}) \boldsymbol{\delta} = \boldsymbol{\delta}^{\top} E(\boldsymbol{W}_i \boldsymbol{W}_{i-h}^{\top}) \boldsymbol{\delta}$ and 555

$$E(\boldsymbol{W}_{i}\boldsymbol{W}_{i-h}^{\top}) = E[\boldsymbol{F}_{ih} \otimes (\boldsymbol{z}_{i-1}^{*} - \boldsymbol{\mu}^{*})(\boldsymbol{z}_{i-h-1}^{*} - \boldsymbol{\mu}^{*})^{\top}] + E[\boldsymbol{F}_{ih} \otimes \boldsymbol{e}_{i-1}^{*}\boldsymbol{e}_{i-h-1}^{*\top}] + E[\boldsymbol{F}_{ih} \otimes (\boldsymbol{z}_{i-1}^{*} - \boldsymbol{\mu}^{*})\boldsymbol{e}_{i-h-1}^{*\top}] - \boldsymbol{\Psi}\boldsymbol{\Psi}^{\top}$$

with $F_{ih} = (q_i + e_i - Be_{i-1}^*)(q_{i-h} + e_{i-h} - Be_{i-h-1}^*)^{\top}$. Thus, using some matricial results and simple expectation rules we can solve these expectations as follows

$$E(\boldsymbol{W}_{i}\boldsymbol{W}_{i-h}^{\scriptscriptstyle +}) = \boldsymbol{0} \qquad ext{for} \quad |h| < r,$$

$$E(\boldsymbol{W}_{i}\boldsymbol{W}_{i-h}^{\top}) = -(\boldsymbol{B}_{r}\boldsymbol{\Sigma}_{e}) \otimes \boldsymbol{\Gamma}_{r}(h) \quad \text{for} \quad h = r,$$

$$E(\boldsymbol{W}_{i}\boldsymbol{W}_{i-h}^{\top}) = -(\boldsymbol{\Sigma}_{e}\boldsymbol{B}_{|r|}^{\top}) \otimes \boldsymbol{\Gamma}_{r}(h) \quad \text{for} \quad h = -r,$$

$$E(\boldsymbol{W}_{i}\boldsymbol{W}_{i-h}^{\top}) = [\boldsymbol{B}(\boldsymbol{J}_{-h}\otimes\boldsymbol{\Sigma}_{e})\boldsymbol{B}^{\top}] \otimes \boldsymbol{\Gamma}_{r}(h) - (\boldsymbol{B}_{h}\boldsymbol{\Sigma}_{e}) \otimes \boldsymbol{\Gamma}_{r}(h) \quad \text{for} \quad h = 1, \dots, r-1,$$

$$E(\boldsymbol{W}_{i}\boldsymbol{W}_{i-h}^{\top}) = [\boldsymbol{B}(\boldsymbol{J}_{-h}\otimes\boldsymbol{\Sigma}_{e})\boldsymbol{B}^{\top}] \otimes \boldsymbol{\Gamma}_{r}(h) - (\boldsymbol{\Sigma}_{e}\boldsymbol{B}_{|h|}^{\top}) \otimes \boldsymbol{\Gamma}_{r}(h) \quad \text{for} \quad h = -1, \dots, 1-r$$

$$E(\boldsymbol{W}_{i}\boldsymbol{W}_{i-h}^{\top}) = [\boldsymbol{B}(\boldsymbol{J}_{-h}\otimes\boldsymbol{\Sigma}_{e})\boldsymbol{B}^{\top}] \otimes \boldsymbol{\Gamma}_{r}(h) - (\boldsymbol{\Sigma}_{e}\boldsymbol{B}_{|h|}^{\top}) \otimes \boldsymbol{\Gamma}_{r}(h) \quad \text{for} \quad h = -1, \dots, 1-r$$

$$E(\boldsymbol{W}_{i}\boldsymbol{W}_{i-h}^{\top}) = \boldsymbol{\Sigma}_{\vartheta} \otimes \boldsymbol{\Gamma}_{r}(0) + \boldsymbol{\Sigma}_{\vartheta} \otimes (\boldsymbol{I}_{r}\otimes\boldsymbol{\Sigma}_{e}) + \boldsymbol{B}^{\top} \otimes [\boldsymbol{\Sigma}_{e}\boldsymbol{B}(\boldsymbol{I}_{r}\otimes\boldsymbol{\Sigma}_{e})] \quad \text{for} \quad h = 0,$$

where J_l is a $(r \times r)$ matrix of zeros with one's in the $|l|^{th}$ diagonal above (below) 563 the main diagonal if l > 0 (l < 0) and J_0 is a $(r \times r)$ matrix of zeros. That is, 564 $x_1 \ldots, x_n$ is a strictly M-dependent sequence of random variables with mean zero 565 (where M = r) and, therefore, we can use the result stated in Shumway and Stoffer 566

for h = 0,

$$_{567}$$
 (2000), which says that

$$\sqrt{n}\bar{x} \xrightarrow{\mathcal{D}} \mathcal{N}(0, V_r)$$

where 568

558

$$V_r = \sum_{h=-r}^{r} \operatorname{Cov}(\boldsymbol{\delta}^{\top} \boldsymbol{W}_i, \boldsymbol{\delta}^{\top} \boldsymbol{W}_{i-h}) = \boldsymbol{\delta}^{\top} \boldsymbol{T}_r \boldsymbol{\delta}$$

with 569

$$\begin{aligned} \boldsymbol{T}_{r} &= \boldsymbol{\Sigma}_{\vartheta} \otimes \boldsymbol{\Gamma}_{r}(0) + \boldsymbol{\Sigma}_{\vartheta} \otimes (\boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e}) + \boldsymbol{B}^{\top} \otimes [\boldsymbol{\Sigma}_{e} \boldsymbol{B}(\boldsymbol{I}_{r} \otimes \boldsymbol{\Sigma}_{e})] + \\ &- \sum_{h=1}^{r} \left\{ (\boldsymbol{B}_{h} \boldsymbol{\Sigma}_{e}) \otimes \boldsymbol{\Gamma}_{r}(h) + (\boldsymbol{\Sigma}_{e} \boldsymbol{B}_{h}^{\top}) \otimes \boldsymbol{\Gamma}_{r}(-h) \right\} + \\ &+ \sum_{h=1-r}^{r-1} [\boldsymbol{B}(\boldsymbol{J}_{-h} \otimes \boldsymbol{\Sigma}_{e}) \boldsymbol{B}^{\top}] \otimes \boldsymbol{\Gamma}_{r}(h). \end{aligned}$$

As $\sqrt{n} \delta^\top \bar{W}$ is asymptotically normally distributed for all $\delta \neq \mathbf{0}_r$ then, by the 570 Cramer-Wold device (see Theorem 10.4.5 on page 336 in Athreya and Lahiri, 2006), 571 we have that 572

$$\sqrt{n} \bar{\boldsymbol{W}} \stackrel{\mathcal{D}}{\longrightarrow} \mathcal{N}(\boldsymbol{0}, \boldsymbol{T}_r).$$

Then, by the Propositions 1 and 2, the prove of Theorem 2 follows 573

$$\sqrt{n}(\operatorname{vec}(\widehat{B}^{\top}) - \operatorname{vec}(B^{\top})) \xrightarrow{\mathcal{D}} \mathcal{N}(\mathbf{0}, [\mathbf{I}_p \otimes \mathbf{\Gamma}_r(0)^{-1}]\mathbf{T}_r[\mathbf{I}_p \otimes \mathbf{\Gamma}_r(0)^{-1}]).$$

References

- B. Abler, A. Roebroeck, R. Goebel, A. Hose, C. Schonfeldt-Lecuona, G. Hole, H. Walter, Investigating directed influences between activated brain areas in a motor-response task using fMRI, *Magnetic Resonance Imaging*, **24** (2006) 181–185.
- D.J. Aigner, C. Hsiao, A. Kapteyn, T. Wansbeek, Latent Variables in Econometric Time-Series. In Handbook of Econometrics, Z. Griliches and M. Intriligator (eds.), Amsterdam: North-Holland, 1984.
- M.G. Akritas, M.A. Bershady, Linear regression for astronomical data with measurement errors and intrinsic scatter, *The Astrophysical Journal*, **470** (1996) 706–714.
- J. Andersson, Testing for Granger causality in the presence of measurement errors, *Economics Bulletin*, 3 (2005) 1–13.
- K.B. Athreya, S.N. Lahiri, Measure Theory and Probability Theory, Springer, 2006.
- L.A. Baccala, K. Sameshima, Partial directed coherence: a new concept in neural structure determination, *Biological Cybernetics*, **84** (2001) 463–474.
- N. Beck, Estimating Dynamic Models Using Kalman Filtering, *Political Analysis*, 1 (1990) 121–156.
- B. Biswal, F.Z. Yetkin, V.M. Haughton, J.S. Hyde, Functional connectivity in the motor cortex of resting human brain using echo-planar MRI, *Magnetic Resonance* in Medicine, **34** (1995) 537–541.
- C.L. Cheng, J. Riu, On estimating linear relationships when both variables are subject to heteroscedastic measurement errors, *Technometrics*, 48 (2006) 511– 519.
- J.D. Cohen, F. Tong, The face of controversy, *Science*, **293** (2001) 2405–2407.
- A. Fujita, J.R. Sato, H.M. Garay-Malpartida, R. Yamaguchi, S. Miyano, M.C. Sogayar, C.E. Ferreira, Modeling gene expression regulatory networks with the sparse vector autoregressive model, *BMC Systems Biology*, **30** (2007a) 1-39.
- A. Fujita, J.R. Sato, H.M. Garay-Malpartida, P.A. Morettin, M.C. Sogayar, C.E. Ferreira, Time-varying modeling of gene expression regulatory networks using the wavelet dynamic vector autoregressive method, *Bioinformatics*, 23 (2007b) 1623–1630.

- W. Fuller, Measurement Error Models, Wiley: Chichester, 1987.
- J. Geweke, "The Dynamic Factor Analysis of Econometric Time-Series." In Latent Variables in Socio-Economic Modelse, Dennis J. Aigner and Arthur S. Goldberger (eds.), Amsterdam: North-Holland, 1977.
- R. Goebel, A. Roebroeck, D.S. Kim, E. Formisano, Investigating directed cortical interactions in time-resolved fMRI data using vector autoregressive modeling and Granger causality mapping, *Magnetic Resonance Imaging*, **21** (2003) 1251–1261.
- S. Gottesman, Bacterial regulation: global regulatory networks, Annual Review of Genetics, 18 (1984) 415–441.
- C.W.J. Granger, Investigating causal relations by econometric models and crossspectral methods, *Econometrica*, **37** (1969) 424–438.
- K. Hasan, J. Hossain, A. HaqueGranger, Parameter estimation of multichannel autoregressive processes in noise, *Signal Processing*, 83 (2003) 603–610.
- M. Katoh, Networking of WNT, FGF, Notch, BMP, and Hedgehog signaling pathways during carcinogenesis, *Stem Cell Review*, **3** (2007) 30–38.
- P. Kellstedt, G.E. McAvoy, J.A. Stimson, Dynamic Analysis with Latent Constructs, *Political Analysis*, 5 (1996) 113–150.
- B.C. Kelly, Some aspects of measurement error in linear regression of astronomical data, *The Astrophysical Journal*, **665** (2007) 1489–1506.
- B.C. Kelly, J. Bechtold, J.R. Trump, M. Vertergaard, A. Siemiginowska, Observational constraints on the dependence of ratio-quiet quasar X-ray emission on black hole mass and accretion rate, *Astrophysical Journal Supplement Series*, **176** (2008) 355–373.
- S.B. Kulathinal, K. Kuulasmaa, D. Gasbarra, Estimation of an errors-in-variables regression model when the variances of the measurement error vary between the observations, *Statistics in Medicine*, **21** (2002) 1089–1101.
- E.L. Lehmann, G. Casella, *Theory of Point Estimation*, 2nd ed. Springer-Verlag: New York, 1998.
- H. Liu, G. Rodríguez, Human activities and global warming: a cointegration analysis, *Environmental Modeling & Software*, **20** (2005) 761–773.

- N.K. Logothetis, J. Pauls, M. Augath, T. Trinath, A. Oeltermann, Neurophysiological investigation of the basis of the fMRI signal, *Nature*, **412** (2001) 150–157.
- X.Y. Long, X.N. Zuo, V. Kiviniemi, Y. Yang, Q.H. Zou, C.Z. Zhu, T.Z. Jiang, H. Yang, Q.Y. Gong, L. Wang, K.C. Li, S. Xie, Y.F. Zang, Default mode network as revealed with multiple methods for resting-state functional MRI analysis, *Journal Neuroscience Methods*, **171** (2008) 349–355.
- H. Lütkepohl, New Introduction to Multiple Time Series Analysis, Springer-Verlag, Berlin, 2005.
- N.D. Mukhopadhyay, S. Chatterjee, Causality and pathway search in microarray time series experiment, *Bioinformatics*, **23** (2007) 442–449.
- A. Maravall, D.J. Aigner, "Identification of the Dynamic Shock-Error Model: The Case of Dynamic Regression." In Latent Variables in Socio-Economic Models, Dennis J. Aigner and Arthur S. Goldberger (eds.), Amsterdam: North-Holland, 1977.
- S. Ni, D. Sun, Noninformative priors and frequentist risks of Bayesian estimators of vector-autoregressive models, *Journal of Econometrics*, **115** (2003) 159–197.
- A.G. Patriota, H. Bolfarine, M. de Castro, A heteroscedastic structural errors-invariables model with equation error, *Statistical Methodology*, **6** (2009) 408–423.
- R Development Core Team, R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. ISBN 3-900051-07-0, URL http://www.R-project.org, 2008.
- J.R. Sato, J.E. Amaro, D.Y. Takahashi, M. de Maria Felix, M.J. Brammer, P.A. Morettin, A method to produce evolving functional connectivity maps during the course of an fMRI experiment using wavelet-based time-varying Granger causality, *Neuroimage*, **31** (2006) 187–196.
- C.A. Sims, Macroeconomics and reality, *Econometrica*, 48 (1980) 1–48.
- R.H. Shumway, D.S. Stoffer, *Time Series Analysis and Its Applications*, Springer-Verlag, New York, 2000.
- J.T. Williams, M.D. McGinnis, The Dimension of Superpower Rivalry: A Dynamic Factor Analysis, *Journal of Conflict Resolution*, **36** (1992) 68–118.

Table 1: Rejection rates (%) of the hypothesis H_0 : $b_{12} = b_{21} = 0$ (at 5% nominal level) using the Wald statistics (8) for n = 50, n = 100, n = 250 and n = 500. The bold numbers at the center are test sizes (they are expected to be 5%) and the numbers around them are empirical powers.

	Corrected approach					Usual a	approach	(OLS)			
				b_{12}					b_{12}		
		-0.4	-0.2	0.0	0.2	0.4	-0.4	-0.2	0.0	0.2	0.4
	n = 50										
	-0.4	88.79	43.95	21.55	44.37	83.03	83.17	31.40	19.27	52.19	88.55
	-0.2	82.95	27.38	7.75	22.52	61.89	75.11	17.19	10.37	39.04	77.59
b_{21}	0.0	82.31	21.89	4.70	17.44	54.01	75.81	15.33	13.06	46.38	81.33
	0.2	87.81	27.67	8.41	24.10	59.58	84.42	25.11	24.30	65.27	92.08
	0.4	93.98	42.31	16.19	34.09	67.33	93.36	43.33	38.86	81.89	97.09
	n = 100										
	-0.4	99.81	81.63	44.50	70.98	98.06	99.47	62.79	34.27	79.88	99.35
	-0.2	99.23	57.85	12.33	35.84	87.49	98.05	32.81	12.62	64.40	97.10
b_{21}	0.0	99.15	45.22	5.03	28.26	83.06	98.01	26.66	19.03	76.63	98.53
	0.2	99.50	49.03	11.12	42.27	88.25	99.03	41.35	42.17	93.19	99.83
	0.4	99.91	69.40	28.78	61.56	92.37	99.89	70.19	67.81	98.92	100.0
	n = 250										
	-0.4	100.0	99.75	85.97	97.86	100.0	100.0	96.74	71.29	99.41	100.0
	-0.2	100.0	95.11	26.42	69.13	99.79	100.0	71.89	21.48	95.93	99.99
b_{21}	0.0	100.0	85.09	5.63	59.33	99.69	100.0	58.01	39.23	99.21	100.0
	0.2	100.0	87.79	19.95	80.56	99.85	100.0	80.67	80.51	99.99	100.0
	0.4	100.0	97.21	62.91	94.57	99.91	100.0	97.65	97.66	100.0	100.0
	n = 500										
	-0.4	100.0	100.0	99.29	99.99	100.0	100.0	99.97	95.71	100.0	100.0
	-0.2	100.0	99.93	48.41	93.75	100.0	100.0	95.21	37.71	99.95	100.0
b_{21}	0.0	100.0	99.11	5.34	88.17	100.0	100.0	88.13	67.50	100.0	100.0
	0.2	100.0	99.45	36.79	98.01	100.0	100.0	98.17	98.19	100.0	100.0
	0.4	100.0	99.99	90.51	99.88	100.0	100.0	99.99	99.99	100.0	100.0

			b_{12}		
Model	-0.4	-0.2	0.0	0.2	0.4
n = 50					
Proposed Model	42.65	13.51	4.93	7.35	14.10
Usual Model	36.54	9.79	6.53	17.78	34.56
n = 100					
Proposed Model	71.01	21.85	5.41	11.09	25.52
Usual Model	61.75	12.97	8.51	31.87	61.65
n = 250					
Proposed Model	97.57	43.83	5.28	21.50	55.67
Usual Model	94.40	22.07	14.17	69.65	95.53
n = 500					
Proposed Model	99.99	70.28	5.37	40.33	85.12
Usual Model	99.94	36.90	24.39	94.27	99.93

Table 2: Rejection rates (%) of the hypothesis $H_0: b_{12} = 0$ (at 5% nominal level) using the Wald statistics (8) for n = 50, n = 100, n = 250 and n = 500.

	Proposed model		Usual model	
	Bias	MSE	Bias	MSE
n = 50				
b_{11}	-0.0034	1.4357	-0.1446	0.0454
b_{12}	-0.0713	1.7832	0.1098	0.0434
b_{21}	0.0323	0.1504	0.0250	0.0143
b_{22}	-0.0813	0.2005	-0.1589	0.0461
n = 100				
b_{11}	-0.0032	0.0218	-0.1313	0.0290
b_{12}	-0.0334	0.0352	0.1209	0.0293
b_{21}	0.0140	0.0120	0.0165	0.0067
b_{22}	-0.0364	0.0195	-0.1265	0.0258
n = 250				
b_{11}	-0.0004	0.0079	-0.1252	0.0203
b_{12}	-0.0143	0.0119	0.1299	0.0224
b_{21}	0.0039	0.0043	0.0112	0.0027
b_{22}	-0.0125	0.0066	-0.1086	0.0156
n = 500				
b_{11}	-0.0008	0.0040	-0.1235	0.0175
b_{12}	-0.0072	0.0058	0.1326	0.0203
b_{21}	0.0023	0.0021	0.0097	0.0013
b_{22}	-0.0068	0.0031	-0.1024	0.0124

Table 3: Empirical bias and mean squared error for the proposed and usual model. Note that, the biases

Table 4: Rejection rates under null univariate hypothesis (at 5% nominal level). The model is generated considering $b_{12} = b_{13} = b_{21} = b_{23} = b_{24} = b_{31} = b_{32} = b_{34} = b_{42} = b_{43} = 0$ and the other parameters were taken similar to which estimated for the application. Each cell depicts the nominal level for univariatly testing if $b_{ij} = 0$. The closer to 5% the better is the result.

	Proposed model			Usual model		
	n = 100	n = 200	n = 400	n = 100	n = 200	n = 400
$H_0: b_{12} = 0$	4.67	4.65	4.60	6.21	7.21	9.78
$H_0: b_{13} = 0$	5.15	4.78	4.79	5.95	5.43	5.86
$H_0: b_{21} = 0$	5.35	4.75	4.83	7.30	7.55	8.99
$H_0: b_{23} = 0$	5.15	5.20	4.74	5.55	5.72	4.89
$H_0: b_{24} = 0$	5.48	5.18	4.81	6.08	5.17	4.93
$H_0: b_{31} = 0$	5.61	5.25	4.91	6.42	5.73	5.67
$H_0: b_{32} = 0$	4.94	5.13	5.09	5.55	5.56	5.30
$H_0: b_{34} = 0$	5.28	5.21	5.36	5.75	5.30	5.68
$H_0: b_{42} = 0$	5.06	4.73	4.89	4.91	4.59	5.21
$H_0: b_{43} = 0$	5.11	5.25	4.96	5.09	5.26	5.33

Parameter	Estimate	Standard Deviation	p-value
b_{11}	0.537	0.065	< 0.001
b_{12}	0.105	0.063	0.097
b_{13}	0.003	0.060	0.967
b_{14}	-0.181	0.059	0.002
b_{21}	0.179	0.068	0.008
b_{22}	0.378	0.066	< 0.001
b_{23}	0.145	0.063	0.002
b_{24}	0.047	0.062	0.442
b_{31}	0.165	0.076	0.030
b_{32}	-0.074	0.074	0.319
b_{33}	0.242	0.071	< 0.001
b_{34}	-0.061	0.069	0.378
b_{41}	0.294	0.070	< 0.001
b_{42}	-0.060	0.068	0.381
b_{43}	0.092	0.065	0.154
b_{44}	0.350	0.064	< 0.001

Table 5: Application to real data - usual approach: coefficient estimates, standard deviations and respective p-values (H_0 : coefficient is equal to zero).

Parameter	Estimate	Standard Deviation	p-value
b_{11}	0.935	0.137	< 0.001
b_{12}	-0.032	0.127	0.803
b_{13}	-0.095	0.103	0.357
b_{14}	-0.287	0.091	0.002
b_{21}	0.132	0.137	0.332
b_{22}	0.581	0.126	< 0.001
b_{23}	0.199	0.103	0.053
b_{24}	0.027	0.092	0.765
b_{31}	0.279	0.156	0.073
b_{32}	-0.184	0.143	0.201
b_{33}	0.346	0.117	0.004
b_{34}	-0.111	0.106	0.294
b_{41}	0.538	0.147	< 0.001
b_{42}	-0.252	0.135	0.063
b_{43}	0.044	0.110	0.687
b_{44}	0.528	0.099	< 0.001

Table 6: Application to real data - proposed approach: coefficient estimates, standard deviations and respective p-values (H_0 : coefficient is equal to zero).



Figure 1: Corrected power *versus* sample size. The full line refers to the proposed approach and the dot line refers to the usual one. It is expected that the corrected power converges to one.



Figure 2: Four areas were selected for connectivity evaluation using the VAR model: Left M1: left primary motor cortex, Right M1: right primary motor cortex, SMA: supplementary motor area and Right Cerebellum.



Figure 3: Observed signal at each brain region.



Figure 4: Identified network of information flow by testing the parameters of VAR model ($\alpha = 5\%$)



Figure 5: **QQplot for Normal distribution:** Residuals (Observed values - Predicted) at each brain region.