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Granger-Geweke causality: Estimation and interpretation

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ABSTRACT

In a recent PNAS article¹, Stokes and Purdon performed numerical simulations to argue that Granger-Geweke causality (GGC) estimation is severely biased, or of high variance, and GGC application to neuroscience is problematic because the GGC measure is independent of 'receiver' dynamics. Here, we use the same simulation examples to show that GGC measures, when properly estimated either via the spectral factorization-enabled nonparametric approach or the VAR-model based parametric approach, do not have the claimed bias and high variance problems. Further, the receiver-independence property of GGC does not present a problem for neuroscience applications. When the nature and context of experimental measurements are taken into consideration, GGC, along with other spectral quantities, yield neurophysiologically interpretable results.

In a recent paper, Stokes and Purdon (2017) claim that Granger-Geweke causality (GGC) (Geweke, 1982, 1984) estimation and application to neuroscience are problematic. Their main conclusions are: (i) GGC estimates can be either severely biased or of high variance, (ii) GGC estimates alone are not interpretable without examining the component behaviors of the system model, and (iii) GGC ignores critical components of a system's dynamics. Critically, Stokes and Purdon fail to recognize the nature of GGC as a statistical formulation intended to make inferences about the direction and strength of synaptic transmission, or information flow, in the brain.

The problem with the Stokes-Purdon study lies in its use of a suboptimal estimation approach for conditional GGC (as pointed out in commentaries (Barnett et al., 2017; Faes et al., 2017) and admitted by Stokes and Purdon in their reply (Stokes et al., 2017)), and a lack of understanding of the GGC measure in relation to other widely used spectral interdependency measures such as coherence. Here, with the same examples used in the Stokes-Purdon study, we show that their main conclusions are invalid.

Geweke's pairwise (Geweke, 1982) and conditional (Geweke, 1984) measures of Granger causality (GC) and total interdependence (TI) between wide-sense stationary processes are based on an elegant decomposition of variance for multiple time series. Neuroscientifically, in systems where the direction of synaptic transmission and information flow is known *a priori*, inferences from these measures are consistent with the ground truth (see, for example, Trongnetrpunya et al., 2015).

For a pair of dynamic processes (1 and 2), the sum of three terms [GC from 1 to 2 (F $_{1\rightarrow2}$), GC from 2 to 1 (F $_{2\rightarrow1}$) and instantaneous GC (F $_{2.1}$) due to common input] is shown to be equal to TI1.2 (i.e., $TI_{1,2} = F_{1\to 2} + F_{2\to 1} + F_{2,1}$ (Wen et al., 2013) in the time domain, which is related to the commonly applied coherence measure between 1 and 2 (C1.2) in the frequency domain because TI is directly related to the summation of coherence over all frequencies (Geweke, 1984). This relationship between TI and Granger causality holds true for conditional measures as well (Geweke, 1982). Geweke also showed for conditional causality that: $F_{1\rightarrow 2|3} = F_{13\rightarrow 2} - F_{3\rightarrow 2} = F_{13^*\rightarrow 2^*}$, where * denotes a moving average representation and 13 represents a combination of processes 1 and 3. The decomposition of $F_{1\rightarrow 2|3}$ by frequency may therefore be derived from appropriately normalized moving average representations for 2* and 13*, a logic for the state-space (SS) model-based estimation framework. All of these measures are invariant with respect to scaling in time series of a general kind, i. e., measures remain unchanged for filtered time series by invertible linear filters. In addition, because GGC is expressed as the ratio of decomposed variances, the magnitude of GGC can be interpreted as the explained variance of one time series by another time series.

For interacting processes 1 (transmitter) and 2 (receiver), frequency-

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Fig. 1. Parametric (VAR-based) and Nonparametric Methods. Power spectra in dB (subplots along the diagonal) and conditional Granger causality (GC) spectra with the parametric method (vector autoregressive (VAR) model-based, p = 3) and the nonparametric method applied to the simulated time series of a 3-node system in Example 1 (Stokes and Purdon, 2017) (Stokes and Purdon, 2017). In this model, there is unidirectional causal driving from node 1 to node 2 to node 3. The nodes (1, 2 and 3) oscillate respectively at 40 Hz, 10 Hz and 50 Hz. Here, both parametric (VAR-based) and nonparametric (based on spectral matrix factorization of the power density spectra) methods, when applied to 1000 trials each of 500 time points, recover the true network interactions as constructed. The parametric estimation framework for conditional GC first builds a vector autoregressive (VAR) model for the full process from the time series and performs spectral matrix factorization on the full spectral matrix and the block of that matrix, related to the sub-process. It thereby avoids two separate model fits. The nonparametric method first estimates the spectral matrix for the full process by direct Fourier transforms of time series and similarly uses the spectral matrix factorization on the full spectral matrix and the sub-process-related block of the spectral matrix.

domain Granger causality from 1 to 2 $(M_{1\rightarrow 2})$ can be defined in terms of the total power of 2 (S_{22}) and its intrinsic power (S_{2i}) or its causal power (S_{2c}) at the receiver due to the transmitter. Specifically,

$$M_{1\to 2} = \log_{e} \frac{S_{22}}{S_{2i}}$$
(1)

Since $S_{22} = S_{2i} + S_{2c}$,

$$M_{1\to 2} = -\log_e \left(1 - \frac{S_{2c}}{S_{22}} \right)$$
 (2)

From (2), without going back to the model components, we can thus obtain the causal power at 2 as:

$$S_{2c} = S_{22} \left(1 - e^{-M_{1 \to 2}} \right) \tag{3}$$

Thus, the causal power at the receiver (S_{2c}) can be derived from the GGC measure (dependent on the total variance (S_{22}) of the activity at the receiver). This result means that GGC does in fact reflect the causal power at the receiver, if one accounts for the total power at the receiver. This conclusion applies in neuroscience just as well as it does in any other field.

In addition to the rigorous mathematical foundation, the framework for estimating GGC is also well-established. Here, we simulate the same model systems as in the PNAS source article (Stokes and Purdon, 2017) and show that: (i) GGC estimates can be obtained reliably by using both the nonparametric approach and the parametric approach (either vector autoregressive (VAR) model-based or state-space (SS) model-based) (as shown in Figs. 1 and 2, Fig. 2 showing excellent agreement between VAR and SS estimates); (ii) GGC is consistent with spectral interdependency measures like coherence, and its estimates are interpretable in terms of the causal power contributed to the



Fig. 2. VAR- and SS-based Parametric Methods. Conditional GC spectral estimates for $1 \rightarrow 2|3$ (in Example 1) (Stokes and Purdon, 2017) from VAR and SS (state space) model-based parametric methods applied to 100 trials. The GC estimates from VAR and SS methods are identical and are close to the true GC spectra obtained from the AR coefficients of the model. The 5th-95th percentile dispersion of GC estimates (shown for VAR in aqua green shading), computed from 100 bootstrap samples, also overlaps with the dispersion from the SS method.



Fig. 3. Granger causality, coherence (total interdependence), power spectra, the effects of intrinsic noise and coupling for the two-node ("transmitter-receiver") system of Example 2¹, in which node 1 (50Hz-transmitter) drives node 2 (receiver). Granger causality spectra (A) and total interdependence (or coherence) spectra (B) are the same for two different cases: node 1 driving node 2 (10Hz-receiver) and node 1 driving node 2 (30Hz-receiver). The definition of Granger causality spectral measure is consistent with total interdependence (or coherence) measure. (C) The causal contributions of power at the receiver (dashed lines in blue and green) reflecting the transmitter's frequency peak at 50 Hz (black line) are different, and so is the intrinsic power spectra, which show the frequency peaks (blue solid line for 10 Hz-receiver, green for 30 Hz-receiver) due to own internal dynamics. (D, F, E) GC spectra depend on transmitter-receiver coupling strength (defined by a variable coefficient in front of $x_{1,t-1}$ in the equation for $x_{2,t}$ in the 2-node system example of the PNAS source article (Stokes and Purdon, 2017)) and intrinsic noise of the receiver: spectra in (D) for (coupling, noise) = (0.5, 1) (solid line) and (coupling, noise) = (1, 0.5) (dashed line) are not the same as in (A) for (coupling, noise) = (1, 1), and integrated GC (or time-domain GC) shows dependence with noise (E) and with coupling (F).



Fig. 4. GC spectra at different model orders (p = 3, 6, 20) for $1 \rightarrow 2|3$ of Example 1¹. Here, the right model order for the system is 3. A higher arbitrary model order can produce a systematic change or deviation in peak amplitude in GC spectra as seen here.

'receiver' relative to the intrinsic power of the 'receiver' (Fig. 3 (A, B, C)); and (iii) GGC estimates scale with the intrinsic noise variance at the 'receiver' and depend on the coupling strength of the 'transmitter-receiver' (Fig. 3 (D, E, F)). The commentary by Faes and colleagues (Faes et al., 2017) has also shown that the SS-based method provides reliable GC estimates.

The issue of bias and variance in conditional GGC estimates from fitting separate full and reduced AR models was recognized a decade ago (Chen et al., 2006) and addressed using matrix-partitioning of full estimated model (Wen et al., 2013; Chen et al., 2006) and factorization of the spectral matrix in the VAR modeling framework (Wen et al., 2013; Barnett and Seth, 2014; Dhamala et al., 2008) and in the SS modeling framework (Barnett and Seth, 2015; Solo, 2016). The receiver-independence property of GGC was also previously identified and investigated (Barrett et al., 2010).

In sum, the main conclusions of Stokes and Purdon's PNAS paper (Stokes and Purdon, 2017) are invalid. Geweke's definition of Granger causality in the frequency domain, along with other spectral measures like coherence, form a logical system of spectral measures, and GGC in combination with power spectra already allows its interpretation in terms of intrinsic and causal variances. The receiver-independence property of GGC is not a problem for applications in neuroscience studies, but the nature and context of experimental measurements need to be considered for applications and interpretations of the GGC results.

Appendix

1. MATLAB codes for generating Fig. 1 along with the main codes for estimating GGC are included in this zipped file: http://www.physics.

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gsu.edu/dhamala/codes/MatlabCodesDhamala.zip, or https:// scholarworks.gsu.edu/phy_astr_facupub/13/, and also included as part of online supplementary material to this article.

2 Fig. 4. GC spectra from the VAR-based parametric approach with different model orders (p = 3, 6, 20) for GC: $1 \rightarrow 2|3$ for the three-node example (Example 1) of the PNAS article (Stokes and Purdon, 2017).

References

- Barnett, L., Seth, A.K., 2014. The MVGC multivariate Granger causality toolbox: a new approach to Granger-causal inference. J. Neurosci. Methods 223, 50–68. https:// doi.org/10.1016/j.jneumeth.2013.10.018.
- Barnett, L., Seth, A.K., 2015. Granger causality for state-space models. Phys. Rev. E Stat. Nonlin Soft Matter Phys. 91, 040101. https://doi.org/10.1103/ PhysRevE.91.040101.
- Barnett, L., Barrett, A.B., Seth, A.K., 2017. Reply to Stokes and Purdon: a study of problems encountered in Granger causality analysis from a neuroscience perspective. arXiv.Org.
- Barrett, A.B., Barnett, L., Seth, A.K., 2010. Multivariate Granger causality and generalized variance. Phys. Rev. E Stat. Nonlin Soft Matter Phys. 81, 041907. https://doi.org/ 10.1103/PhysRevE.81.041907.

- Chen, Y., Bressler, S.L., Ding, M., 2006. Frequency decomposition of conditional Granger causality and application to multivariate neural field potential data. J. Neurosci. Methods 150, 228–237. https://doi.org/10.1016/j.jneumeth.2005.06.011.
- Dhamala, M., Rangarajan, G., Ding, M., 2008. Analyzing information flow in brain networks with nonparametric Granger causality. Neuroimage 41, 354–362. https:// doi.org/10.1016/j.neuroimage.2008.02.020.
- Faes, L., Stramaglia, S., Marinazzo, D., 2017. On the interpretability and computational reliability of frequency-domain Granger causality. F1000Res 6, 1710,. https:// doi.org/10.12688/f1000research.12694.1.
- Geweke, J., 1982. Measurement of linear dependence and feedback between multiple time series. J. Am. Stat. Assoc. 77, 304–313.
- Geweke, J., 1984. Measures of conditional linear dependence and feedback between time series. J. Am. Stat. Assoc. 79, 907–915.
- Solo, V., 2016. State-space analysis of granger-geweke causality measures with application to fMRI. Neural comput. 28, 914–949. https://doi.org/10.1162/NECO_a_ 00828.
- Stokes, P.A., Purdon, P.L., 2017. A study of problems encountered in Granger causality analysis from a neuroscience perspective. Proc. Natl. Acad. Sci. U. S. A. https:// doi.org/10.1073/pnas.1704663114.
- Stokes, P.A., Purdon, P.L., 2017. In reply to Faes et al. and Barnett, et al. regarding "A study of problems encountered in Granger causality analysis from a neuroscience perspective". arXiv.Org.
- Trongnetrpunya, A., et al., 2015. Assessing granger causality in electrophysiological data: removing the adverse effects of common signals via bipolar derivations. Front. Syst. Neurosci. 9, 189,. https://doi.org/10.3389/fnsys.2015.00189.
- Wen, X., Rangarajan, G., Ding, M., 2013. Multivariate Granger causality: an estimation framework based on factorization of the spectral density matrix. Philos. Trans. A Math. Phys. Eng. Sci. 371 https://doi.org/10.1098/rsta.2011.0610, 20110610.