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Analyzing Coherent Brain Networks with Granger Causality

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Abstract: **Multielectrode neurophysiological recording and functional brain imaging produce massive quantities of data. Multivariate time series analysis provides the basic framework for analyzing the patterns of neural interactions in these data. Neural interactions are directional. Being able to assess the directionality of neuronal interactions is thus a highly desired capability for understanding the cooperative nature of neural computation. Research over the last few years has identified Granger causality as a promising technique to furnish this capability. In this paper, we first introduce the concept of Granger causality and then present results from the application of this technique to multichannel local field potential data from an awake-behaving monkey.**

I. Introduction

COGNITIVE functions are achieved through cooperative neural computation. Multielectrode recording and functional imaging afford us the opportunity to study brain mechanisms of cognition from a network perspective. Traditional multivariate time series analysis relies on cross-correlation and coherence to measure the interdependence between two signals. These measures are symmetric and do not yield directional information. Phase spectra may be used under very ideal conditions to infer directions of interaction. It is often the case that the relative phase between two signals is zero at the frequencies of interest [1]. Cross-correlation functions could be helpful if the peak occurs at a nonzero time lag. Similar to the phase spectra, this peak value often happens at a zero time lag, yielding no information regarding the direction of interaction between two signals. A different framework exists for addressing the question of causal influence and direction of information transmission. The basic idea can be traced back to Wiener [2]. He proposed that, for two simultaneously measured time series, one series can be called causal to the other if we can better predict the second series by incorporating past knowledge of the first one. This concept was later adopted and formalized by Granger [3] in the context of linear regression models of stochastic processes. In this paper we start by reviewing the basic mathematical formulation of Granger causality and then proceed to test this method using local field potential data recorded from V4 of a monkey trained to perform an auditory discrimination task.

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II. Methods

Let p channels of neural recordings at time t be denoted by $\mathbf{X}_t = (x_{1t}, x_{2t}, \cdots, x_{pt})^T$ where T stands for matrix transposition. Assume that the data over an analysis window are described by a MultiVariate AutoRegressive (MVAR) model:

$$\sum_{k=0}^{m} \mathbf{A}_k \mathbf{X}_{t-k} = \mathbf{E}_t \quad , \tag{1}$$

where $\mathbf{E}_t$ is a temporally uncorrelated residual error series with covariance matrix $\mathbf{\Sigma}$, and $\mathbf{A}_k$ are $p \times p$ coefficient matrices which are obtained by solving the multivariate Yule-Walker equations (of size mp^2) [5][6]. Here, repeated trials for the same experimental condition can be used as realizations of a locally stationary stochastic process. The order m of the MVAR model is determined by the Akaike Information Criterion (AIC) [7]. Once the model coefficients $\mathbf{A}_k$ and $\mathbf{\Sigma}$ are estimated, the spectral matrix can be evaluated as

$$\mathbf{S}(f) = \left\langle \mathbf{X}(f)\mathbf{X}^*(f) \right\rangle = \mathbf{H}(f)\mathbf{\Sigma}\mathbf{H}^*(f) , \tag{2}$$

where the asterisk denotes matrix transposition and complex conjugation, $< \bullet >$ stands for ensemble average, and $\mathbf{H}(f) = (\sum_{k=0}^{m} \mathbf{A}_k e^{-2\pi i k f})^{-1}$ is the transfer function. The power spectrum of channel l is given by $S_{ll}(f)$ which is the l-th diagonal element of the spectral matrix $\mathbf{S}(f)$. The coherence spectrum between channel l and channel k is:

$$C_{lk}(f) = |S_{lk}(f)| / (S_{ll}(f) S_{kk}(f))^{1/2} . \tag{3}$$

The value of coherence can range from 1, indicating maximum linear interdependence between channel l and channel k at frequency f, down to 0, indicating no linear interdependence.

The phase of the complex quantity $S_{lk}(f)$ plotted as a function of f gives the phase spectrum. Adaptive computation of the MVAR model with moving analysis windows can reveal temporal dynamics of neuronal interactions.

To introduce Granger causality let us consider two simultaneously acquired time series: $x_1, x_2, ..., x_n, ...; y_1, y_2, ..., y_n, ...$. Suppose that one would like to build a linear predictor of the current value of the x series from m previous values: $x_n = a_1 x_{n-1} + a_2 x_{n-2} + ... + a_m x_{n-m} + \varepsilon_n$. This is nothing but a single variable autoregressive model (setting p=1 in Eq. (1)). The variance of the error series ε_n is a gauge of the prediction accuracy. Now consider a predictor of the current values of the x series by including both the previous values of the x series and the previous values of the y series, namely, $x_n = b_1 x_{n-1} + b_2 x_{n-2} + ... + b_m x_{n-m} + c_1 y_{n-1} + c_2 y_{n-2} + ... + c_m y_{n-m} + \eta_n$. The variance of the error series η_n is a gauge of the prediction accuracy of the new expanded predictor. Based on Wiener's idea [2], Granger formulated that if $\mathrm{var}(\eta_n) / \mathrm{var}(\varepsilon_n)$ is less than one in some suitable statistical sense, meaning that the prediction of x is improved by incorporating past knowledge of the y series, then we say the y series has a causal influence on the x series [3]. The role of the x and y series can be reversed to address the influence from x to y. The spectral Granger causality was developed by Geweke [4]. It can be shown that for a bivariate autoregressive model the Granger causality spectrum from x_{2t} to x_{1t} can be computed as [6][8],

$$I_{2\to 1}(f) = -\ln\left(1 - \frac{(\Sigma_{22} - \frac{\Sigma_{12}^2}{\Sigma_{11}})\left|H_{12}(f)\right|^2}{S_{11}(f)}\right) . \quad (4)$$

Similarly, the Granger causality spectrum from x_{1t} to x_{2t} can be obtained by switching the indices 1 and 2 in Eq. (4).

The variability of the spectral quantities derived from the MVAR model above can be assessed by a bootstrap resampling technique. It involves randomly sampling a pool of trials with replacement from the total ensemble, and then estimating the MVAR model for this pool. Repeating this process many times for different pools of the same size, we estimate the mean and standard deviation of any given spectral quantity over the whole collection of estimated bootstrap values. The standard deviation gives a measure of the variability of the estimator.

To assess whether interdependence measures such as coherence and Granger causality spectra are significantly different from zero, we can apply a random permutation approach. Briefly, consider two channels of recordings with many repeated trials. We can reasonably assume that the data from different trials are independent of one another. Randomly pairing data for channel 1 from a certain trial with data for channel 2 from a different trial leads to the creation of a synthetic ensemble of trials for which there is no interdependence between the two channels based on construction. This procedure preserves the temporal structure within a channel. Performing such random pairing with many different permutations will result in a distribution of coherence or causality spectra corresponding to the null hypothesis (i.e. distribution under the condition of no statistical interdependence). Then the calculated value for a given statistic from the actual data is compared with this baseline null hypothesis distribution for the assessment of significance levels.

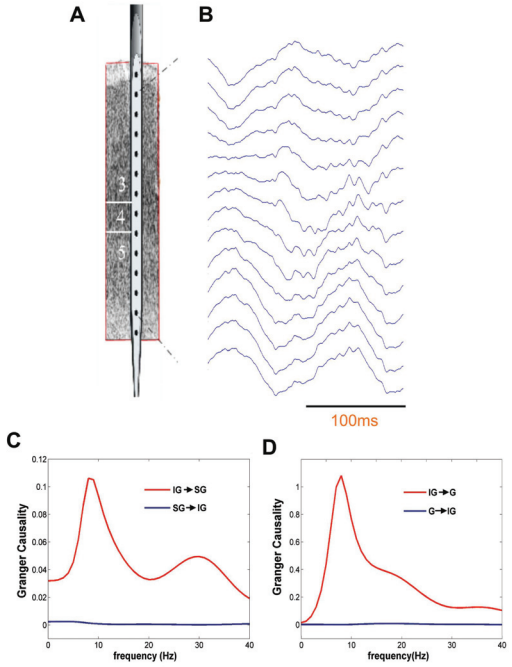

Fig. 1. A: Schematic of the multi-electrode with 14 equally spaced (200μm) contacts. B: A short segment (200 ms) of LFPs showing alpha oscillations. C: Granger causality between alpha generators in infragranular layers (IG) and in supragranular layers (SG). D: Granger causality between alpha generators in infragranular (IG) layers and in granular layer (G).

III. Application to Neural Data

Field oscillations in the alpha band (8 to 12 Hz) are prominent over human occipital-parietal cortex. More than 80 years after the initial discovery, the physiological mechanisms of alpha oscillations remain not well understood. Prior to the 1970s, the thalamus was thought to be the pacemaker of cortical alpha [9]. More recent studies using lesion techniques have tested the role of infragranular layer pyramidal cells in alpha pacemaking in cortical slice preparations [10]. Here we demonstrate that Granger causality can be used in lieu of the lesion technique to identify the cortical pacemakers of alpha activity.

Local field potential (LFP) were sampled (2 kHz) with a linear array electrode with 14 contacts spanning all six cortical layers in visual area V4 of a macaque monkey trained to perform an auditor discrimination task. The inter-contact spacing was 200 μm. To examine the laminar organization of alpha oscillations we followed a two-step analysis protocol. First, laminar generators of LFP oscillations at the alpha frequency are identified by calculating the current source density (CSD) using the phase realigned averaging technique (PRAT) [11]. Second, the patterns of interaction between different laminar alpha generators are identified using Granger causality. Figure 1A and 1B display the schematic of the linear multielectrode and 200 ms unfiltered single sweep LFPs. Oscillations around 10 Hz is apparent. Current source density reveals alpha current generators in granular (G), infragranular (IG) and supragranular (SG) layers. Applying Granger causality to these alpha current generators we show in Figures 1C and 1D that there are large IG→SG and IG→G causal influences in the alpha band whereas the SG→IG and G→IG causal influences are close to zero. This finding is consistent with the in vitro result mentioned earlier that alpha frequency pacemakers are located in deep layers. This finding also helps to validate Granger causality as a method to infer direction of synaptic transmission in neuronal circuits.

IV. Conclusion

In neuroscience, commonly used methods to study the effect of one neuronal ensemble on another include stimulation and lesion. In this paper we have described a third methodology called Granger causality. This method is statistical in nature, is data-driven, and does not require perturbing the nervous system. Our results demonstrate that Granger causality yield physiologically interpretable results and can complement the traditional stimulation and lesion techniques. With the advent of advanced recording technology, multivariate data are becoming commonplace, which promise unparalleled insights into how different areas of the brain work together to achieve thought and behavior, and how such coordinated brain activity breaks down in disease. While the accumulation of data continues at an astonishing rate, how to effectively analyze these data to extract information about the workings of the brain remains a key challenge. Granger causality is an important method to help meet the challenge.

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