Causal Assessment of Neural Interactions by Analysis of Electrophysiological Recordings

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SUMMARY

Neural interaction is a basic property in nervous systems. In the analysis of electrophysiological recordings, it is often desirable to determine whether or not one signal is causal relative to another. For example, correlations or coherences between recording sites can result from stimulus-locked transients, evoked by a common afferent input, or reflects stimulus-induced oscillations and phasic coupling of neural assemblies, mediated by synaptic connections. As such, it is often necessary to remove the confounding effects of stimulus-locked transients (that introduce correlations not causally mediated by direct neural interactions) in order to reveal an underlying connectivity. The ability to determining causal relationships among cortical areas is critical to the understanding of bottom-up and top-down influences in neuronal systems.

A number of attempts has been made to assess the causal influences between cortical sites. Directed Transfer Function (DTF) [1] is one, among others, that has been thoroughly explored. It is a statistical measure of directional influences between two cortical areas based on spectral analysis of multivariate autoregressive time series models. Although this technique has produced promising results [2], it also has some inherent limitations (see below). In this contribution, we describe a direct causal influence measure based on the fundamental concept of Granger causality and present its application to cortical field potentials recorded from monkeys.

The concept of causality, commonly referred to as Granger causality [3], has been well established in the field of econometrics. A simple, formal description of Granger causality can be described by two time series, $x_1(t)$ and $x_2(t)$, from two recording sites which form a bivariate autoregressive process:

$$x_1(t) = \sum_{k=1}^{p} a_{11}(k)x_1(t-k) + \sum_{k=1}^{p} a_{12}(k)x_2(t-k) + w_1(t)$$

$$x_2(t) = \sum_{k=1}^{p} a_{21}(k)x_1(t-k) + \sum_{k=1}^{p} a_{22}(k)x_2(t-k) + w_2(t) \tag{1}$$

if the variance of the prediction error w_1 (or w_2) is reduced by the inclusion of the x_2 (or x_1) terms in the first (or second) equation, then, based on Granger causality, we say that x_2 (or x_1) cause x_1 (or x_2). An equivalent but more convenient way of expressing the same

concept is that coefficient $a_{12}(k)$ (or $a_{21}(k)$), $k = 1, \cdots, p$, are not uniformly zero under suitable statistical criteria.

As a generalization of multivariate process, we say, if $a_{ij}(k), k = 1, \cdots, p$, are not uniformly zero, then there is direct causal influence from channel j to i. In practice, direct examination of the model coefficients makes it hard to infer whether there is direct causal influence from one to another. We found that the Granger causality from channel j to i in spectral domain defined by $a_{ij}(f)$ makes itself easy to test the existence of direct causal influence because the coefficients along different lag k effectively integrate one term in the frequency domain. Significance tests can be performed by means of the bootstrap resampling procedure. More importantly, such definition is directly based on the well-accepted Granger causality, thus it is straightforward to interpret within the multivariate regression framework. The utility of the method was demonstrated through analysis of simulated time series and contrasted with DTF results.

We consider two different coupling schemes in a model of three-channel time series. In the first scheme, as shown in Fig.1 (left), the signal propagates from channel 1 to channel 2, then relays to channel 3. There is no direct coupling from channel 1 to 3 as revealed by Granger causality (Fig. 1, middle), which is in agreement with the built-in network connectivity pattern and the analytic result (0). But DTF gives erroneous result by showing strong directional influence from channel 1 to 3 (Fig. 1, right) because of the intermediate connection of channel 2. In the second coupling scheme (Fig. 2, left), there is a direct pathway from channel 1 to 2, also an indirect pathway from from channel 1 to 2 through channel 3. As expected, Granger causality is able to correctly measure the direct causal influence from channel 1 to 2 (Fig. 2, middle). DTF, however, shows no causal influence from channel 1 to 2 (Fig. 2, right)! It is not surprising because DTF essentially is a linear combination of both the direct influence from one channel to another and the indirect influence mediated by other channels. Thus a zero DTF value occurs when the direct and indirect influences are even. This again will inevitably hamper its application in the analysis of neurobiological recordings.

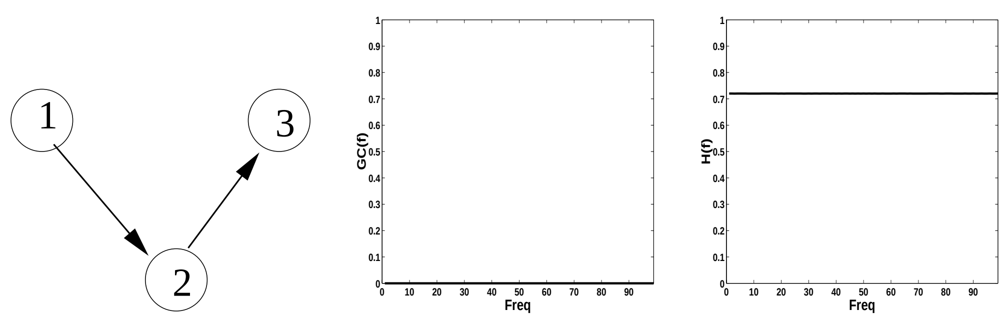

Figure 1: Coupling scheme (left) based on a three-channel model: $x_1(t) = w_1(t); x_2(t) = 0.8x_1(t-1) + w_2(t); x_3(t) = 0.9x_2(t-1) + w_3(t)$ and $w_1(t), w_2(t), w_3(t)$ are three independent white noise processes with zero means and unity variances. Granger causality (middle) and DTF (right) from channel 1 to 3.

For evaluation of the technique on neural data, it was applied to event-related local field potentials (LFPs) (600 msec long digitized at 200 points/sec). The LFPs were recorded transcortically from bipolar electrodes at up to 15 unilateral sites in highly trained macaque monkeys performing a visuomotor task in which they discriminated dot patterns arranged as either diamonds or lines. In each recording session, a GO response was contingent on

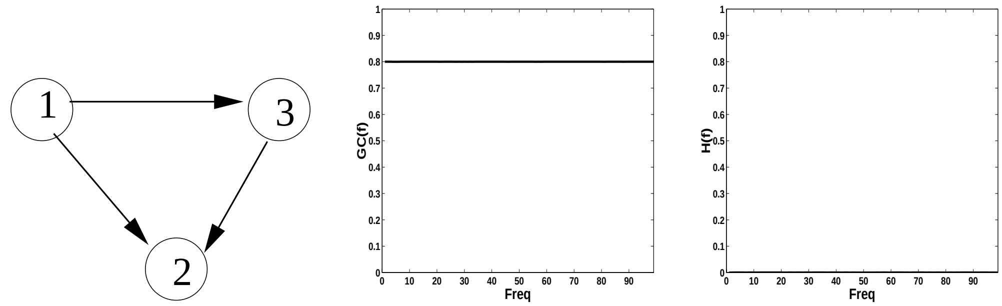

Figure 2: Coupling scheme (left) based on a three-channel model: $x_1(t) = w_1(t); x_2(t) = 0.8x_1(t-2) + 2x_3(t-1) + w_2(t); x_3(t) = -0.4x_1(t-1) + w_3(t)$, and $w_1(t), w_2(t), w_3(t)$ are three independent white noise processes with zero means and unity variances. Granger causality (middle) and DTF (right) from channel 1 to 3.

one pattern type and a NO-GO response on the other. The contingency was reversed across sessions. Trials from sessions having mixed response contingencies were pooled, forming balanced data sets that differed only in stimulus pattern (Diamond vs Line) or response type (GO vs NO-GO).

An example of the influences between two sites, P1 and P2, in the parietal cortex is used for illustration. The DTF is shown in Fig. 3 (left) where a Strong feedforward influence from P1 to P2 (solid line) is observed around the stimulus onset. The Granger causality shown in Fig.3 (right) reveals no significant direct causal influence between these two sites, although the Granger causality has much small, yet similar waveshapes. It means that DTF has no differentiation between direct and indirect connections, whereas Granger causality can resolve the existence of direct influence between two sites.

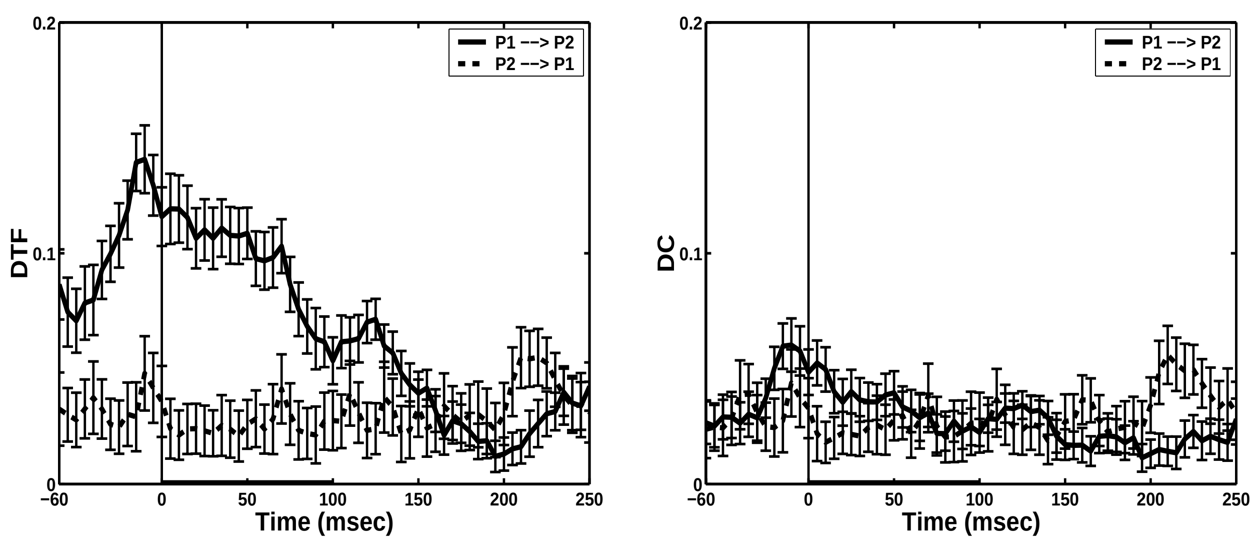

Figure 3: DTF (left) and Granger causality (right) at 20 Hz with error bar obtained by bootstrap procedure. There is stronger feedforward influence (solid line) compared to the feedback (dashed line) in DTF, but not seen in Granger causality. The results suggested that there is no direct causal influence between two cortical sites studied. The vertical lines indicate the stimulus onsets; The horizontal thick bar shows the stimulus duration.

In this contribution, we present a frequency domain picture of Granger causality. We demonstrate the application of the technique to simulated data and real neurobiological recordings from monkeys. Comparison with DTF measure is also made. It is suggested that the Granger causality can be used to assess whether a direct link exists between two given channels.

References

[1] Kaminski & Blinowska (1991) Biological Cybernetic 65: 203-210.

[2] Liang et al. (2000) NeoroReport 11: 2875-2880.

[3] Granger (1969) Econometrica 37: 424-438.