# Adaptive Frequency-domain Granger Causal Inference from Neuronal Ensemble Data

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***Abstract*—Granger causality is an increasingly prevalent tool in extracting the functional networks that underlie neural processes. While its time domain formulation yields useful insights into these functional networks, the inferred Granger causal influences leave the spectral properties of said functional networks ambiguous: this is a question of particular interest when neural processes exhibit oscillatory behavior. The frequency-domain formulation of Granger causality proposed by Geweke has addressed the spectral properties of functional links between stationary processes. Based on Geweke's method of conditional Granger causality, we introduce a framework to derive direct spectro-temporal causal interactions in a population of neurons from multivariate ensemble spiking observations, using point process modeling, state space estimation and multitaper spectral analysis. Further, we propose statistical tests that characterize the significance of these functional links. The utility of our methods is demonstrated through application to simulated and real data.**

## I. Introduction

The advent of neural data acquisition techniques such as two photon calcium imaging and multielectrode array recording has enabled the observation of brain oscillations at the neuronal scale, manifest in ensemble spiking activity. Cross spectral and coherence analyses of such neural data provide insights into the spectro-temporal coupling between neurons, and have been the focus of active research [1]–[3]. However, such analyses do not capture directionality of neuronal interactions, an essential component of understanding the roles of different neurons within a population. Granger-Geweke causality [4]–[13] is a widely used statistical method of characterizing such frequency domain directional interactions in continuous processes.

In time domain analysis, if the prediction of one time series is improved by incorporating the past samples of a second one, the second process is said to have a Granger Causal (GC) influence on the first one. Geweke [4], [5] extended this notion to frequency domain analysis, further introducing a statistical characterization of conditional GC links [5]. The conditional measure quantifies the fraction of total power of the first process at a given frequency that is *directly* contributed by the second process [5]. Even though various applications and extensions of this method have been introduced in the literature [6], [7], [10], [11], [13], they are tailored for the analysis of continuous observations, and hence are not directly applicable to binary spiking observations.

Point processes and Generalized Linear Models are widely-applied methods for modeling the underlying non-linear mappings between binary spiking observations and latent intrinsic/extrinsic oscillatory neural covariates [1], [3], [14], [15]. Existing work [8], [9], [12] on conditional GC analysis of spiking observations applies methods developed for continuous processes to spike trains, undermining the aforementioned non-linearities and thus leading to biased estimates that cannot be guaranteed to identify the true directional interactions underlying neuronal oscillations. Further, existing methods analyze spectro-temporal coupling using sliding windows, independently estimating GC links at each time window. Brain oscillations underlying neuronal spiking are in general non-stationary and may exhibit dynamics corresponding to brain state or behavior [2], [16]. These dynamics may not be accounted for if the selected window length is too large; at the same time, smaller window lengths can adversely affect the accuracy of spectral estimation.

To address the aforementioned challenges, we introduce a unified method to estimate spectro-temporal conditional GC links from binary spiking observations in a Generalized Linear Model framework. We employ state space modeling techniques to characterize the latent process driving ensemble spiking activity, and use the multitaper method [17]–[19] for spectral estimation to subsequently infer conditional Geweke-Granger causal interactions non-parametrically [10]. Furthermore, we introduce two tests to quantify the statistical significance of the inferred links. Finally, we demonstrate the utility of the proposed methods in a simulation study and through application to multi-unit recordings from rat cortical neurons during sleep [16], [20].

## II. Methods

In this section, we summarize the proposed methods for frequency domain conditional GC analysis. We denote the $i^{\mathsf{th}}$ element of vector $\mathbf{v}$ by $v^{(i)}$ and the $(i,j)^{\mathsf{th}}$ element of matrix $\mathbf{M}$ by $M^{(i,j)}$ in subsequent expositions. Suppose that the spiking activity of $N$ neurons is observed over $L$ independent trials. Let $n_{t,l}^{(i)}$ denote the spiking activity of the $i^{\mathsf{th}}$ neuron at discrete time frame $t$ in the $l^{\mathsf{th}}$ trial. Further, suppose that spiking events $n_{t,l}^{(i)}$ for $l = 1, \cdots, L$, are driven

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by an underlying latent process $x_t^{(i)}$ corresponding to latent intrinsic/extrinsic oscillatory covariates. Given the ensemble spiking observations $\{n_{t,l}^{(i)}\}_{i,t,l=1}^{N,T,L}$, we seek to identify the direct causal interactions in the latent oscillations at different frequencies and time windows. To this end, we employ conditional Granger-Geweke Causality (GC) [5].

### A. Geweke's Conditional Granger Causality framework

First, we briefly review the non-parametric formulation of conditional Granger-Geweke causality [10]. Let $\mathrm{GC}_{j\to i|\mathbf{w}}(f,m)$ denote the conditional GC from the $j^{\mathsf{th}}$ neuron to the $i^{\mathsf{th}}$ neuron, at frequency $f$ and time window $m$. Here $\mathbf{w}$ represents the $N-2$ neurons in the population excluding $i$ and $j$. To compute the conditional link $\mathrm{GC}_{j\to i|\mathbf{w}}(f,m)$, we first derive the Power Spectral Density (PSD) matrix [21] within the $m^{\mathsf{th}}$ time window of the process $\mathbf{x}_t := [x_t^{(1)},\cdots,x_t^{(N)}]^\top$, denoted by $\mathbf{S}_m(f)$. Re-arranging the entries of $\mathbf{S}_m(f)$, the full $\left(\mathbf{S}_m^{\mathsf{full}}(f)\right)$ and reduced $\left(\mathbf{S}_m^{\mathsf{red}}(f)\right)$ PSD matrices can be formed as:

$$\mathbf{S}_m^{\mathsf{full}}(f)=\begin{bmatrix} S_m^{(i,i)}(f) & S_m^{(i,j)}(f) & \mathbf{S}_m^{(i,\mathbf{w})}(f)\\ S_m^{(j,i)}(f) & S_m^{(j,j)}(f) & \mathbf{S}_m^{(j,\mathbf{w})}(f)\\ \mathbf{S}_m^{(\mathbf{w},i)}(f) & \mathbf{S}_m^{(\mathbf{w},j)}(f) & \mathbf{S}_m^{(\mathbf{w},\mathbf{w})}(f)\end{bmatrix},\ \mathbf{S}_m^{\mathsf{red}}(f)=\begin{bmatrix} S_m^{(i,i)}(f) & \mathbf{S}_m^{(i,\mathbf{w})}(f)\\ \mathbf{S}_m^{(\mathbf{w},i)}(f) & \mathbf{S}_m^{(\mathbf{w},\mathbf{w})}(f)\end{bmatrix}.$$

Next, the symmetric minimum phase factorizations of these matrices, defined as:

$$\mathbf{S}_m^{\mathsf{full}}(f)=\mathbf{H}_m(f)\,\boldsymbol{\Sigma}_m\mathbf{H}_m^*(f),\ \mathbf{S}_m^{\mathsf{red}}(f)=\mathbf{G}_m(f)\,\boldsymbol{\Omega}_m\mathbf{G}_m^*(f),$$

are obtained using Wilson's algorithm for factorization of matrix spectral densities [22]. This method has been used extensively in previous work [10], [11], [13], but, importantly, requires a high spectral sampling frequency and smooth PSD estimates to ensure stability and convergence. Finally, the conditional Granger causal influence of the $j^{\mathsf{th}}$ neuron on the $i^{\mathsf{th}}$ neuron is defined as:

$$\mathrm{GC}_{j\to i|\mathbf{w}}(f,m)=\log\left(\frac{\Omega_m^{(i,i)}}{\left(Q_m^{(i,i)}(f)\right)\Sigma_m^{(i,i)}\left(Q_m^{(i,i)}(f)\right)^*}\right),\quad(1)$$

where the matrix $\mathbf{Q}_m(f)$ is a function of the spectral factors $\mathbf{H}_m(f)$ and $\mathbf{G}_m(f)$ whose explicit form is given in [10].

### B. Proposed forward model

Note that the oscillatory process $\mathbf{x}_t$ is latent, indirectly observed through spiking processes $n_{t,l}^{(i)}$; hence, recovering the PSD matrix is the key challenge in computing conditional GC links as described previously. Though a method for direct spectral estimation from spiking observations without requiring estimation of $\mathbf{x}_t$ is introduced in [3], the computational complexity of this method increases considerably with the increase of frequency bins, and consequently is not well-suited to the conditional GC estimation framework. Alternatively, PSD estimates with minimum bias and variance can be obtained with considerably lower computational complexity and higher sampling frequency using direct multitaper spectral estimation [17]–[19], if accurate estimates of $\mathbf{x}_t$ are available. Hence, we propose the use of Generalized Linear Models for point processes [2], [3], [14], [15] to estimate the latent oscillations $\mathbf{x}_t$ from the spiking observations $n_{t,l}^{(i)}$, and subsequently estimate the PSD matrix using multitaper spectral estimation as in [2].

We model the binary spiking process $n_{t,l}^{(i)}$ as a Bernoulli process with a logistic link to the latent oscillatory continuous process $\mathbf{x}_t$:

$$n_{t,l}^{(i)}\sim\text{Bernoulli}\left(\frac{\exp\left(x_t^{(i)}+\mu^{(i)}\right)}{1+\exp\left(x_t^{(i)}+\mu^{(i)}\right)}\right),$$

where $\mu^{(i)}$, for $i=1,\cdots,N$ are the baseline firing rate parameters; these are taken to be hyper-parameters in the proposed model, but in practice may be separately estimated based on the average firing rates of neurons. The latent process $\mathbf{x}_t$ is assumed to be jointly stationary within windows of length $W$. The oscillatory process is explicitly modeled at the $m^{\mathsf{th}}$ time window as a multivariate autoregressive (AR) process:

$$\mathbf{x}_t=\sum_{p=1}^{P}\mathbf{A}_{m,p}\mathbf{x}_{t-p}+\boldsymbol{\varepsilon}_t,\quad\boldsymbol{\varepsilon}_t\sim\mathcal{N}(\mathbf{0},\boldsymbol{\Sigma}_m),\quad(2)$$

for $(m-1)W+1\le t<mW$. Stochastic continuity across time windows is imposed by a first order state space model on the AR coefficients across time windows:

$$A_{m,p}^{(i,j)}=\beta A_{m-1,p}^{(i,j)}+v_{m,p}^{(i,j)},\quad v_{m,p}^{(i,j)}\sim\mathcal{N}\left(0,\sigma^2\right),$$

where $\beta\in[0,1]$ is the state transition parameter. Finally, to compensate for potential overfitting arising from the sparsity of typical spiking observations, we impose a conjugate prior over the noise covariance:

$$\boldsymbol{\Sigma}_m\sim\text{InverseWishart}_N(\boldsymbol{\psi},\gamma),$$

where $\boldsymbol{\psi}$ and $\gamma$ are hyper-parameters.

### C. MAP estimation via Expectation-Maximization

Integrating the various facets of the forward model, the joint log-likelihood of the spiking observations $\mathbf{n}:=\{n_{t,l}^{(i)}\}_{i,t,l=1}^{N,T,L}$, the latent variables $\mathbf{x}:=\{x_t^{(i)}\}_{i,t=1}^{N,T}$ and the parameters $\mathbf{A}:=\{\mathbf{A}_{m,p}\}_{m,p=1}^{M,P}$ and $\boldsymbol{\Sigma}:=\{\boldsymbol{\Sigma}_m\}_{m=1}^{M}$ takes the form:

$$\begin{aligned}\log p(\mathbf{n},\mathbf{x},\mathbf{A},\boldsymbol{\Sigma}|\beta,\sigma^2)=&-\tfrac{1}{2}\sum_{m=1}^{M}\Big((W+\gamma+N+1)\log|\boldsymbol{\Sigma}_m|\\&+\mathrm{Tr}(\boldsymbol{\psi}\boldsymbol{\Sigma}_m^{-1})\Big)+\sum_{i,t=1}^{N,T}\Big(\sum_{l=1}^{L}n_{t,l}^{(i)}\left(x_t^{(i)}+\mu^{(i)}\right)-L\log\left(1+\exp\left(x_t^{(i)}+\mu^{(i)}\right)\right)\Big)\\&-\tfrac{1}{2}\sum_{m=1}^{M}\sum_{t=(m-1)W+1}^{mW}\Big(\mathbf{x}_t-\sum_{p=1}^{P}\mathbf{A}_{m,p}\mathbf{x}_{t-p}\Big)^\top\boldsymbol{\Sigma}_m^{-1}\Big(\mathbf{x}_t-\sum_{p=1}^{P}\mathbf{A}_{m,p}\mathbf{x}_{t-p}\Big)\\&-\tfrac{1}{2}\left(N^2PM\log\sigma^2+\tfrac{1}{\sigma^2}\sum_{i,j,m,p=1}^{N,N,M,P}\left(A_{m,p}^{(i,j)}-\beta A_{m-1,p}^{(i,j)}\right)^2\right)+\Delta,\end{aligned}\quad(3)$$

where $\Delta$ cumulatively represents terms independent of $\mathbf{n},\mathbf{x},\mathbf{A},\boldsymbol{\Sigma},\beta$ or $\sigma^2$. We fix the hyper-parameters $\boldsymbol{\mu}$, $\boldsymbol{\psi}$, $\gamma$ and $P$, and derive the maximum *a posteriori* (MAP) estimates of the latent variables $\mathbf{x}$ and the parameters $\mathbf{A}$, $\boldsymbol{\Sigma}$, $\beta$ and $\sigma^2$ using Expectation-Maximization (EM) [23].

*1) E-step:* The autocovariance function of $\mathbf{x}_t$ up to lag $P$ will be required for subsequent computations, so we first perform a state augmentation $\widetilde{\mathbf{x}}_t:=[\mathbf{x}_t^\top,\mathbf{x}_{t-1}^\top,\cdots,\mathbf{x}_{t-P+1}^\top]^\top$, to derive the first order formulation equivalent to Eq. (2): $\widetilde{\mathbf{x}}_t=\widetilde{\mathbf{A}}_m\widetilde{\mathbf{x}}_{t-1}+\widetilde{\boldsymbol{\varepsilon}}_t$. The first two conditional moments of the augmented state variable $\widetilde{\mathbf{x}}_t$, i.e. $\mathbb{E}[\widetilde{\mathbf{x}}_t|\mathbf{x}_{1:T},\widehat{\mathbf{A}},\widehat{\boldsymbol{\Sigma}},\hat{\beta},\hat{\sigma}^2]$ and $\mathbb{E}[\widetilde{\mathbf{x}}_t\widetilde{\mathbf{x}}_t^\top|\mathbf{x}_{1:T},\widehat{\mathbf{A}},\widehat{\boldsymbol{\Sigma}},\hat{\beta},\hat{\sigma}^2]$, are obtained by point process smoothing [15] and covariance smoothing [24]. The conditional mean and autocovariance of $\mathbf{x}_t$ can subsequently be recovered using the first two conditional moments of $\widetilde{\mathbf{x}}_t$.

*2) M-step:* The parameter updates for $\mathbf{A}$, $\mathbf{\Sigma}$, $\beta$ and $\sigma^2$ are derived by maximizing the expected log-likelihood $\mathbb{E}_{\mathbf{x}}[\log p(\mathbf{n}, \mathbf{x}, \mathbf{A}, \mathbf{\Sigma}|\beta, \sigma^2)]$. First, we address the updates for $\mathbf{A}_{m,p}$, for $m = 1, \cdots, M$ and $p = 1, \cdots, P$. Note that the joint log-likelihood in Eq. (3) is quadratic in $\mathbf{A}_{m,p}$, and hence the posterior distribution $p(\mathbf{A}|\mathbf{n}, \mathbf{x}_{1:T}, \widehat{\mathbf{\Sigma}}, \hat{\beta}, \hat{\sigma}^2)$ is in fact Gaussian. Thus, the maximization of $\mathbf{A}_{m,p}$ can be obtained by computing the conditional mean, for which we use fixed interval smoothing [25]. The updated $\widehat{\mathbf{A}}$ is then used to derive closed form expressions for the updates of $\mathbf{\Sigma}$, $\sigma^2$, and $\beta$ by maximizing $\mathbb{E}_{\mathbf{x}}[\log p(\mathbf{n}, \mathbf{x}, \widehat{\mathbf{A}}, \mathbf{\Sigma}|\beta, \sigma^2)]$.

We iterate between the aforementioned expectation and maximization steps until convergence. The resulting estimates are used to obtain the MAP estimate of the latent oscillatory process $(\widehat{\mathbf{x}}_t)_{\mathsf{MAP}} := \mathbb{E}[\mathbf{x}_t|\mathbf{x}_{1:T}, \widehat{\mathbf{A}}, \widehat{\mathbf{\Sigma}}, \hat{\beta}, \hat{\sigma}^2]$. Then, the PSD matrix $(\mathbf{S}_m(f))_{\mathsf{proposed}}$ is estimated non-parametrically by performing sliding window multitaper spectral estimation [19] on $(\widehat{\mathbf{x}}_t)_{\mathsf{MAP}}$. Notably, the proposed model enables the full PSD matrix to alternatively be parametrically obtained using the estimated AR coefficients $\widehat{\mathbf{A}}_{m,p}$ and the estimated noise covariance $\widehat{\mathbf{\Sigma}}_m$ [6]. However, $(\mathbf{S}_m(f))_{\mathsf{proposed}}$ is in fact the better PSD estimate, since $(\widehat{\mathbf{x}}_t)_{\mathsf{MAP}}$ for $t = 1, \cdots, T$ capture the underling dynamics with a much larger number of parameters than $\widehat{\mathbf{A}}$ and $\widehat{\mathbf{\Sigma}}$ combined. Thus, the presented results focus on non-parametric spectral estimation using $(\widehat{\mathbf{x}}_t)_{\mathsf{MAP}}$, which we denote by $(\mathbf{S}_m(f))_{\mathsf{proposed}}$. Finally, employing Wilson's factorization method and conditional Granger-Geweke analysis as described in Eq. (1), we derive the proposed estimates of the GC links $\mathrm{GC}^{\mathsf{proposed}}_{j\to i|\mathbf{w}}(f, m)$.

### *D. Testing statistical significance*

Estimated GC links with non-zero values do not necessarily indicate a meaningful effect; this necessitates statistical inference to identify the salience of estimated influences. The significance of estimated links, $\mathrm{GC}^{\mathsf{proposed}}_{j\to i|\mathbf{w}}(f, m)$, may be tested using either of two proposed approaches.

The first approach is to empirically obtain the distribution of GC links under the null hypothesis that there is no contribution from process $j$ at frequency $f$ to the power spectrum of $i$ over time window $m$. Time indices were shuffled for each neuron individually in order to decorrelate neuronal activity and spectral GC analysis was applied to shuffled data. The distribution of the resulting links are used as the empirical null distribution against which estimated links $\mathrm{GC}^{\mathsf{proposed}}_{j\to i|\mathbf{w}}(f, m)$ are tested.

The second approach is based on an analytically derived distribution of the spectral power under the previously stated null hypothesis. For a window length $W = f_s \cdot K$, an integer multiple of the sampling frequency, let $\{\varepsilon_t\}_{t=1:W}$ be a noise process given by a sequence of independent Gaussian random variables $\varepsilon_t \sim \mathcal{N}(0, \sigma^2_\varepsilon)$, for $t = 1, \ldots, W$. The DTFT of $\varepsilon_t$ is $\mathcal{E}(f) = \sum_{t=1}^{W} \varepsilon_t e^{-j' \frac{2\pi f}{f_s} t}$, where $j'$ represents the unit imaginary number: $(j')^2 = -1$. The DTFT is written in terms of $f$ rather than normalized frequency $2\pi f/f_s$, for clarity in the following arguments.

Each term in the summation is complex Gaussian with zero-mean, covariance $\Gamma_t = \mathbb{E}\left[\left(\varepsilon_t e^{-j' \frac{2\pi f}{f_s} t}\right)\left(\varepsilon_t e^{j' \frac{2\pi f}{f_s} t}\right)\right] = \sigma^2_\varepsilon$, and relation $C_t = \mathbb{E}\left[\left(\varepsilon_t e^{-j' \frac{2\pi f}{f_s} t}\right)^2\right] = \sigma^2_\varepsilon \left(e^{-j' \frac{2\pi f}{f_s} t}\right)^2$. It follows that $\mathcal{E}(f)$ is also complex normal; specifically,

$$\mathcal{E}(f) \sim \mathcal{N}_C\left(0, \Gamma = W\sigma^2_\varepsilon, C = \sigma^2_\varepsilon \textstyle\sum_{t=1}^{W} \left(e^{-j' \frac{2\pi f}{f_s} t}\right)^2\right).$$

The power of the spectrum is denoted by $Z := \frac{\mathcal{E}(f)\mathcal{E}^*(f)}{W}$. In general, when $\mathcal{E}(f)$ is complex normal, $Z$ follows a Hoyt distribution [26], [27]. However, recalling that $W = f_s \cdot K$,

$$\frac{C}{\sigma^2} = \left(1 - e^{-j' \frac{4\pi f}{f_s} W}\right) \Big/ \left(1 - e^{-j' \frac{4\pi f}{f_s}}\right) = 0.$$

Thus, $\mathcal{E}(f)$ is specifically a circularly symmetric complex normal random variable, in which case, $Z \sim \text{Exponential}\left(\sigma^2_\varepsilon\right)$.

This result is used to derive the null distribution of the spectral power. Following standard procedures for conditional GC analysis [5], [10], it can be derived that if there is no link, the spectrum of the $i^{\mathsf{th}}$ process at the $m^{\mathsf{th}}$ window is given by $X^{(i)}_m(f) = Q^{(i,i)}_m(f)\mathcal{E}^{(i)}_m(f)$, where $\mathcal{E}^{(i)}_m(f)$ is the DTFT of the Gaussian noise process driving $\{x^{(i)}_t\}_{t=(m-1)W+1}^{mW}$. Invoking the previous result, $\mathcal{E}^{(i)}_m(f) \sim \mathcal{N}_C(0, W\Sigma^{(i,i)}_m, 0)$; consequentially,

$$X^{(i)}_m(f) \sim \mathcal{N}_C\left(0, W\left(Q^{(i,i)}_m(f)\right)\Sigma^{(i,i)}_m\left(Q^{(i,i)}_m(f)\right)^*, 0\right).$$

Thus, the spectral power of $i^{\mathsf{th}}$ process, denoted by the random variable $Z^{(i)}_m := \frac{\left(X^{(i)}_m(f)\right)\left(X^{(i)}_m(f)\right)^*}{W}$ has distribution

$$Z^{(i)}_m \sim \text{Exponential}\left(\left(Q^{(i,i)}_m\right)\Sigma^{(i,i)}_m\left(Q^{(i,i)}_m\right)^*\right),$$

where $\left(Q^{(i,i)}_m(f)\right)\Sigma^{(i,i)}_m\left(Q^{(i,i)}_m(f)\right)^* = S^{(i,i)}_m(f)$ under the null hypothesis.

The significance of the link is determined by testing the full model estimate, $\Omega^{(i,i)}_m$, against the distribution of $Z^{(i)}_m$. Since the full model is tested against multiple null hypotheses (testing multiple candidate links), the Benjamini-Hochberg procedure [28] for controlling false discovery rate is employed.

## III. Results

In this section, we present a simulation and a real data study demonstrating the utility of the proposed method. In both studies, we compare the performance to an existing, widely used method [8], [9], [12] whose results are based on the peristimulus time histogram (PSTH) of spiking activity, which we refer to as PSTH estimates, $\mathrm{GC}^{\mathsf{PSTH}}_{j\to i|\mathbf{w}}(f, m)$. The PSTH is given by the ensemble average of spiking activity $(\widehat{x}^{(j)}_t)_{\mathsf{PSTH}} = \frac{1}{L}\sum_l n^{(j)}_{t,l}$, which is used to estimate the latent oscillatory process, followed by sliding window multitaper spectral estimation. We additionally benchmark the performance of the estimators with respect to the oracle estimator, $\mathrm{GC}^{\mathsf{oracle}}_{j\to i|\mathbf{w}}(f, m)$, in the simulation study. The oracle estimator, which uses the true latent process as an observable, is derived using the multitaper estimates of $\mathbf{x}_t$ in simulations.

### *A. Simulation study*

We simulated the activity of three neurons as a tri-variate ($N = 3$) AR process, with $L = 30$ independent trials per

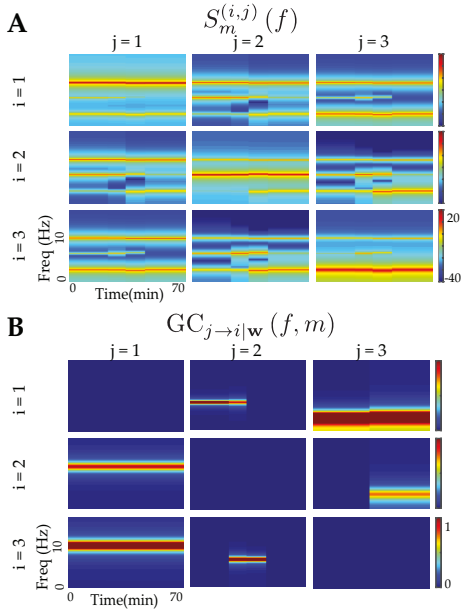


Fig. 1: (A) Magnitude spectrograms of the ground truth PSD matrix $\mathbf{S}_m(f)$ in dB scale and (B) the ground truth conditional GC links $\mathrm{GC}_{j\to i|\mathbf{w}}(f,m)$ between each pair of neurons, in the simulation study.

each latent process. Spikes were sampled at $f_s = 30$ Hz for a total duration of 70 minutes. The ground truth PSD matrix and conditional GC links in Fig. 1 respectively show the true dynamics in spectral coupling and GC connectivity across frequencies. Assuming stationarity within windows of length $W = 2100$, direct causal links are estimated between each pair of processes using the oracle, proposed and PSTH methods.

The conditional GC links inferred by each of the three methods and determined statistically significant by either of the proposed criteria are illustrated in Fig. 2. The proposed estimates closely follow the oracle estimates and the ground truth, recovering most of the spectro-temporal dynamics of ground truth conditional GC links, independently of the statistical test used. However, the PSTH-based approach fails to identify links that are significant according to either statistical test. In fact, PSTH spectral estimates generally capture spurious harmonics masking the true spectral content [3], which in turn adversely affects the corresponding conditional GC estimates, as seen in Fig. 2.

### *B. Application to experimentally recorded data*

Finally, our method is applied to multi-unit recordings of rat cortical neurons during sleep (data from [16], publicly available in the Collaborative Research in Computational Neuroscience data sharing website [20]). The data set includes the spiking activity of putative pyramidal cells (pE) and putative interneurons (pI) recorded during three main brain states: waking (WAKE), rapid eye movement (REM) sleep, and non-rapid eye movement (nonREM) (See [16] for details). We consider a bivariate setting ($N = 2$), denoting spiking observations of pE and pI cells by $n_{k,l}^{(1)}$ and $n_{k,l}^{(2)}$, respectively. We choose 10 spike trains ($L = 10$) from each cell type for the analysis, and consider an observation period of 35 minutes.

Fig. 3 shows the cross power spectral density estimates and the conditional GC estimates from the proposed and PSTH methods during different brain states. The GC link estimates in Fig. 3 are statistically significant with respect to the empirical test at level $\alpha = 0.01$. Similar to the results in [3], the cross PSD estimated from the proposed method (Fig. 3-A left) has greater cross power in low frequencies during nonREM sleep episodes. The GC links estimated with the proposed method, shown in Fig. 3-B (left) and Fig. 3-C (left), indicate steady low frequency links from interneurons to pyramidal cells during

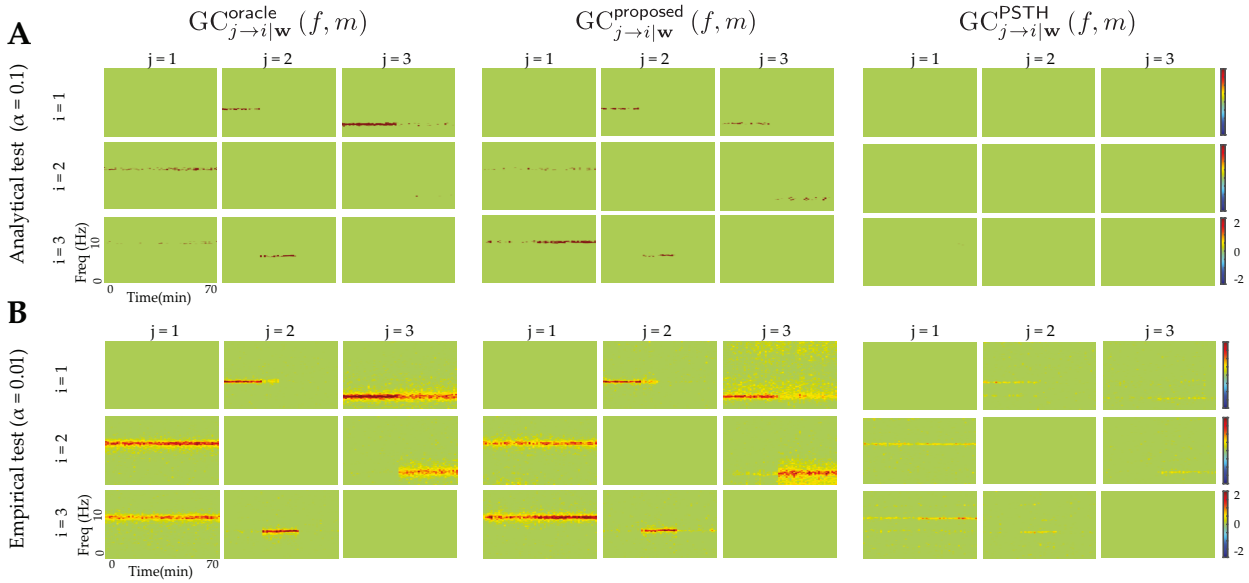


Fig. 2: Statistically significant conditional GC links according to (A) the analytical test with significance level $\alpha = 0.1$ and (B) the empirical test with significance level $\alpha = 0.01$, in the simulation study. Columns from left to right: the Oracle estimates, Proposed estimates and PSTH estimates.

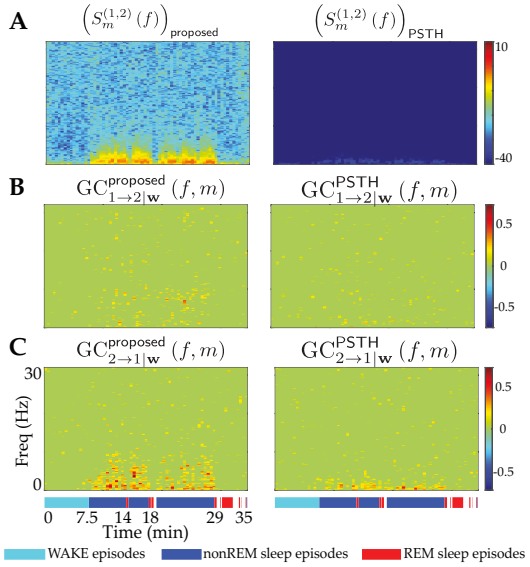


Fig. 3: Spectral GC analysis of rat cortical spiking during sleep. (A) The magnitude spectrogram of estimated cross PSD $\left(S_m^{(1,2)}(f)\right)$ in dB scale, (B) the estimated GC links from pE cells to pI cells $\left(\mathrm{GC}_{1\to 2|\mathbf{w}}(f,m)\right)$ and (C) the estimated GC links from pI cells to pE cells $\left(\mathrm{GC}_{2\to 1|\mathbf{w}}(f,m)\right)$. The Proposed (resp., PSTH) estimates are shown in the left (right) column. State labels of WAKE (cyan), nonREM (blue) and REM (red) are indicated at the bottom of each column. All GC links shown were statistically significant with respect to the empirical test for $\alpha = 0.01$.

nonREM sleep episodes. In contrast, PSTH estimates (Fig. 3 right) of cross spectra and GC links are unable to characterize these spectro-temporal dynamics.

## IV. Conclusion

In this work, we introduce a framework that combines point processes, state space modeling, multitaper spectral estimation, and conditional Granger-Geweke Causality analysis to infer spectro-temporal causal interactions from ensemble neuronal spiking activity, addressing shortcomings in existing methods. We also introduce two methods to test the statistical significance of inferred functional links. The utility of the proposed methods is demonstrated through a simulation study. In an application to cortical neuronal data acquired during sleep, the proposed method identified dynamics in functional connectivity under different brain states. These studies highlight the ability of the proposed method to accurately infer the underlying spectro-temporal interactions in a network of neurons, outperforming existing methods for spiking observations.

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