Inferring functional connectivities of networks with discrete and continuous observables

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Abstract—We here introduce estimating methods of functional connectivities of the networks, under the condition that the observable variables are composed of discrete and continuous ones. The causality estimation in the frequency domain is based on the estimation of the cross-spectrum density matrix. So, the main problem is how do we estimate the cross-specral density matrix. The cross-spectral density matrix is estimated through the multi-variate auto-regressive models for the continuous variables. In the current study, the discrete observables were assumed to be event time-series (e.g. timing of the earth quake and firing timing of the nerve cells). For the discrete variables, the cross-spectral density matrix can be estimated by the Fourier transformation and multitaper methods. In the current study we also consider the situation that the observed variables are composed of the discrete and continuous variables. For example, recording of the brain signals often provides the spike event time-series and the EEG or LFP signals. The spike signal is discrete and the LFP is continuous signals. For such cases, the event-triggered continuous averaging is useful method for the cross-spectral density matrix estimation. The current manuscript provides the outline of the estimation methods for the functional connectivity.

1. Introduction

The systems around us are comprised of the networks. The network structure however is invisible in many cases, e.g., neural systems, economy system, biological systems, and so on. Therefore, to understand the system, inferring the network structure is inevitable. The network structure can be categorized into functional and not functional. Even the nodes are connected, the network is not functional if the connection is not used. We call the collection of the meaningful connections the functional network. The functional network sometimes called the causal network. Estimating the functional network is first proposed by Wiener and it was formulated by the Granger [10, 5]. The Granger causality assumes the linear Gaussian stationary process. The definition of the Granger causality is as follows,

Definition 1 (Granger 1969) *We say that $X_1(t)$ is causing $X_2(t)(X_1(t) \implies X_2(t)$ if we are better able to predict $X_1(t)$ using all available information than if the information apart from $X_2(t)$ had been used.*

In other words,

Definition 2 *If the knowledge of the past of both $X_1(t)$ and $X_2(t)$ reduces the variance of the prediction error of $X_2(t)$ in comparison with the knowledge of the past of $X_2(t)$ alone, then a signal $X_1(t)$ causes the signal $X_2(t)$ in Granger sense.*

In short, if knowing time series X_2 helps predict the future of the other time series X_1, X_2 "Granger causes" X_1. This is applicable to a criterion of conditional independence on probability distributions that is generally applicable to stationary and non-stationary stochastic processes.

To study the functional connectivities of the real systems, it is important how the connectivities are related with different frequency bands which are functionally relevant [2]. In fact, the brain uses several frequency bands and their combinations to process the sensory information. To analyze the functional connectivities ranging frequency bands, several causality measures in spectral domain were proposed, comprising the Geweke spectral measures of Granger causality (for bi-variate signals, [3]; for multi-variate signals, [4]), the Directed Transfer Function (DTF) [7], and the Partial Directed Coherence (PDC) [1]. These measure were applied to analyze brain signals.

The above studies analyzed continuous signals. Some studies, on the other hand, analyses the functional connectivities by using the event time series [9]. For the brain, the event time-series corresponds to the spike timing of the neurons [6, 8].

In the current study, we used both discrete (event) time-series and continuous time-series to estimate the functional connectivities. In the brain, the spike signal and LFP (especially lower frequency range) is relevant and have different functions [11]. We here use the event triggered continuous time-series averaging to estimate the cross-spectral density matrix. The estimation accuracy will be assessed by some toy-models.

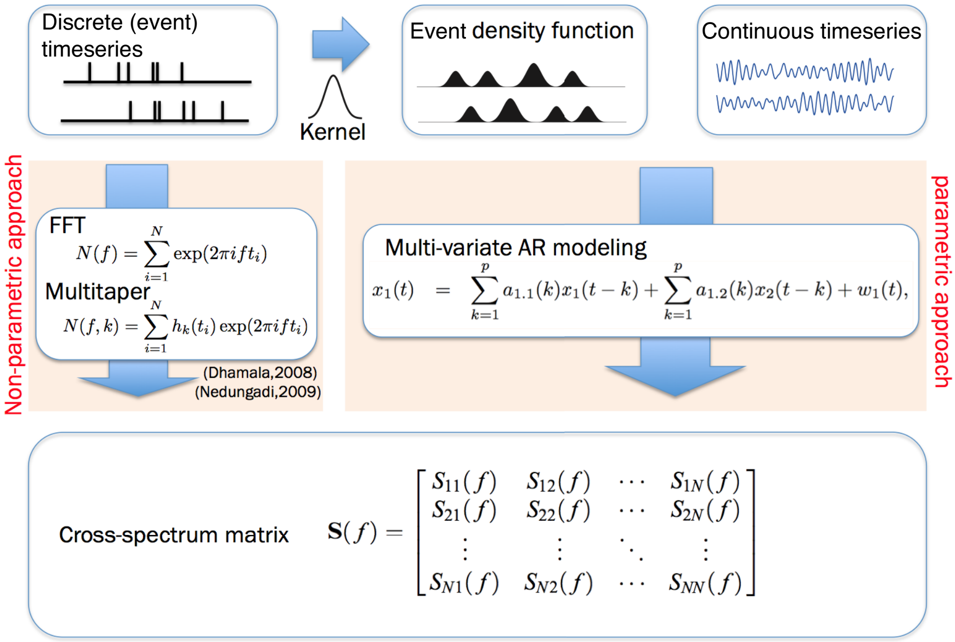

Figure 1: Schematic drawing of the estimation of the cross-spectral density matrix from the discrete and continuous time-series.

2. Causality estimation

2.1. The causality estimation

The estimation of the functional connectivities have relied on the cross-spectral density matrix,

$$S(f)=\begin{pmatrix} S_{11}(f) & S_{12}(f) & \cdots & S_{1N}(f) \\ S_{21}(f) & S_{22}(f) & \cdots & S_{2N}(f) \\ \vdots & \vdots & \ddots & \vdots \\ S_{N1}(f) & S_{N2}(f) & \cdots & S_{NN}(f) \end{pmatrix}.$$

The spectrum matrix can be decomposed into transfer function $H(f)$ and covariance matrix Σ,

$$S(f)=H(f)\Sigma H^T(f)$$

where ^{T} denotes complex conjugate and matrix transpose,

$$H(f)=\begin{pmatrix} H_{11}(f) & H_{12}(f) & \cdots & H_{1N}(f) \\ H_{21}(f) & H_{22}(f) & \cdots & H_{2N}(f) \\ \vdots & \vdots & \ddots & \vdots \\ H_{N1}(f) & H_{N2}(f) & \cdots & H_{NN}(f) \end{pmatrix},$$

and

$$\Sigma=\begin{pmatrix} \sigma_{11}^2 & \sigma_{12} & \cdots & \sigma_{1N} \\ \sigma_{21} & \sigma_{22}^2 & \cdots & \sigma_{2N} \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_{N1} & \sigma_{N2} & \cdots & \sigma_{NN}^2 \end{pmatrix}.$$

Coherence and causality measures in frequency domain
By using the cross-spectral density matrix, the ordinary coherence is defined as

$$C(f)=\frac{|S_{ij}(f)|^2}{S_{ii}(f)S_{jj}(f)}.$$

The Granger causality in the frequency domain,

$$GC_{ij}(f)=\ln\frac{S_{ii}(f)}{\Sigma_{ii}^{(ij)}|H_{ii}^{(ij)}(f)|^2}.$$

The directed coherence,

$$DC_{ij}(f)=\frac{\sigma_{jj}H_{ij}(f)}{\sqrt{S_{ii}(f)}}.$$

The directed transfer function,

$$DTF_{ij}(f)=\frac{H_{ij}(f)}{\sqrt{\sum_{j=1}^{N}|H_{ij}(f)|^2}}.$$

2.2. Continuous variables

The causality measures in the frequency domain is based on the cross-spectral density matrix, so the problem is how do we estimate the cross-spectral density matrix from the observable variables. The cross-spectrum density matrix of the continuous variables are obtained through the multi-variate auto-regressive models.

In the situation that time-series $\boldsymbol{x_n}$, $(n = 1, 2, ..., N)$ are available, each P-th dimensional linear mono-variate auto-regressive model is described as,

$$x_n(t)=\sum_{p=1}^{P}a_n(j)x_n(t-j)+u_n(t),$$

and P-th linear multi-variate auto-regressive model is described as,

$$x_n(t) = \sum_{m=1}^{N}\sum_{p=1}^{P} a_{n.m}(p)x_m(t-p) + w_n(t),$$

where, $u_n(t)$ and $w_n(t)$ are estimation error at moment t.

The estimation error of the mono-variate auto-regressive and multi-variate auto-regressive model of $\boldsymbol{x_n}$, $(n = 1, 2)$ is described as follows,

$$\begin{aligned}
\Sigma_{x_1|x_1} &= \frac{1}{T-p}\sum_{t=1}^{T} u_1^2(t), \\
\Sigma_{x_2|x_2} &= \frac{1}{T-p}\sum_{t=1}^{T} u_2^2(t), \\
\Sigma_{x_1|x_1,x_2} &= \frac{1}{T-2p}\sum_{t=1}^{T} w_1^2(t), \\
\Sigma_{x_2|x_2,x_1} &= \frac{1}{T-2p}\sum_{t=1}^{T} w_2^2(t).
\end{aligned}$$

If the causality $x_2 \to x_1$ is existed, the estimation error of the multi-variate model is expected to be reduced relative to the estimation error of the mono-variate auto-regressive model. Namely, it is expected that $\Sigma_{x_1|x_1,x_2} < \Sigma_{x_1|x_1}$. From this, we define linear time domain Granger causality (LTGC) of x_2 for x_1 as

$$\mathrm{LGC}_{x_2\to x_1} \equiv \ln \frac{\Sigma x_1|x_1}{\Sigma_{x_1|x_1,x_2}},$$

and LTGC of the opposite direction as

$$\mathrm{LGC}_{x_1\to x_2} \equiv \ln \frac{\Sigma_{x_2|x_2}}{\Sigma_{x_1|x_2,x_1}}.$$

Statistical significance

In the case that $x_2 \to x_1$ has no causal relationships, $a_{1.2}(p) = 0$ for $p = 1, \dots, P$. Then the statistical significance based on the Fisher's test is as follows,

$$\begin{aligned}
F_{x_2\to x_1}^{\mathrm{LGC}} &= \frac{T-2p}{p}\frac{\sum_{t=1}^{T} w_1^2(t) - \sum_{t=1}^{T} w_2^2(t)}{\sum_{t=1}^{T} w_2^2(t)} \\
&= \frac{T-p}{p}\Big(\exp(\mathrm{LGC}_{x_2\to x_1}) - \frac{T-2p}{T-p}\Big).
\end{aligned}$$

Partial Directed Coherence

The partial directed coherence is described from the spectral representation of the auto-regressive models. Suppose that the multi-variate auto-regressive model is expressed as follows,

$$\begin{bmatrix} x_1(t) \\ \vdots \\ x_N(t) \end{bmatrix} = \sum_{p=1}^{P} A_p \begin{bmatrix} x_1(t-p) \\ \vdots \\ x_N(t-p) \end{bmatrix} + \begin{bmatrix} w_1(t) \\ \vdots \\ w_N(t) \end{bmatrix},$$

$$A_p = \begin{bmatrix} a_{1.1}(p) & a_{1.2}(p) & \cdots & a_{1.N}(p) \\ \vdots & \vdots & \ddots & \vdots \\ a_{N.1}(p) & a_{N.2}(p) & \cdots & a_{N.N}(p) \end{bmatrix}.$$

Then, the PDC is defined as follows,

$$\mathrm{PDC}_{i\to j}(f) = \frac{\overline{A}_{j.i}(f)}{\sqrt{\sum_{p=1}^{P} |A_{n.k}(f)|^2}}$$

where, $A(f) = \sum_{p=1}^{P} A_k e^{-1i\pi f p}$, $\overline{A}(f) = I - A(f)$, I is P-dimensional identity matrix.

Model order

To apply the AR model to the observations, the dimension of the underlying system is usually unknown. In the current study, we used Akaike Information Criterion (AIC) for the estimation of the dimension of the model order.

Firstly, the estimation error is assumed to follow the normal distribution. Then, for N data and P degrees of freedom statistical model that have the maximum log likelihood $l = \ln L$, we calculated AIC,

$$\mathrm{AIC} = -2l + 2P. \tag{1}$$

The maximum log likelihood model of the regressive model is $\hat{l} = -\frac{N}{2}\{1 + \ln(2\pi\sigma^2)\}$, and

$$\mathrm{AIC} = N\ln(2\pi\sigma^2) + N + 2P. \tag{2}$$

In the current study, the dimension P was determined in the mono-variate auto-regressive model, and the same P was applied to the multi-variate auto-regressive model.

2.3. Discrete variables

Fourier transformation

The cross-spectral density matrix of the event time-series are obtained by the Fourier transformation of the event series,

$$N(f) = \sum_{i=1}^{k} \exp(2\pi f t_i),$$

where t_i is the event timing.

Multitaper method

The multitaper method, a variation of the Fourier transformation, is useful and often used to estimate the power spectrum of the time series,

$$N(f,k) = \sum_{i=1}^{k} h_k(t_i)\exp(2\pi f t_i),$$

where $h_k \in \{h_i\}_{k=1}^{K}$ is data taper. The multitaper method is used in the situations,

1. to estimate the power spectrum of short time-series,
2. to estimate the power spectrum of the short time-series segments of the long time-series, to evaluated temporal variation of the power spectrum.

For situation (2), the wavelet transformation is often used instead. By using the multitaper method, the spectrum matrix estimation is

$$\hat{S}_{ij}(t) = \frac{1}{2\pi KT} \sum_{k=1}^{K} \tilde{N}_i(f,k)\tilde{N}_j(f,k)^*$$

where * denotes matrix transposition and complex conjugate.

Kernel convolution

The other way to estimate the cross-spectral density matrix is convolution of the kernel function. In this study, the kernel function is assumed to be the Hanning window.

2.4. Discrete and Continuous variables

The purpose of the current study is to estimate the cross-spectral density matrix from both the discrete and continuous observable signals. On the situation that both spike and continuous variables are available, the event triggered continuous averaging (ETCA) is applicable (Fig.2). The ETCA is called spike-triggered LFP (EEG) averaging in the neuroscience field. The power spectrum of the ETCA is used as the cross-spectrum density matrix.

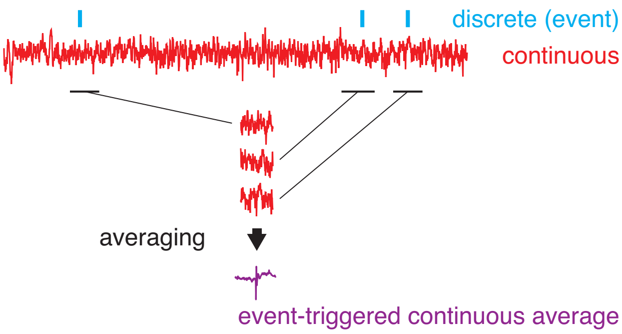

Figure 2: Schematic drawing of the discrete triggered continuous signal averaging.

3. Conclusion

We here introduced the outline of the estimation methods for the functional connectivities. Those methods will be applied to some toy-models, and the result will be shown on the conference.

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