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Estimation of Brain Dynamic Interactions with Time-varying Vector Autoregressive Modeling using fMRI

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Abstract

Analyzing the interaction among regions of the brain is an important step to understand the brain process. There have been many studies of directional effective influence between regions of the brain using fMRI. However, most of the previous studies are based on the assumption of time-invariant connectivity structure, which is insufficient to understand the change of the connectivity during cognitive tasks. In this paper, we propose a method of time-varying connectivity analysis using time-varying vector autoregressive model (tvVAR). The method allows the examination of the dynamic interactions among brain regions during cognitive tasks in the concept of Granger causality. The result of the simulation study indicates that this approach is effective to estimate the time-varying connectivity with short time intervals. Application of the method to real fMRI data was illustrated by the identification dynamic interactions among brain regions during simple sensory-motor task experiment.

Keywords: expectation-maximization algorithm, interactions, Kalman filter, tvVAR.

1. INTRODUCTION

Examining the interactions (effective connectivity) [1] among brain areas during a cognitive task is a challenging work in the field of neuroscience; however, it is a necessary step to understand the brain process. Many previous studies have focused on estimating this directed influences based on neuroimaging data such as functional magnetic resonance image (fMRI), electroencephalography (EEG), magnetoencephalogram (MEG), etc., to address the question of causal connectivity. Dynamic Causal Model (DCM) [2] was performed using fMRI to make inferences about the temporal changes of effective connectivity. The DCM is based on a nonlinear input-state-output system and comprises a bilinear model for neurodynamic to model the interaction at the neural level [4]. However, as DCM is estimated via Bayesian algorithms, it requires the prior densities of the parameters of interest and need the assumption of stationarity. Other methods have been proposed using VAR models and the Granger causality to identify the directed influence among activated brain areas [1], [6]. However, these approaches also assume that the data is stationary, while most neuroimaging data is non-stationary. The above assumptions will likely lead to incorrect inferences. In this paper, we propose a method to examine the time-varying directed influence among active brain areas based on tvVAR model [5]. The tvVAR model provides an easy way to measure the directed influence, the information about the influences is contained in the coefficient matrix. With this method, the multivariate non-stationary signals can be modeled to estimate the time-varying coefficients, which are used to examine the dynamic of brain areas interaction in the context of Granger causality [5]. This paper is organized as follows: In section 2, we present the method of estimate the time-varying coefficients of the tvVAR model using Kalman filter based EM algorithm as well as the application of tvPDC [10] to measure the directed influence between regions. Then in the next section, the simulated data will be used to illustrate the performance of the method and the application of the real fMRI with simple sensory-motor tasks. Finally, we make a conclusion in section IV.

2. METHOD

In this section, we present a method to estimate the time-varying directed influence among active brain areas. First, we estimate the coefficients of tvVAR in the state-space model using the Kalman filter. Finding the parameters for the Kalman filter has been a common issue, in this paper, the optimal parameters will be determined based on expectation maximization (EM) algorithm on a large training dataset. The tvPDC then will be applied on the estimated coefficients to measure the time-varying interaction among active brain areas. The framework of this research is present in the Fig. 1.

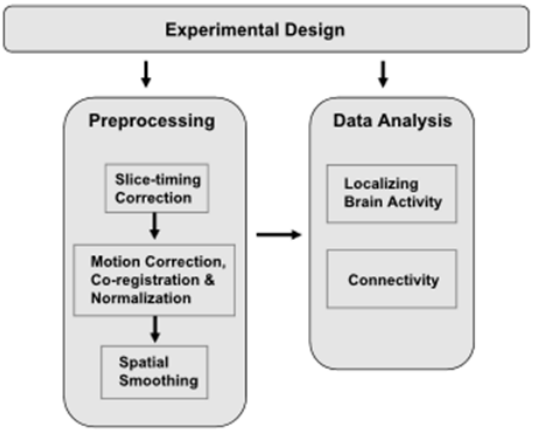

Figure 1. The framework of connectivity analysis.

2.1. Time-varying vector autoregressive (tvVAR) model. Generally, the measuring of the causal influence in the context of Granger causality is achieved by fitting the VAR model. In most cases, because the data is non-stationary, the tvVAR is necessary to model the data. We assume that our fMRI data can be represented by a tvVAR model given by:

$$y_t = \sum_{k=1}^{p} a_{k,t} y_{t-k} + v_k \qquad (1)$$

where p is the model order, y_t is the d –dimensioned observation at time t, $a_{k,t}$ are tvVAR coefficients and v_t is Gaussian noise with zero mean and covariance R.

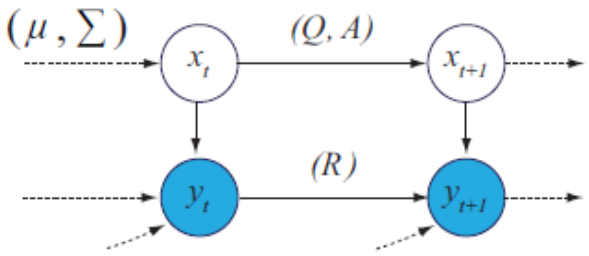

Figure 2. Graph representation of the state-space model.

To apply Kalman filter to estimate the coefficients, we need to represent this model in a state-space model. Kalman filter provides an optimal estimate to the state of a process, in the sense of minimizing the mean square error. We need to rearrange the elements of tvVAR model:

$$x_t = Vec(a_{k,t}^{'}) \qquad (2)$$

$$C_t = (I_d \otimes y_{t-1}^{'} \ldots y_{t-p+1}^{'}) \qquad (3)$$

where Vec operator is used to rearrange the coefficients matrix $a_{k,t}$ to the vector form. I_d is identity matrix of dimension d and $\otimes$ is Kronecker product of matrix.

The tvVAR model can be represented as a state-space model:

$$y_t = C_t x_t + v_t \qquad (4)$$

$$x_{t+1} = Ax_t + w_t \qquad (5)$$

where x_t are tvVAR coefficients, w_t is the state noise with zero mean and covariance Q. A is the state transition matrix and C_t is the observation matrix. The initial state is assumed to be Gaussian with mean μ and covariance Σ. In this model, all the above parameters, denotes as $\Theta = \{A, Q, R, \mu, \Sigma\}$, are assumed to be known. The graph representation of the model is shown in Fig. 2, which is shown the dependencies between variables.

2.2. Coefficients estimation

Given the observations $Y_{1:T}$, we apply Kalman filter to estimate the tvVAR coefficients. We need to calculate two quantities, the condition expectation of the states and the corresponding error covariance:

$$x_{t|k} = E(x_t \mid Y_{1:T}) \qquad (6)$$

$$P_{t|t} = E\left\{(x_t - x_{t|k})(x_t - x_{t|k})^{'} \mid Y_{1:T}\right\} \qquad (7)$$

The above quantities can be obtained using Kalman filter, the detail of Kalman filter implementation is given in [7]. Note that in this case, because of time-varying estimation, the Kalman gain and the observation matrix are varied in time. To estimate the current state $x_{t|t}$, the predictive state $x_{t|t-1}$ is calculated based on only the previous state $x_{t-1|t-1}$. Then the correction step is calculated using the present observation y_t and the predictive state $x_{t|t-1}$. If we have all the observations, we can first apply the Kalman Filter recursively forward until we reach the state x_T. After that, we apply Kalman Smoother backward until we reach the state x_t that we would like to estimate. Because all the observations are used in the estimate, the result will be less noisy compared to the Kalman Filter. In the implementation of Kalman filter, we assume that all the parameters are known. In fact, values of these parameters cannot be known in an exact manner but can be determined using empirical knowledge. In the next section, we will describe the use of an EM algorithm [8] to estimate the model parameter.

2.3. Parameters estimation

The objective of this section is to estimate Θ given an observation sequence using EM algorithm. The EM algorithm is the procedure to perform a maximum likelihood estimation of the observations $Y_{1:T}$, with the presence of hidden variables $x_{t|T}$. Note that the direct maximization cannot be performed because the hidden variables are not available. The maximization must be done with respect to states and model parameters.

The E-step takes the expected value of the complete log-

likelihood as followed:

$$F = E_{X|Y}\left[\log p(Y_{1:T}, X_{1:T} \mid \Theta)\right] \quad (8)$$

We consider Y_t as the observations and state X_t as the hidden variables. Each of the parameter in the M-step is estimated by taking the corresponding partial derivative of the expected log likelihood and setting it to zero [8], [9].

$$\hat{R} = \frac{1}{T}\sum_{t=1}^{T}\left(y_t y_t' - 2C_t\hat{x}_t y_t' + C_t P_t C_t'\right) \quad (9)$$

$$\hat{A} = \left(\sum_{t=2}^{T} P_{t,t-1}\right)\left(\sum_{t=2}^{T} P_{t-1}\right)' \quad (10)$$

$$\hat{Q} = \frac{1}{T-1}\left(\sum_{t=2}^{T} P_t - \hat{A}\sum_{t=2}^{T} P_{t-1,t}\right) \quad (11)$$

$$\hat{\mu} = \hat{x}_1 \quad (12)$$

$$\hat{\Sigma} = P_1 - \hat{x}_1\hat{x}_1' \quad (13)$$

After obtaining the states of the model, we can derive the coefficient matrices of tvVAR model by inverting the vec-operator of state x. These matrices will be the inputs for tvPDC to measure the direct influences among brain regions.

2.4. Time-varying Partial directed coherence

The Partial Directed Coherence (PDC) [10] is a method to analyze the directed interactions among signals in multivariate data set in the context of Granger causality [8]. In order to examine the brain dynamics, a tvPDC, which is obtained from VAR with time-varying coefficients, is employed. In order to define the tvPDC, we need to take the Fourier transformation of the tvVAR coefficients:

$$A(f,t) = I - \sum_{k=1}^{p} a(t-k)\exp^{-ifk} \quad (14)$$

Then the tvPDC from x_j to x_i is defined as:

$$PDC_{i\leftarrow j}(f,t) = \frac{\left|A_{ij}(f,t)\right|}{\sqrt{\sum_{l=1}^{K}\left|A_{ij}(f,t)\right|^2}} \quad (15)$$

3 RESULT

3.1 Application on simulated data

To illustrate the performance of the method, we sue the simulated three-dimensional VAR process of order two, generated as (1) with time-varying coefficients varied as shown in Fig. 3a. In this model, the process x_2 is influenced by x_1 with disrupted change from strong to weak, whereas x_3 is influenced by x_1 with increasing strength in the first half of simulation and with decreasing strength in the second half. The corresponding estimated tvPDC is given in Fig. 3b. We can see that, the spectra of process xi are displayed on the diagonal while the $PDC_{i\leftarrow j}$ are shown in off-diagonal elements. The result shows that the directed influences are estimated correctly by tvPDC. The element (1, 2) shows correctly the influence of process x_2 on x_1 with disrupted change and the element (1, 3) also shows the correctly the influence of x_3 on x_1 with increasing and decreasing strength. The example demonstrates that partial directed coherence provides a frequency domain approach for the identification of causal influences in multivariate systems.

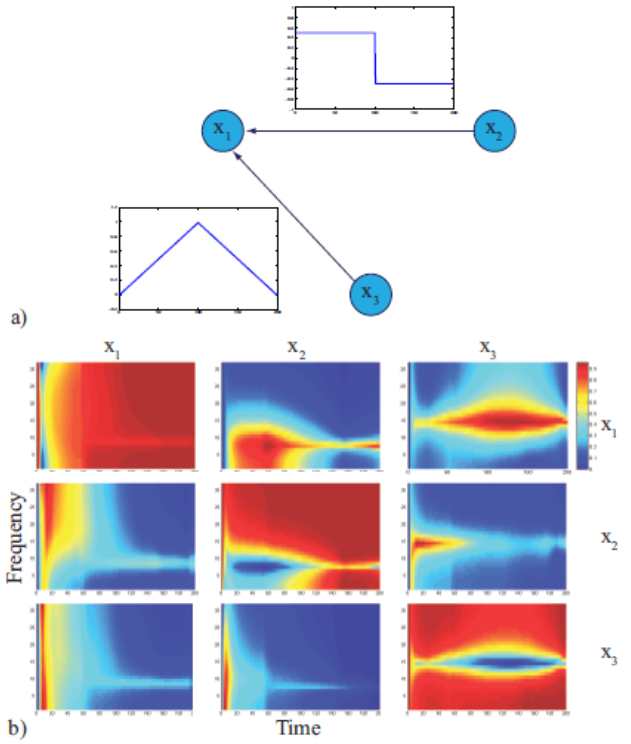

Figure 3. (a) Graph represent the causal influences among 3-dimensional tvVAR[2] process. (b) The causal influences estimated by tvPDC.

3.2 Application on fMRI data

The data used in this method is from Washington University [11]: thirteen subjects with very mild to AD condition were scanned during a simple sensory-motor experiment. During the task, subjects are required to respond with a button press with their right index fingers to a stimulus onset. The visual stimulus was a flashing checkerboard which was presented for 1.5 sec in single or in pairs with a 5.36 sec gap between presentations. The raw data were received from the fMRI Data Center at Dartmouth College and were preprocessed using SPM5 [12]. Images were motion corrected and normalized to coordinates of Talairach and Tournoux [18]. They are also smoothed with a 4 mm Gaussian kernel to decrease spatial noise. We apply group ICA for fMRI Toolbox (GIFT) [13] on a group of subjects with Alzheimer's disease to extract the task related components. Recent researches shows that ICA can be used to separate fMRI data into meaningful components, classified as task-related, transiently task-related, and motion related [3], [14]. From the group ICA,

three significant independent components of interest were identified. They are left motor cortex (LM), supplementary motor area (SMA) and visual cortex (VC). The corresponding time courses are used as an input to the tvVAR to obtain the coefficients. The order of the model is obtained using Bayesian Information Criterion [17]. The tvPDC is then calculated using (3) and the result is show in Fig. 4.

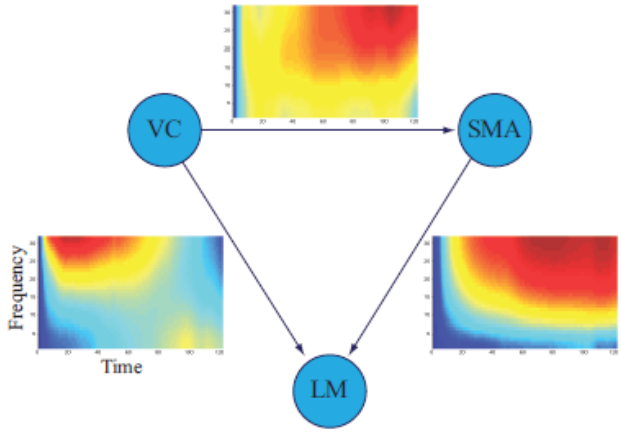

Figure 4. Time-varying directed influences among brain regions.

The diagram describes the time-varying directed influences among three regions in the brain during a task. We observed that the influence of the SMA on the LM is significant during the whole of experiment. It is demonstrated that SMA plays an important role in cognitive motor control, which involves sensory discrimination [15]. The diagram also shows that the influence of the VC on LM is significant during the early experiments and the influence of the VC on SMA is significant in the latter half of experiment. We also investigated the directed influences among three regions with a stationary assumption using VAR model and PDC. The result in Fig. 5 showed the same connectivity structure and the influences are significant at the corresponding oscillation frequencies [16].

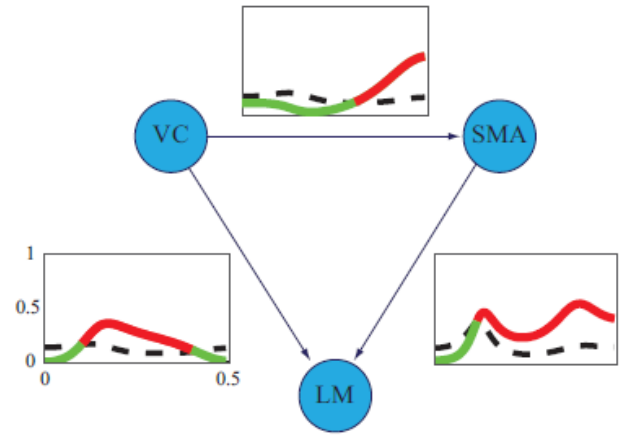

Figure 5. Directed influences among brain regions estimated by PDC.

4 Conclusion

We proposed the method to examine the time-varying interactions among active brain regions. The method attempts to resolve the issue existed in a stationary model, which is the influences is constant during the cognitive task. Our method allows for the investigation of the change in the strength of influences over time. Our results open ways for further research to learn more about the neural system.

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