Functional Connectivity Using Complex-Gaussian Graphical Models of EEG

Anirudh Wodeyar (awodeyar@uci.edu)
Cognitive Sciences and Statistics
University of California
Irvine, California, USA

Ramesh Srinivasan (r.srinivasan@uci.edu)
Cognitive Sciences and Biomedical Engineering
University of California
Irvine, California, USA

Abstract

Functional connectivity can be measured with electroencephalography (EEG) data using a variety of metrics that emphasize different aspects of brain dynamics. Coherence, which measures the consistency of relative phase between channels, is a widely used measure of synchronization in different frequency bands and describes marginal dependence between channels. The interpretation of coherence as reflecting a functional connection in the brain is confounded by volume conduction of current and by common inputs to both channels. In this paper we assume that EEG data in a frequency band are generated by a complex multivariate normal (CMVN) in order to define a complex-Gaussian Graphical Model of the data. Conditional dependence between channels is reflected in the precision values of the model. Compared to coherence, precision estimates suppress volume conduction and common input effects, while providing, by way of the graphical lasso, a sparse estimate of the underlying network. We show through simulation that this model outperforms coherence as an estimate of connectivity and captures the most important features of the network. We apply this technique to estimate how networks in the alpha (8-13 Hz) band is modified in a working memory task and find that connection density as measured by the degrees follows the process of encoding, retention and retrieval.

Keywords: functional connectivity; working memory; EEG; complex gaussian graphical model; graphical lasso

Introduction

Functional connectivity in macroscopic brain data (EEG, LFP) refers to evidence of statistical dependence between two signals. EEG and LFP are sampled on a millisecond time scale capturing aggregate synaptic activity in populations of neurons. These neurophysiological signals have intrinsic time scales of organization, often organized in terms of frequency bands that exhibit distinct behaviors in different cognitive tasks and clinical disease states. Functional connectivity in EEG is usually based on measures of statistical dependence of amplitude and phase in different frequency bands.

Coherence is the most widely used measure of functional connectivity in EEG studies. Coherence is an analogue of the coefficient of variation or squared correlation coefficient for complex-valued data:

$$\gamma^2(f) = \frac{|C_{ab}(f)|^2}{C_{aa}(f)C_{bb}(f)} \tag{1}$$

$C_{ab}(\omega)$ is the cross-spectrum between two channels a and b, and $C_{aa}(\omega)$ is the power spectrum of channel a at frequency ω. This measure is particularly susceptible to volume conduction (Nunez and Srinivasan, 2006) which is the spread of current through the tissues of the brain and to common input effects.

Here we discuss how we gain in interpretation and estimation by applying ideas from Gaussian Graphical models (GGM, Whittaker 2009) to the estimation of functional connectivity from EEG data. In GGMs we perform inference on the inverse of the covariance matrix (called the precision) for a set of random variables that are distributed according to a multivariate normal distribution. By observing the zeros in the precision matrix, we can establish conditional independence between channels. Establishing conditional dependence also has the benefit in the context of EEG of suppressing volume conduction and common input effects. Additionally, we sidestep the problem of determining a threshold for coherence by applying the graphical lasso to estimate graphs from the precision.

Methods and Materials

Complex Gaussian Graphical Modeling

We frame the problem of estimating functional connectivity in terms of the complex values in the frequency domain. Every epoch (any one trial) of the EEG data gives us a realization of the CMVN random process at each channel for any one frequency band.

We define the complex vectors $z = x + iy$ and $z^H = x - iy$, and the complex augmented vector Z for a specific frequency ω, for any one epoch, at all channels C.

Using $Z = [z, z^H]$, we define the CMVN for a complex Gaussian process (Schreier and Scharf, 2010) over the channels as (assuming $E(Z) = 0$):

$$\rho(Z) = \frac{1}{\pi^n det^{\frac{1}{2}}(\Theta_{zz})} \exp(-\frac{1}{2} Z^H \Theta_{zz}^{-1} Z) \tag{2}$$

$$\Theta_{zz} = \begin{bmatrix} R_{zz} & \widetilde{R}_{zz} \\ \widetilde{R}^*_{zz} & R^*_{zz} \end{bmatrix} \tag{3}$$

$$R_{zz} = E[zz^H]; \widetilde{R}_{zz} = E[zz^T] \tag{4}$$

When the data is not circularly symmetric, we must examine the complementary covariance alongside the cross spectrum R_{zz}. The complementary covariance $\widetilde{R}_{zz}$ is an estimate of the similarity in variance between the real and imaginary parts of the complex-valued process.

$$\widetilde{R}_{zz} = R_{xx} - R_{yy} + i(R_{xy} + R_{xy}^T) \tag{5}$$

Any value in the precision matrix is an estimate of the conditional covariance between any two variables (here channels) given the other variables (Whittaker, 1990). When the value for precision is zero in the Schur complements of both the covariance and complementary covariance matrix, we can state that those channels are conditionally independent under the CMVN. By establishing the framework of the CMVN, we possess the ability to estimate which pairs of electrodes are in fact conditionally independent, and by its complement, which are conditionally dependent i.e. *functionally connected*.

Graphical Lasso

The graphical lasso (Friedman, Hastie and Tibshirani, 2008) helps to identify the zeros in the precision matrix by optimizing a penalized likelihood function. In this way, we allow our estimates to be more robust for the precision values that are retained. In order to apply the lasso, we define optimization for the precision as follows :

$$\hat{\Theta}^{-1} = argmin_{P \succ 0} \left(log(detP) + tr(\Theta P) + \lambda \sum_{j<k} |P_{jk}| \right) \quad (6)$$

The parameter λ determines the cachet of precision values retained through the process of optimization. Using simulations of networks with different number of edges, we found that a λ in the range of $0.2 * max(Covariance)$ is appropriate to maximize accuracy and minimize volume conduction.

Volume Conduction Model

We built a finite element model of the brain, skull and scalp based on estimates of these layers from MRI data. We place a independent, identically distributed standard normal source at each point of the estimated cortical brain mesh to see how they linearly combine when measured at the scalp. By doing this we can then estimate the connectivity for these random sources at the channel level, which ideally should be completely disconnected functionally but are not because of volume conduction.

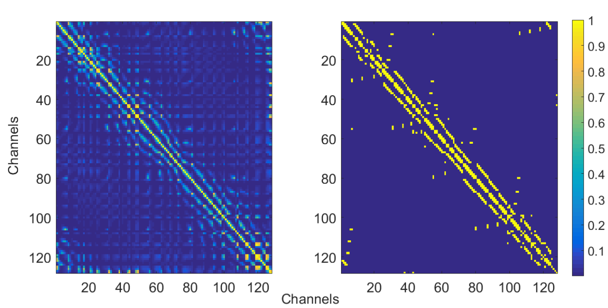

Figure 1: On left coherence matrix from pure volume conduction from IID sources. On right the graph from the precision matrix at 0.2*max(covariance) penalization

Working Memory Task

Working memory experiments follow an encoding, delay and retrieval paradigm. Alpha networks reflect the act of maintenance of items over the delay (Sauseng et al., 2010). We ran an experiment where participants remember the orientations of two gabor patterns over a delay period of random length before being tested on their recollection of one of the gabors. We collected EEG from 128 channels for 400 trials. EEG data was cleaned of gross movement artifacts manually. An ICA was performed to remove eyeblink components. We used the cleaned data (300 trials) to perform graph theoretical analysis of the dynamic structures present over the pre-encoding (500ms), encoding (1 sec split into 500 ms chunks), maintenance (1 sec split into 500 ms chunks) and retrieval (500 ms) periods.

Results

We forward simulated samples from a multivariate normal for different connection densities in the precision matrix. We tested the efficacy of the graphical lasso against thresholding the covariance. The lasso provides accuracies above 60 percent in cases with less than 50 percent connection density, and up to 90 percent accuracy when the model is genuinely sparse. The method consistently estimates the strongest connections in the precision.

We also looked at the reduction in volume conduction effects from applying the lasso over a range of λ. The lasso removes volume conduction based connections from all but nearest neighbor channels as seen in Figure 1.

Finally, the alpha band networks suggest that there is a reduction in connections over occipital lobe during the trial, with respect to the pre-encoding period. There is an increase in connections over right parietal, as well as right temporal past the first 500 ms of the trial. This change may reflect that participants were able to encode items within the first 500 ms and subsequently began to structure attention internally towards the items in working memory.

References

Friedman, J., Hastie, T., & Tibshirani, R. (2008). Sparse inverse covariance estimation with the graphical lasso. *Biostatistics*, *9*(3), 432–441.

Nunez, P. L., & Srinivasan, R. (2006). *Electric fields of the brain: the neurophysics of eeg*. Oxford University Press, USA.

Sauseng, P., Klimesch, W., Doppelmayr, M., Pecherstorfer, T., Freunberger, R., & Hanslmayr, S. (2005). Eeg alpha synchronization and functional coupling during top-down processing in a working memory task. *Human brain mapping*, *26*(2), 148–155.

Schreier, P. J., & Scharf, L. L. (2010). *Statistical signal processing of complex-valued data: the theory of improper and noncircular signals*. Cambridge University Press.

Whittaker, J. (2009). *Graphical models in applied multivariate statistics*. Wiley Publishing.