PHASE SYNCHRONY IN MULTIVARIATE GAUSSIAN DATA WITH APPLICATIONS TO CORTICAL NETWORKS

Sergul Aydore† *Dimitrios Pantazis*⋆ *Richard M. Leahy*†

† Signal and Image Processing Institute, University of Southern California, Los Angeles, CA, USA
⋆ McGovern Institute for Brain Research, Massachusetts Institute of Technology, Cambridge, MA, USA

ABSTRACT

Phase relationships between neuronal sources are often quantified by the phase locking value (PLV). Since the PLV is a bivariate measure and computed pairwise between sources, it cannot differentiate between direct and indirect connections in a multidimensional network. Schelter described a non-parametric partial phase synchronization index by extending sample PLV to the multivariate case by analogy to the relationship between full and partial network correlations. Here we derive an analytical expression for partial PLV for a multivariate circular Gaussian model and show that a partial PLV can be computed from partial coherence. We demonstrate our method in simulations with Roessler oscillators and experimental data of multichannel local field potentials from a macaque monkey. We show that the multivariate non-parametric and circular complex Gaussian based models suggest similar synchronization networks while the latter has a lower variance.

***Index Terms*—** Phase locking value, multivariate network, Gaussian signals

1. INTRODUCTION

Brain functional connectivity, or the study of interactions between cortical regions and their modulation during experimental tasks, has begun to reveal the highly organized structure of large scale networks. It is now believed that cortical networks are mediated by the coordinated activation of thousands of neurons that oscillate synchronously in specific frequency bands. Sample phase locking value (PLV) is one of the most widely used measures of brain synchronization [1],[2]. It quantifies the phase relationship between two signals with high temporal resolution without making any statistical assumptions of the data.

A significant limitation of PLV is that it is a bivariate measure which cannot differentiate between direct and indirect interactions in a multiple-node network. To overcome this problem, Schelter et al. [3] investigated the inversion of the matrix of pairwise PLVs to compute a non-parametric estimate of partial PLV. Their approach is analogous to the inversion of cross-correlation and cross-spectral matrices to compute partial correlations and partial-coherence, respectively. An alternative parametric approach was proposed by Cadieu et al. [4] via multivariate extension of the von Mises distribution. Direct phase coupling measures can be determined in a straightforward manner from this model.

This work was supported by NIH under grants R01 EB009048 and R01EB000473 and the NSF under grant BCS-1134780.

In this paper, we derive an analytical expression for partial PLV under the multivariate circular complex Gaussian model [5]. We show that under this model, partial PLV is a nonlinear function of partial coherence, which is computed from both the phase and amplitude information of the signals. We demonstrate our partial PLV measure in detection of synchronization of Roessler oscillators. We further show that local field potentials from a macaque monkey study approximately follow our modeling assumptions and our measure of partial PLV has reduced estimator variance compared to the non-parametric PLV in [3].

2. METHODS

The PLV between two coupled oscillators $s_a(t)$ and $s_b(t)$ is defined as $PLV = \left|\mathrm{E}\left[e^{j\phi_{a,b}}\right]\right|$, where $\phi_{a,b} = \phi_a(t) - \phi_b(t)$ is the relative phase of the two oscillators a and b with instantaneous phase $\phi_a(t)$ and $\phi_b(t)$ respectively [6]. The instantaneous phase of an arbitrary signal $s(t)$ is often derived from its Hilbert transform and the construction of the analytic signal [7]. If the signal is broadband, it must first be filtered into a frequency band of interest [8].

In this section, we discuss three different measures of phase synchrony. We first describe the bivariate sample PLV, which is the maximum likelihood estimator of PLV under the assumption of Von Mises distribution for the relative phase. We also describe the non-parametric multivariate partial PLV measure proposed by Schelter et al. [3]. Finally, we derive a parametric measure of partial PLV using the multivariate circular complex Gaussian model.

2.1. Sample PLV

The sample estimate of PLV between $s_a(t)$ and $s_b(t)$ at time instant t is:

$$PLV_{\text{sample}} = \left|\frac{1}{N}\sum_{n=1}^{N} e^{j\phi_{a,b}^{(n)}(t)}\right| \quad (1)$$

where N is the total number of trials. In the following we drop the term t for convenience. Even though this measure is non-parametric, it is also the maximum likelihood estimator of PLV when the distribution of relative phase $\phi_{a,b}$ is Von Mises [9], i.e. the relative phase has probability density function:

$$p(\phi_{a,b}|\mu_{ab},\kappa_{ab}) = \frac{1}{2\pi I_0(\kappa_{ab})} e^{j\kappa_{ab}\cos(\phi_{a,b}-\mu_{ab})} \quad (2)$$

where $-\pi \le \theta \le \pi$, $\kappa_{ab} \in [0, \infty)$ is the concentration parameter, $\mu_{ab} \in (-\pi, \pi]$ is the mean offset between the two oscillators and $I_0(\kappa_{ab})$ is the modified Bessel function of zeroth order.

Since sample PLV captures only pairwise phase interactions, it is not suitable to separate direct and indirect connections in the case of multiple oscillators. In the following we present non-parametric and parametric extensions of PLV for multivariate case.

2.2. Non-parametric Partial PLV

Schelter et al. [3] proposed inverting the matrix of pairwise PLVs to compute a non-parametric partial PLV. This is motivated by the analogous inversion of cross-correlation and cross-spectral matrices to compute partial correlation and partial coherence, respectively [10]. First, the matrix of pairwise phase synchronization indices is constructed such that $P_{mn} = \mathrm{E}\left[e^{j\phi_{m,n}}\right]$, where $m, n \in \{1, \cdots, M\}$ and M is the total number of oscillators.

Then, inverting matrix $\mathbf{P}$ and normalizing with the diagonal elements leads to the partial PLV:

$$PPLV_{\text{nonparam}} \triangleq \frac{\left(\mathbf{P}^{-1}\right)_{ab}}{\sqrt{\left(\mathbf{P}^{-1}\right)_{aa}\left(\mathbf{P}^{-1}\right)_{bb}}}. \tag{3}$$

Since the above expression is based on the sample bivariate PLV, it is a non-parametric estimate of partial PLV.

2.3. Parametric partial PLV Using the Multivariate Circular Complex Gaussian Model

In this paper we introduce a parametric measure of partial PLV using the multivariate circular complex Gaussian model. Given jointly Gaussian, zero mean, time series $s_i(t)$, $i = \{1, \cdots, M\}$, $j = \sqrt{-1}$, the analytic random vector $\mathbf{z}(t)$ is constructed with elements

$$z_i(t) = A_i(t) e^{j\phi_i(t)} \tag{4}$$

where $A_i(t) = \sqrt{s_i^2(t) + \tilde{s}_i^2(t)}$ and $\phi_i(t) = \tan^{-1}(\tilde{s}_i(t)/s_i(t))$ are the instantaneous amplitude and phase of $s_i(t)$, respectively, and $\tilde{s}_i(t)$ is the Hilbert transform of $s_i(t)$. Again we drop the time index t for convenience. The probability density function of $\mathbf{z}$ is circular complex Gaussian distribution [5]:

$$p(\mathbf{z}) = \frac{1}{\pi^2 |\mathbf{K_z}|} \exp\left\{-\mathbf{z}^H \mathbf{K_z}^{-1} \mathbf{z}\right\} \tag{5}$$

where $\mathbf{K_z}^{-1}$ is the inverse covariance matrix of $\mathbf{z}$ with mn-th entry $\kappa_{mn} e^{j\mu_{mn}}$,$\kappa_{mn} = \kappa_{nm} > 0$ and $-\pi < \mu_{mn} = -\mu_{mn} < \pi$.

For $M > 2$, let $\mathbf{z} = \begin{bmatrix} \mathbf{x} \\ \mathbf{y} \end{bmatrix}$ where $\mathbf{x} = \begin{bmatrix} z_1 \\ z_2 \end{bmatrix}$ and $\mathbf{y} = \begin{bmatrix} z_3 & \cdots & z_M \end{bmatrix}^T$; then the distribution of $\mathbf{x}$ conditioned on $\mathbf{y}$ is also circular Gaussian with conditional inverse covariance matrix $\mathbf{K}_{\mathbf{x}|\mathbf{y}}^{-1} = \begin{bmatrix} \kappa_{11} & \kappa_{12} e^{j\mu_{12}} \\ \kappa_{21} e^{j\mu_{21}} & \kappa_{22} \end{bmatrix}$. Hence, the conditional distribution can be written as:

$$p(\mathbf{x}|\mathbf{y}) = p(z_1, z_2 | z_{\mathcal{M}}) = \frac{1}{\pi^2 |\mathbf{K}_{\mathbf{x}|\mathbf{y}}|} \exp\left[\mathbf{x}^H \mathbf{K}_{\mathbf{x}|\mathbf{y}}^{-1} \mathbf{x}\right] \tag{6}$$

where $\mathcal{M} = \{3, \cdots, M\}$. We represent this in terms of phases and amplitudes as $p(\phi_1, \phi_2, A_1, A_2 | \phi_{\mathcal{M}}, A_{\mathcal{M}})$. Further conditioning on A_1 and A_2 reveals the distribution of the pair-wise phase conditioned on all the other variables.

$$p(\phi_{1,2} | A_1, A_2, A_{\mathcal{M}}, \phi_{\mathcal{M}}) = \frac{1}{2\pi I_0(-2\kappa_{12} A_1 A_2)} e^{-2\kappa_{12} A_1 A_2 \cos(\phi_{1,2} - \mu_{12})}. \tag{7}$$

This is a von Mises distribution with coupling parameter $-2\kappa_{12} A_1 A_2$, verifying that the distribution of relative phase is a function of amplitudes and thus not independent of amplitude. As a final step we marginalize with respect to (A_1, A_2) to compute the parametric partial PLV:

$$\begin{aligned} PPLV_{\text{param}} &\triangleq \left|\mathrm{E}\left[e^{j\phi_{1,2}} | \mathbf{A}_{\mathcal{M}}, \phi_{\mathcal{M}}\right]\right| \\ &= \left|\frac{\pi}{\sqrt{2}}\left(1 - \frac{\kappa_{11}\kappa_{22}}{\kappa_{12}^2}\right)\left[w^{3/2} {}_2F_1\left(\frac{3}{4}, \frac{5}{4}, 1, w^2\right)\right.\right. \\ &+ \left.\left.\frac{3}{4} w^{5/2} {}_2F_1\left(\frac{5}{4}, \frac{7}{4}, 2, w^2\right)\right]\right| \end{aligned} \tag{8}$$

where $w = \frac{\kappa_{12}^2}{2\kappa_{11}\kappa_{22} - \kappa_{12}^2}$ and ${}_2F_1$ is the hypergeometric function (derivation of this equation is too long to include here). The data can be re-indexed in order to find the PPLV between any pair of nodes or channels. Since the signals have been band-pass filtered before computing their Hilbert transform, the inverse of the conditional covariance matrix, $\mathbf{K}_{\mathbf{x}|\mathbf{y}}$, effectively corresponds to the partial coherence matrix for that frequency indicating that the partial phase locking value for Gaussian time series is simply a function of the partial coherence, $\kappa_{12}/\sqrt{\kappa_{11}\kappa_{22}}$. To estimate $PPLV_{\text{param}}$, we find the maximum likelihood estimate of the partial coherence and than perform the transformation in (8).

3. RESULTS

3.1. Roessler Oscillator Simulations

Roessler oscillators are commonly used models of weakly coupled stochastic oscillators. To test whether the aforementioned meaures of partial PLV can separate direct from indirect phase relationships, we generated 3 Roessler oscillators ξ_i using the equations as described in [3]:

$$\begin{aligned} \dot{\xi}_j &= \begin{pmatrix} \dot{X}_j \\ \dot{Y}_j \\ \dot{Z}_j \end{pmatrix} \\ &= \begin{pmatrix} -\omega_j Y_j - Z_j + \left[\sum_{i \neq j} \epsilon_{i,j}(X_i - X_j)\right] + \sigma_j \eta_j \\ \omega_j X_j + a Y_j \\ b + (X_j - c) Z_j \end{pmatrix} \end{aligned} \tag{9}$$

where $i, j \in \{1, 2, 3\}$. We set the parameters $a = 0.5$, $b = 0.2$, $c = 10$, $\omega_1 = 1.03$, $\omega_2 = 1.01$, $\omega = 0.99$ and $\sigma_j = 3.5$ for all j and η_j is standard Gaussian noise. Parameters

$\epsilon_{i,j}$ control the amount of coupling from the i^{th} to the j^{th} oscillator and are set such that $\epsilon_{12} = \epsilon_{21} = \epsilon_{13} = \epsilon_{31} = \epsilon$ implying a bidirectional coupling. We also set $\epsilon_{23} = \epsilon_{32} = 0$, so that there is no direct coupling between the 2nd and 3rd oscillators.

We used the above equations to produce time series of $10,000$ samples with sampling interval $\Delta t = 0.02$, and then estimated the sample PLV (1), non-parametric partial PLV (3) and parametric partial PLV (8) between each pair of oscillators. By repeating the above procedure 1000 times, we computed the distribution of the above PLV measures. The corresponding box plots are shown in Fig. 1(a) for the coupling between ξ_2 and ξ_3. Given that the true coupling is zero between ξ_2 and ξ_3, the parametric partial PLV is not only the

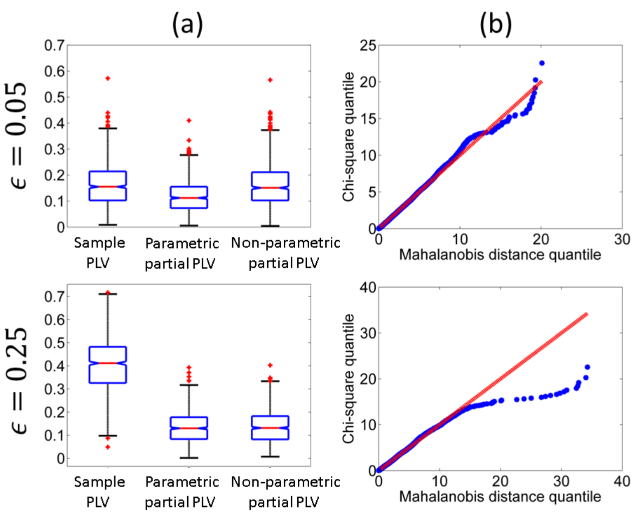
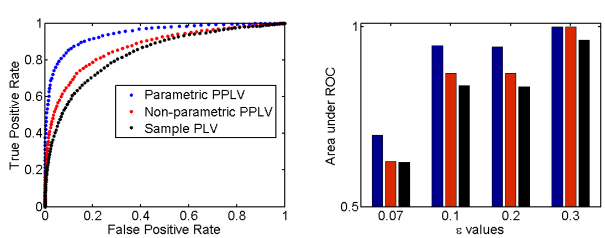


Fig. 1. (a) Estimated coupling between the 2nd and 3rd Roessler oscillators. For each boxplot, the central mark is the median, the edges of the box are the 25-th and 75-th percentiles, and the whiskers extend to the most extreme data points not considered outliers. The true coupling between is zero. (b) Q-Q plot of ranked Mahalanobis distance r_i^2 versus the expected corresponding value of χ_3^2 for the Roessler oscillators.



(a) (b)

Fig. 2. ROC analysis of the Roessler oscillators (a) ROC curves for $\epsilon = 0.2$ (b) Area under ROC curves for different values of ϵ (legend as (a)).

least biased, but also has the smallest variance.

To evaluate whether the signals X_1, X_2, and X_3 are jointly Gaussian, we used an extension of a univariate graphical procedure (Q-Q plot of a Gaussian distribution) to the multivariate case [11]. The Mahalanobis distance:

$$r_i^2 = (\mathbf{X}_i - \bar{\mathbf{X}})^T \mathbf{S}^{-1} (\mathbf{X}_i - \bar{\mathbf{X}}) \qquad (10)$$

where $\mathbf{X} = \begin{bmatrix} X_1 & X_2 & X_3 \end{bmatrix}^T$, will be distributed approximately as a chi-square distribution with 3 degress of freedom if the Roessler oscillators are jointly Gaussian. Multivariate normality is rejected if the Q-Q plot of the ordered Mahalanobis distances versus the corresponding chi-square quantile is significantly non-linear. Fig.1(b) shows that the Roessler oscillators can deviate significantly from multivariate normality, depending on the selected parameter ϵ. Despite the deviation from normality, the parametric partial PLV measure is able to detect the zero direct connection between 2nd and 3rd. The parametric partial PLV performs similarly to the non-parametric one when there is significant deviation from normality as shown in the second row of Fig.1.

We also performed Receiver Operating Characteristic (ROC) analysis to compare the accuracy of methods in detecting coupled versus non-coupled nodes. For the same Roessler system described above, we computed estimates of PLV between ξ_2 and ξ_3 ($\epsilon_{23} = 0$; non-coupled) and ξ_1 and ξ_2 or ξ_1 and ξ_3 ($\epsilon > 0$; coupled). For each threshold value, we computed the false positive and true positive rates, producing the ROC curve given in Fig. 2(a). We then measured the area under the ROC curves for different values of ϵ, as shown in Fig. 2(b). Both plots indicate the non-parametric partial PLV has better performance than the other two methods.

3.2. Local field potentials from a macaque monkey

We performed a similar synchronization analysis to investigate oscillatory interactions of local field potential (LFP) time series, sampled at 200Hz, from a macaque monkey implanted with transcortical bipolar electrodes at 15 sites in the right hemisphere (Fig. 3) while the monkey performed a GO, NO-GO visual pattern discrimination task [12]. In this work, we used only 313 GO trials and focused on 120 msec and 265

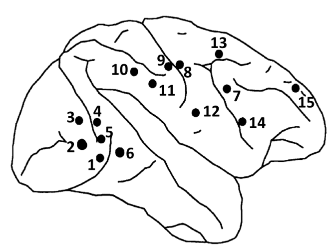
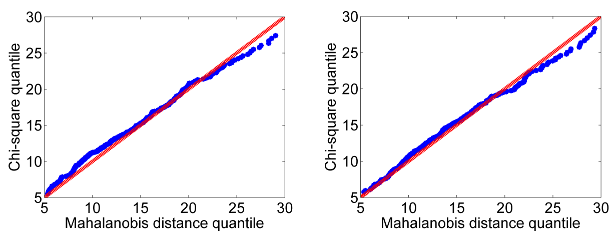


Fig. 3. Right hemisphere of monkey GE, showing positions of 15 cortical recording sites (from [12]).

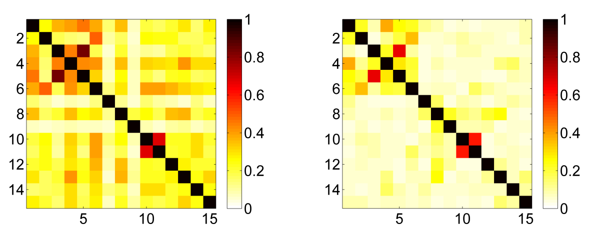
msec after stimulus presentation in the frequency range of $[10-15]$ Hz. Fig. 4 shows the Q-Q plot of ranked Mahalanobis distances versus χ^2_{15} quantiles indicating that the data is approximately Gaussian at time instants 120 msec (early stimulus) and 265 msec (response onset) .

We then calculated channel-to-channel synchrony and repeated the procedure over 500 bootstrap samples of the data to estimate the variance of the PLV estimates. Figure 5 (a-c) shows the mean bootstrapped PLVs. The synchronization network from the bivariate sample PLV is quite different from the partial PLV ones. The synchronization networks from the two partial PLV measures are surprisingly similar, however the standard deviation of the parametric model is somewhat smaller than the non-parametric estimate (Fig. 5(d)).

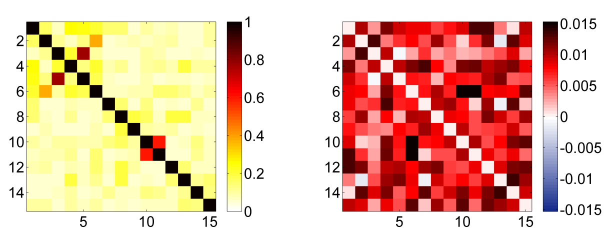


(a) at 120 msec (b) at 265 msec

Fig. 4. Q-Q plot of ranked Mahalanobis distance versus the corresponding quantile of χ^2_{15} for macaque LFP data.



(a) Sample PLV (b) Parametric partial PLV



(c) Non-parametric partial PLV (d) Std $_{\text{nonparametric}}$-Std $_{\text{parametric}}$

Fig. 5. (a-c) Bootstrap mean of the PLV measures. (d) Difference of bootstrap standard deviation of non-parametric minus parametric partial PLV.

4. CONCLUSION

The use of multivariate phase synchrony measures is a valuable approach to detecting interactions in dynamic networks with multiple nodes. We have shown the qualitative difference between bivariate and multivariate approaches both in simulations with Roessler oscillators and macaque monkey LFP data. The parametric partial PLV measure outperformed the non-parametric one in detecting non-coupled nodes when the data was approximately Gaussian (Fig. 1, top). Both measures performed similarly when the data was non-Gaussian (Fig. 1, bottom). ROC analysis further demonstrated that the parametric partial PLV is better able to distinguish direct and indirect coupled Roessler oscillators.

Since the parametric partial PLV is a non-linear function of partial coherence, does not constitute a novel interaction measure. Rather, it provides a new insight into phase synchronization in multivariate networks. When the time series are approximately Gaussian, which is often the case in experimental data, partial coherence and partial PLV contain equivalent information about the system dynamics.

5. ACKNOWLEDGEMENTS

We thank Dr. Steven Bresler of Florida Atlantic University for providing the macaque data used here.

6. REFERENCES

[1] M. Rosenblum, A. Pikovsky, J. Kurths, C. Schäfer, and P.A. Tass, "Phase synchronization: from theory to data analysis," *Handbook of biological physics*, vol. 4, pp. 279–321, 2001.

[2] J.P. Lachaux, E. Rodriguez, J. Martinerie, and F.J. Varela, "Measuring phase synchrony in brain signals," *Human brain mapping*, vol. 8, no. 4, pp. 194–208, 1999.

[3] B. Schelter, M. Winterhalder, R. Dahlhaus, J. Kurths, and J. Timmer, "Partial phase synchronization for multivariate synchronizing systems," *Physical review letters*, vol. 96, no. 20, pp. 208103, 2006.

[4] C.F. Cadieu and K. Koepsell, "Phase coupling estimation from multivariate phase statistics," *Neural computation*, vol. 22, no. 12, pp. 3107–3126, 2010.

[5] NR Goodman, "Statistical analysis based on a certain multivariate complex gaussian distribution (an introduction)," *The Annals of mathematical statistics*, vol. 34, no. 1, pp. 152–177, 1963.

[6] F. Mormann, K. Lehnertz, and P. David, "Mean phase coherence as a measure for phase synchronization and its application to the eeg of epilepsy patients," *Physica D: Nonlinear Phenomena*, vol. 144, no. 3-4, pp. 358–369, 2000.

[7] L. Cohen, *Time-frequency analysis: theory and applications*, Prentice-Hall, Inc., 1995.

[8] J. Bhattacharya, H. Petsche, and E. Pereda, "Long-range synchrony in the γ band: role in music perception," *The Journal of Neuroscience*, vol. 21, no. 16, pp. 6329, 2001.

[9] S.R. Jammalamadaka and A. Sengupta, *Topics in circular statistics*, vol. 5, World Scientific Pub Co Inc, 2001.

[10] R. Dahlhaus, "Graphical interaction models for multivariate time series 1," *Metrika*, vol. 51, no. 2, pp. 157–172, 2000.

[11] C.J. Mecklin and D.J. Mundfrom, "An appraisal and bibliography of tests for multivariate normality," *International Statistical Review*, vol. 72, no. 1, pp. 123–138, 2004.

[12] S.L. Bressler, R. Coppola, and R. Nakamura, "Episodic multiregional cortical coherence at multiple frequencies during visual task performance," *Nature*, vol. 366, no. 6451, pp. 153–156, 1993.