Analysis of Time-Varying Cortical Connectivity In The Newborn EEG

B.Vagya Naik, Addanki Srinu, Dr. V. Venkata Rao ,
PG Student, Department of ECE, Narasaraopeta Engg. College, Narasaraopet, Guntur(D.T),India.
Asst Professor, Department of ECE, Narasaraopeta Engg. College, Narasaraopet, Guntur(D.T),India.
Professor & Head, Department of ECE, Narasaraopeta Engg. College, Narasaraopet, Guntur(D.T),India.
Chinni.vag@gmail.com, Addanki6@gmail.com, venkatarao2k9tec@gmail.com

Abstract : The usefulness of the connectivity measures (such as different types of correlation coefficients, different types of coherence, Granger causality measures etc) for extracting connectivity in adult EEG studies and considering the differences between mature and immature brains, the applicability of these methods for neonatal functional connectivity applications needs to be investigated. This paper aims to evaluate the performance of the time-varying versions of the two popular Granger causality measures, namely Partial Directed Coherence (PDC) and direct Directed Transfer Function (dDTF). Using Dual Extended Kalman Filter (DEKF) as it accounts for both non-stationarity and non-linearity behaviors of the EEG. Using simulated data, we show that fast changing cortical connectivity between channels can be measured more accurately using the time-varying PDC. Neonatal seizure propagation can also be investigated by using time-varying cortical connectivity measures.

Keywords: Granger causality, EEG, PDC, DEKF and dDTF.

I. INTRODUCTION

Investigation on the functional development of the brain structures and their interactions during the maturational age is another interesting topic for research. Since the newborn brain structure is varying during this time period, most of the adult EEG signal processing techniques including EEG source localization approaches are not applicable for the neonatal EEG analysis. Therefore, development of new mathematical tools in time and/or frequency domains to deal with such a time-varying and unstable situation deserves more careful investigation.

II. PREVIOUS WORK

Studies on the dynamical interrelations between different brain structures may potentially identify neural mechanisms of pathophysiological diseases and, therefore, improve clinical interventions [1]. Due to its non-invasive nature, high temporal resolution and low cost, scalp EEG remains the preferred neural activity monitoring tool for investigating temporospatial connectivity of the different cortical areas. In essence, the nature of the transient changes in the newborn EEG is different from that of adults. Many of the neonatal EEG patterns have completely different medical implications than when observed in later ages [1]. Moreover, rapid maturational changes are observed in the newborn brain until early infancy [2]. This imposes high inter- and intra-individual differences in the EEG transients during the neonatal period [3]. In fact, some EEG features that are normal at a certain stage of development become abnormal in a later stage [1]. As a consequence, interactions between the brain regions in neonates differ from those of the mature brain [2].

Multivariate autoregressive (MVAR) process, as a linear representation of multichannel EEG data, is able to model interactions between EEG channels in the form of linear difference equations [4]. By using this EEG representation, not only can the direction of the information flow between channels be inferred, but also the direct or indirect influences detected. Directed Coherence [4], Partial Directed Coherence (PDC) [4], Directed Transfer Function (DTF) [5] and direct Directed Transfer Function (dDTF) [6] are MVAR-based measures which have been introduced to determine directional influence in multivariate systems. The above measures assume that the underlying signals are stationary and that their
Interactions are constant over time. However, EEG signals are non-stationary [7, 8]. This implies that the mutual influence of brain cortical regions and, therefore, those of EEG channels do not necessarily show a stationary behavior. Therefore, time-varying forms of connectivity measures should be used. In this paper, nonstationary PDC and dDTF measures are computed for the simulated data using Dual Extended Kalman Filter to estimate the coefficients of the MVAR model. Then, the PDC measure is extracted from the neonatal EEG signals and the results are discussed. Previous studies have shown that Dual Extended Kalman Filter (DEKF) [9] can accurately track fast changing parameters of MVAR models [10]. The aim of the study is to investigate appropriate time-frequency representations of cortical connectivity during neonatal EEG seizures.

### III. METHODS

**A. The model:** For a time series, a time-varying MVAR model of order $p$ is defined as:

$$
\begin{align*}
[y_2(n)] & = \sum_{r=1}^{p} A_r(n) [y_2(n-r)] + [w_2(n)] \\
y_N(n) & = \sum_{r=1}^{p} A_r(n) [y_N(n-r)] + [w_N(n)]
\end{align*}
$$

The matrices $A_r$ is given by

$$
A_r(n) = \begin{bmatrix}
    a_{21}^r(n) & \cdots & a_{2n}^r(n) \\
    \vdots & \ddots & \vdots \\
    a_{N2}^r(n) & \cdots & a_{NN}^r(n)
\end{bmatrix}
$$

for $r = 1, \ldots, p$. The parameters reflect the time-varying linear relationship between channel $i$ and channel $j$ at the delay $r$. In the stationary case, the optimum order $p$ of MVAR models can be estimated using different methods such as Akaike Information Criterion (AIC) and Schwarz’s Bayesian Criterion (SBC) [11]. The model order selection is not straightforward for time-varying MVAR models, as this order can vary over time. In this study, the optimal model order is estimated using the ARFIT module [11] which evaluates the SBC for a range of $p$ values over the entire data and is kept constant during the process.

**B. Parameter estimation using DEKF**

The DEKF [9] adapts two interlaced Extended Kalman filters, one for state estimation and the other for parameter estimation. The equivalent state space can be presented as

$$
\begin{align*}
(a(n) & = a(n-1) + n_a(n) \\
(x(n) & = F(a(n-1), x(n-1)) + n_x(n) \\
y(n) & = Cx(n) + n_y(n)
\end{align*}
$$

The state $x$ and the output $y$ are assumed to be generated by a nonlinear system of equations.

**C. Time-varying PDC and dDTF measures**

A number of time-varying connectivity measures can be defined based on the following transformation of the MVAR parameters ($A_r(n)$) to the frequency domain:

$$
A(n,f) = 1 - \sum_{r=1}^{p} A_r(n) z^{-r} |_{z=e^{j\omega f}}
$$

The time-varying version of the PDC [4] is defined as:

$$
\pi_{ij}(n,f) = \frac{\text{abs}(A_{ij}(n,f))}{\sqrt{A_{ii}(n,f)A_{jj}(n,f)}}
$$

Time-varying PDC and dDTF can be computed based on the time-varying MVAR model fitted to the signal using Dual Extended Kalman Filtering. A surrogate data method with 50 realizations is then used to select the statistically significant values of the time-varying PDC and dDTF measures at 99% confidence level. All values below the confidence level are set to zero for illustration purposes.

Surrogates are obtained by randomizing all samples of the signal to remove all causal relationships between them [12]. Because of the summation over frequencies in the denominator (Eq. 10), the dDTF function is usually much smaller than one. In this paper, dDTF values are focused in 0 to 0.005 for magnifying the result and obtaining a clear representation.

### IV. RESULTS AND DISCUSSION

**A. Data**

1) **Simulated data**

The data is obtained from a 3-dimensional MVAR(2) process, two damped stochastically driven oscillators ($y_2$ and $y_3$) and a stochastically driven relaxator (Eq. 13). This process has previously been used to evaluate time-varying directed interactions in multivariate neural data [10].

2) **Newborn EEG data**

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Seven monopolar channels (C3, P3, Pz, Cz, O1, T3, T5) out of 14 channels recorded according to the 10-20 standard [13] were selected from a newborn EEG dataset. Beforehand, channel P3 was identified by a matching pursuit-based algorithm [14] as the main location of seizure. Then, P3 and its six peripheral electrodes were selected for further analysis. The results of the source localization will appear elsewhere. The data was recorded using a Medelec Profile system (Medelec, Oxford Instruments, Old Woking, UK) at 256 Hz sampling rate and marked by a pediatric neurologist from the Royal Children’s Hospital, Brisbane, Australia. To decrease the computational load, the data was filtered using a 0.5-30 Hz band pass filter and down-sampled at the rate of 1/8.

B. RESULTS

1) Simulated data

Figure 2 shows the most significant values of both time-varying PDC and dTDF measures at 99% level of significance after applying the surrogate data method. Both representations are able to reflect the time-varying partial connectivity from channel 2 to channel 1 and from channel 3 to channel 1.

However, the dDTF plots represent two extra direct influences from channel 1 to channels 2 and 3, while corresponding PDC measures, multiplication of two smaller than 1 values makes the measure even smaller. In contrast, there is no problem with the time-varying PDC. For a better illustration of the dDTF measures, all significant values are zoomed in the interval of 0 to 0.005 in Fig. 2.

![Fig. 2: PDC (panel a) and dDTF (panel b) of the model using the DEKF. The y-axis represents normalized frequency ([0 0.5] corresponding to [0 Fs/2]) and the x-axis represents time direction in terms of data samples.](image)

2) Newborn EEG data

Due to the superiority of the time-varying PDC compared to the time-varying dDTF illustrated above, only the former measure was applied to the EEG data. Fig. 3 illustrates the time-varying PDC values extracted from a 10-sec ictal EEG epoch.

The optimum AR model order was evaluated by Schwarz’s Bayesian Criterion and fixed to 4 during the analysis. Based on visual inspection of the plots in Fig. 3 for all pairs of channels, a directed path graph can be suggested as the model of the seizure propagation within the seven utilized electrodes for this particular infant (Fig. 4). Note that the relationships within the graph are time-varying.
IV. CONCLUSION

The results presented in this paper show the superiority of the DEKF-based PDC in terms of its ability to track fast parameter changes and at the same time, accurately identify interactions compared to the dDTF using the simulated data. This advantage is valuable for characterizing EEG.

Abnormalities such as seizure in the newborn, during which the dynamics change rapidly [15]. The findings also suggest that the time-varying cortical connectivity analysis may potentially lead to a source localization approach within the inner layers of the newborn brain. This would be a significant development in the neonatal EEG signal processing field of research, as adult EEG source localization methods are not applicable for analysis of neonatal brain interactions [16].

REFERENCES


