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Estimating Cortical Connectivity in Functional Near Infrared Spectroscopy Using Multivariate Autoregressive Modeling

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***Abstract*— Performing cognitive tasks requires close interaction between cortical regions of the brain. Monitoring the functional connectivity during a particular task could contribute to a better understanding of the role and interactions of underlying brain regions. In this paper, we employ time variant Multivariate Autoregressive (MAR) modeling to establish functional connectivity between regions involved in a cognitive task. Data is collected from neonates whose brain activity was monitored by functional Near Infrared Spectroscopy (fNIRS) while being exposed to 2 different types of auditory stimuli. The method was applied to data from 3 subjects on a predefined set of channels known to be involved in auditory and structural processing. The connectivity analysis reveals a common connectivity pattern among the subjects which is neuroanatomically and functionally relevant. Moreover, investigation of temporal evolution of connectivity between temporal and frontal areas shows an increase in connection strength towards the end of the experiment.**

I. INTRODUCTION

The interaction between spatially separated cortical regions plays an important role in performing a cognitive task. Functional imaging methods such as functional Near Infrared Spectroscopy (fNIRS) are capable of detecting activated areas of the brain based on hemodynamic changes associated with increased neural activity. fNIRS is a non invasive optical method for investigating hemodynamic changes in the brain based on changes in oxygenated and deoxygenated hemoglobin. fNIRS is inexpensive, portable and has higher temporal resolution compared to other functional imaging methods such as functional Magnetic Resonance Imaging (fMRI) and is well suited for applications in which subjects movement is inevitable.

Even though functional images acquired by fNIRS can help identify different cortical regions involved in a given cognitive task, possible functional connections and interactions among activated areas are not directly reflected in such images without further processing.

Different methods have been proposed for detecting functional connectivity in the brain. Multivariate Autoregressive (MAR) modeling is a common approach to studying the interaction between brain regions in fMRI [1] and Electroencephalography (EEG) [2]. MAR can establish a direct measure of functional relation between brain regions. Time domain correlation strength between fNIRS channels has been shown to detect resting state functional connectivity in the language system [3]. fNIRS via Gauss-Markov modeling has also been used to study temporal connectivity of prefrontal cortex in adult subjects [4]. Wavelet correlation is also capable of detecting connectivity differences under pathological conditions [5].

We use MAR modeling to measure time varying connectivity between temporal and frontal areas of neonates brain during a neurocognitive study using fNIRS. Higher temporal resolution along with non-confining nature of fNIRS makes it a natural choice for study of functional connectivity and its temporal evolution in infants. Study of connectivity and its changes on infant can contribute to a better understanding of the early learning process.

II. METHOD

An AR model for multichannel fNIRS signal can be written as [6]

$$Y(n) = \sum_{i=1}^{p} A(i)Y(n-i) + \epsilon(n) \qquad n = p \dots N \tag{1}$$

where $Y(n) = [y_1(n)\ y_2(n) \dots y_L(n)]^T$ is the L channel fNIRS measurement at time point n, p is the maximum lag and N is the total number of available samples. $A(i) = [a_{jk}(i)]$ is an L×L matrix in which $a_{jk}(i)$'s are the AR coefficients describing $y_j(n)$ in terms of $y_k(n-i)$. $a_{jk}(i)$ can give a measure of connection in terms of causality between signals in different channels and shows how much of the energy of signal in channel j can be represented by signal in channel k. $\epsilon(n)$ is normal identically and independently distributed noise with zero mean. Eq. 1 can be rewritten as

$$\mathbf{Y} = \mathbf{X}\mathbf{A} + \mathbf{E} \tag{2}$$

where $\mathbf{A} = [A^T(1)\ A^T(2) \dots A^T(p)]^T$ is a (p × L)× L matrix of MAR coefficients at lags 1 to p, $\mathbf{Y} = [Y^T(n)\ Y^T(n-1) \dots Y^T(p+1)]^T$ is an (N-p)×L matrix, and $\mathbf{X}$ defined as

$$\mathbf{X} = \begin{pmatrix} Y(n-1) & Y(n-2) & \cdots & Y(n-p) \\ Y(n-2) & Y(n-3) & \cdots & Y(n-p-1) \\ \vdots & \vdots & \ddots & \vdots \\ Y(p) & Y(n-p-1) & \cdots & Y(1) \end{pmatrix} \tag{3}$$

is an (N-p)×(L×p) matrix.

The maximum likelihood estimator of A is [6]

$$\mathbf{A} = (\mathbf{X}^T\mathbf{X})^{-1}\mathbf{X}^T\mathbf{Y} \tag{4}$$

In order to track possible changes in a_{jk} in the time course of the signal, one can divide the signal into smaller segments and estimate $\mathbf{A}$ in each segment:

$$\mathbf{A}^m = (\mathbf{X}_{s_m}^T \mathbf{X}_{s_m})^{-1} \mathbf{X}_{s_m}^T \mathbf{Y}_{s_m} \tag{5}$$

in which $\mathbf{X}_{s_m}$ and $\mathbf{Y}_{s_m}$ are formed by replacing $Y(n)$ with $Y_{s_m}(n)$:

$$Y_{s_m}(n) = \begin{cases} Y(n), & mW \leq n < (m+1)W \\ 0, & \text{else} \end{cases} \tag{6}$$

in which W is the sliding window width. In other words, we fit the AR model to a small window of the signals. The window is then shifted one sample in the forward direction and the model is fitted again to the data in the new window.

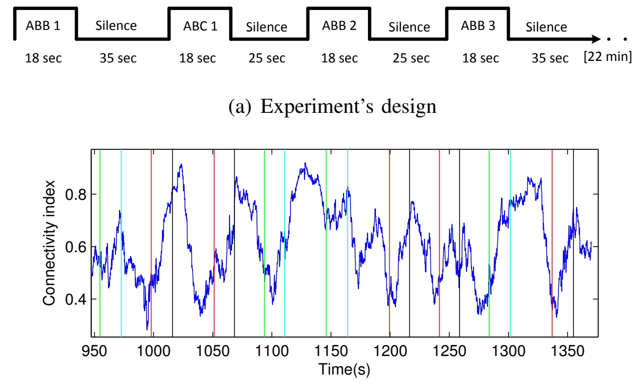
In order to summarize the effect of AR coefficients at different time lags between 2 channels, we define a connectivity index as

$$c_{jk}(n) = \frac{\sum_{i=1}^{p} \tilde{a}_{jk}(i)^2}{\sum_{k=1}^{L} \sum_{i=1}^{p} \tilde{a}_{jk}(i)^2} \tag{7}$$

where $\tilde{a}_{jk}(i)$'s are the elements of $\mathbf{A}^m$. $\sum_{i=1}^{p} \tilde{a}_{jk}(i)^2$ represent the contribution of signal in channel k in minimizing the prediction error of AR model in channel j. Larger value for this parameter means information in channel k can be used to better predict values in channel j given the past values of both channels. This parameter has also been referred to as Direct Causality (DC) in the literature [7]. The denominator in Eq. 7 is the sum of such effects from all other channels. Normalization ensures comparable values over different subjects. $c_{jk}(n)$ is evaluated for every time window as defined in Eq. 6. We now define the connectivity matrix as $C(n) = [c_{jk}(n)]$. Each element of connectivity matrix $C(n)$ shows the causal effect of channel k on channel j at time point n.

III. Experiment

The purpose of this experiment is to study the changes in functional connectivity in neonates brain when exposed to two different types of audio stimulations. The experiment was originally designed to study the ability of neonates to learn simple underlying structures in speech [8]. To establish the feasibility of our method, we applied it to 3 representative cases from the original study [8]. The selected subjects were all female with ages 2,3 and 4 days, respectively. Informed consent was acquired from parents when the experiment was being conducted. The study design was approved by the ethics committee of the Azienda Ospedaliera Universitaria di Udine, Italy where the experiments were conducted [8]. During the 22-25 minute long testing session, audio stimulus was administered to subjects while the subjects were in state of quiet rest or sleep. The audio stimuli consisted of consonant-vowel syllables organized into syllable pairs and were divided into 2 major "grammar" groups named "ABB" and "ABC" based on their syllables repetition order. Each grammar was presented in blocks of 18 seconds long



(a) Experiment's design

(b) Representative connectivity index

Fig. 1. Experiment design and a representative connectivity index (between channels 2 and 5 for subject 3). Red and green lines denote the beginning of the ABB and ABC blocks, while cyan and black indicate the end of blocks.

followed by a silence of randomly varying duration (25-35 seconds). A total of 14 blocks for each stimulus was presented. Figure 1(a) shows the experiment design.

The hemodynamic changes associated with increased neural activity in response to the 2 types of stimuli were monitored by an fNIRS device (24 channel Hitachi ETG-4000 machine with 695 and 830 nm lasers, interoptode distance of 3 cm and sampling rate of 10 Hz). The optode placement and the location of channels is shown in Figure 2. The tragus and the vertex were used as landmarks for optode positioning to ensure data is recorded from perisylvian and anterior brain regions.

Earlier study using the same dataset indicated that subjects were capable of discriminating between grammars [8]. The discrimination was indicated by significant increase in oxygenated hemoglobin in response to one type of stimulus in temporal and frontal regions of neonates brain. The temporal region is known to be responsible for auditory processing in infants [9] while the frontal areas are responsible for computation of structure and higher order representations in infants and adults [9]. Since the process of learning the grammar types involves 2 spatially separate areas of the brain, it is natural to assume a functional connectivity network should be involved. The purpose of current pilot study was to use the data collected in the same experiment and detect possible changes in such connections as a result of exposure to stimuli using the proposed method.

Before applying functional connectivity analysis, raw optical data collected by fNIRS device was converted to changes in oxygenated and deoxygenated hemoglobin concentration using Modified Beer Lambert law [10]. The signals were highpass filtered to remove any overall trend in the signals. A window of length 200 samples (20 seconds) was used to estimate AR coefficients in each step according to Eq. 6.

Channels 1 to 6 on the left hemisphere were chosen to study the functional connectivity. This choice is based on the fact that temporal region (represented by channels 3 and 6) and frontal region (represented by channels 2,5 and possibly 1) are the major areas involved in processing audio

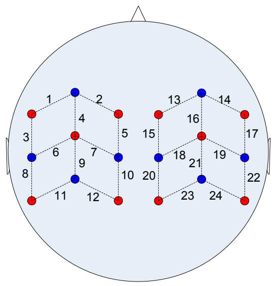


Fig. 2. Top view of fNIRS optode holder overlaid on schematic representation of neonates head. The red and blue dots indicate the source lasers and detectors, respectively. The numbers between the dots are the channel numbers. The optodes are placed such that they sample data from perisylvian and anterior brain regions.

stimuli and processing structures, respectively. Earlier studies have also shown that language function is left hemispheric dominant [8] [11]. Therefore, we limited our study to the left hemisphere only. Also, only oxygenated hemoglobin changes were used for this study. It has been shown that oxygenated hemoglobin is more sensitive to regional cerebral blood flow changes [8] [12].

MAR model is estimated for channels 1-6. We are interested in overall connectivity difference between conditions (grammars), which means a function of $C(n)$ must be used to summarize the connectivity matrix in each block for the conditions. We use simple averaging as

$$\bar{c}_{jk}^{B_i} = \frac{1}{M} \sum_{n \in B_i} c_{jk}(n) \tag{8}$$

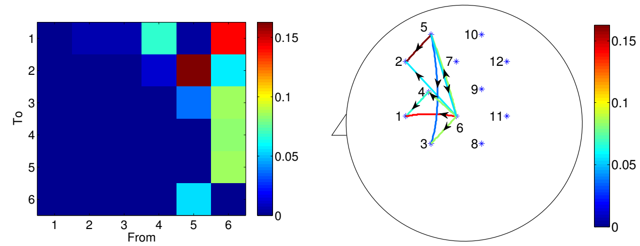
to form $\bar{C}^{B_i} = [\bar{c}_{jk}^{B_i}]$ where B_i is the ith block of condition B, where B is either type "ABB" or "ABC". M is the total number of calculated matrices in the block.

The resulting connectivity matrices $\bar{C}^{B_i}$ are grand averaged to yield overall connectivity matrix for each condition in every subject. Blocks involving motion artifacts are excluded from this procedure. Motion artifacts are identified by changes larger than 0.5 mMol.mm/s in the concentration changes.

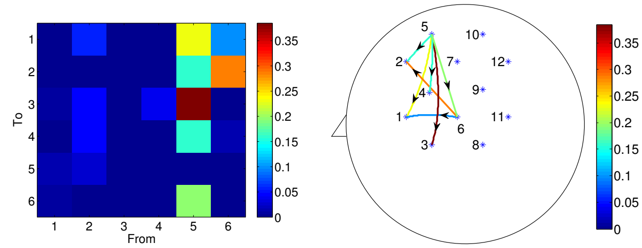
IV. Results

Figure 1(b) shows a representative connectivity index between channels 2 and 5 ($c_{52}(n)$). The duration of each stimulus is indicated by vertical lines. The figure suggests that the connection between the 2 channels becomes stronger when the stimulus is being presented.

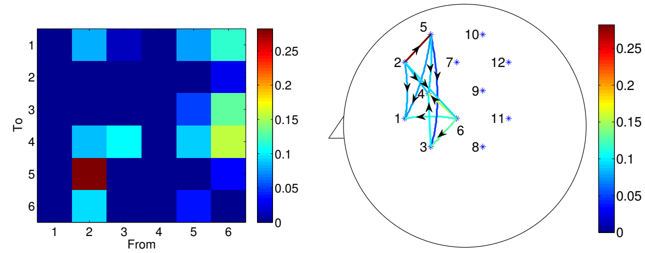
Figure 3 shows the connectivity matrix for 3 test subjects. Self connections are not shown in the figure. Connections with strength of less than 15% of maximum strength in each subject are not shown in the connectivity network in the right panels of figure 3. In order to differentiate conditions, overall connectivity matrix for condition "ABC" is subtracted from that of condition "ABB" to yield the difference in average connectivity between 2 conditions. This difference matrix shows channels whose connectivity is stronger in one



(a) Subject 1



(b) Subject 2



(c) Subject 3

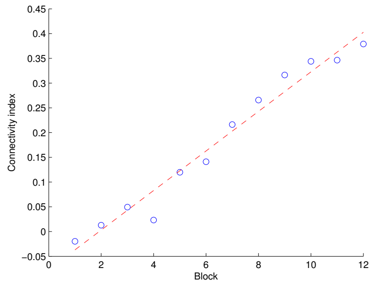
Fig. 3. Connectivity matrices and networks for 3 test subjects. Connection strength is color coded. Only connection paths which are stronger in condition "ABB" compared to condition "ABC" are shown. The rest are set to zero. Figures on the right show a graphical representation of the connectivity network overlaid on a head model (lateral view).

condition compared to the other. This is important as there may be larger and more complicated networks involved in accomplishing a particular task while we are only interested in connections which are stronger for the "ABB" grammar.

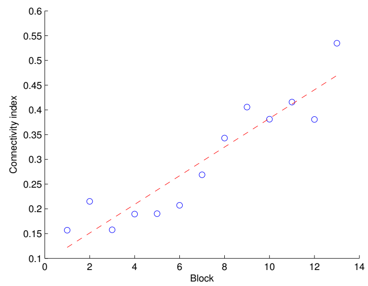
All three subjects demonstrate strong connectivity between temporal and frontal areas. This is indicated by connection from channel 6 to 2 and 5 in subject 1, 6 to 2 in subject 2 and 2 to 6 in subject 3.

Also in subject 1, channel 6 shows strong connection with channels 3 which in turn has connection with channel 5 in temporal region. Possible explanation can be that channel 6 is the lowest/first level of auditory processing, its output feeds into channel 3. The next level of auditory processing, channel 3 then connects with the frontal area, channel 5 for higher level structural processing. This can also be observed in subject 3.

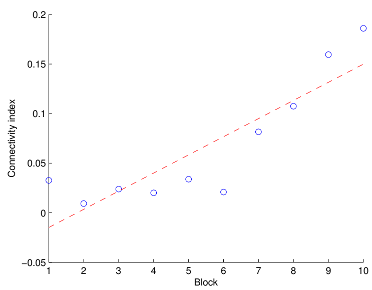
The connectivity matrices provide an overall comparison of functional connections between temporal and frontal areas. Another interesting analysis would be to investigate the temporal evolution of connectivity matrices $\bar{C}^{B_i}$ across the blocks. The hypothesis is that this evolution should be associated with learning in infants and should therefore change as the subjects are exposed further to the stimuli.



(a) Subject 1



(b) Subject 2



(c) Subject 3

Fig. 4. Temporal evolution of connection strength between temporal region and frontal region. For subjects 1 and 2, plots represent connection from channel 6 to 2. For subjects 3, plot represents connection from channel 2 to 6. r^2=0.97, r^2=0.87, r^2=0.76 for subjects 1 to 3, respectively.

We studied this by investigating temporal evolution of connection strength between representative temporal and frontal channels. Channels 6 and 2 are selected as they have strong temporal-frontal connection in all 3 subjects . Figure 4 shows the plots of connection strength vs block number. Each point corresponds to average connectivity strength within a stimulus block. All three subjects show an increase in connection strength in the time course of the experiment.

V. Discussion and Conclusion

We used MAR modeling to identify changes in connection strength in cortical network involved in a speech perception study on neonates. The hemodynamic changes associated with increased neural activity were detected by fNIRS device. The purpose of this pilot study was to detect the changes in functional connectivity in response to exposure to 2 different types of stimuli.

The cortical signals were modeled as a MAR signal in which AR coefficients represented connection strength at different lags. An overall connection strength measure was defined and was evaluated for every block of the 2 stimulus types. The grand average of blocks in the 3 test subjects indicated strong connections from temporal to frontal areas. Connections were also observed from lower level audio processing areas to higher audio processing levels which in turn mediated the connection to structural processing regions.

Another observation was the temporal increase in connection strength for one type of stimulus compared to the other across experiment blocks. This is perhaps associated with learning in the time course of experiment.

The results of the current study are functionally and neuroanatomicaly relevant. However, further validation on a larger number of subjects is required.

VI. Acknowledgment

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