Localizing the Neonatal and Fetal Spontaneous Brain Activity by Hilbert Phase Analysis

Rathinaswamy B. Govindan Member, IEEE, Srinivasan Vairavan Member, IEEE, Naim Haddad, James D. Wilson, Hubert Preissl Member, IEEE and Hari Eswaran, Member, IEEE

Abstract— We propose a novel method to characterize the spontaneous brain signals using Hilbert phases. The Hilbert phase of a signal exhibits phase slips when the magnitude of the successive phase difference exceeds π . To this end we use standard deviation ($\sigma\Delta\tau$) of the time ($\Delta\tau$) between successive phase slips to characterize the signals. We demonstrate the application of this approach to neonatal and fetal magnetoencephalographic signals recorded using a 151-sensor array to identify the sensors containing the neonatal and fetal brain signals. To this end we propose a spatial filter using $\sigma(\Delta\tau)$ as weights to reconstruct the brain signals.

I. INTRODUCTION

Signals from a physical or biological system can be decomposed into amplitude and phase components. The Hilbert transform [1] is a commonly used approach to compute the instantaneous phase of a signal. Using the phases of two signals, it is possible to characterize the synchrony between them and this is a well-established technique [1,2]. Information theoretic measures have been used to quantify the direct and indirect connection between the signals originating from multichannel systems [3]. Phases are less sensitive to the mixing property (smearing of the signal from the local region to neighboring regions), a common problem in spatio-temporal systems such as multi-channel electro/magnetoencephalogram (E/MEG). Hence, to char-

This work was supported by the National Institute of Health, through the following grants, 5R01-NS-36277 and NIBIB/1R01EB0782601A1, USA.

Rathinaswamy B. Govindan, Hari Eswaran and Hubert Preissl are with the Department of Obstetrics and Gynecology, University of Arkansas for Medical Sciences, Little Rock, AR 72205 USA. rbgovindan@uams.edu

S. Vairavan and J.D. Wilson are with the Graduate Institute of Technology, University of Arkansas at Little Rock, Little Rock, AR 72204 USA

N. Haddad is with the Department of Neurology, University of Arkansas for Medical Sciences, Little Rock, AR 72205 USA

H. Preissl is also with the MEG-Center, University of Tuebingen, D-72076 Tuebingen, Germany.

acterize the signals from these systems, techniques involving phases are preferred over other conventional techniques. Here, we propose a uni-variate approach to characterize the signal using Hilbert phases. The phase of a signal exhibits slips when the magnitude of the successive differences exceed π . We use the standard deviation $\sigma(\Delta \tau)$ of the time difference $\Delta \tau$ to characterize the system. We extend this approach to spatio-temporal neonatal and fetal MEG data to identify the sensors containing the spontaneous brain activity. Finally, we propose a construct for a spatial filter using $\sigma(\Delta \tau)$ to reconstruct the brain signals.

II. METHODOLOGY

For a uniformly sampled signal x(t), Hilbert transform h(t) is defined through the following convolution integral:

$$h(t) = \frac{1}{\pi} \text{P.V.} \int_{-\infty}^{\infty} \frac{x(\tau)}{t-\tau} d\tau,$$

where P.V. denotes Cauchyś Principle Value. Basically this integral introduces a phase shift of -90° to the signal x(t). The signal together with its Hilbert transform can be represented as a complex-value analytic function a(n) as follows: $a(n) = x(n) + i \cdot h(n)$, where $i = \sqrt{-1}$ and t = n/sf, n is the sample number and sf is the sample frequency in Hertz. All the calculations reported in this work are done using Matlab (Mathworks Inc. Natick, MA, USA) and the hilbert function in this software directly provides a(n). For the complex-value function a(n), the (Hilbert) phase is defined as $\varphi(n) = \tan^{-1} \{h(n)/x(n)\}$. The Hilbert phase $\varphi(n)$ exhibits slips when the magnitude of the successive difference between the phase exceeds π . We define the time difference between successive phase slips as $\Delta \tau(i) = \tau_{i+1} - \tau_i$. A histogram of $\Delta \tau$ for periodic signals will have a δ -distribution with the peak centered at the periodicity of the signal and with the amplitude equal to the number of such cycles in the signals. Thus, spectral properties can be studied using $\Delta \tau$ and this has been attempted in an earlier work [4] to study spectral content of atmospheric variables. In this work, we quantify the dynamics of the system by computing the standard deviation $\sigma(\cdot)$ of $\Delta \tau$. It is easy to infer that for periodic signals $\sigma(\Delta \tau)$ will be zero and for aperiodic signals it will have nonzero value. For white noise, which is a high frequency process, $\Delta \tau$ will be small and hence $\sigma(\Delta \tau)$ will also be small while for correlated noise (such as EEG) and quasi-periodic signals, $\sigma(\Delta \tau)$ will be large. Thus it is possible to distinguish different types of signals based on the $\sigma(\Delta \tau)$ values [5]. In the next section, we will apply this approach to neonatal and fetal MEG recorded using a 151 sensor array system and identify the sensors that contain the brain signals. Further, we propose a spatial filter using $\sigma(\Delta \tau)$ to reconstruct the neonatal and fetal MEG sources.

III. APPLICATION TO NEONATAL AND FETAL MEG

Neonatal and fetal MEG are recorded using an instrument called SARA (SQUID Array for Reproductive Assessment), which is specifically designed to study the maternal-fetal physiology [6]. This instrument is completely non-invasive, and detects weak biomagnetic fields associated with the electrophysiological activity in the human body. SARA is equipped with 151 primary magnetic sensors with an approximate distance between the sensors of 3 cm and spread over an area of 1300 cm². The sensor array spans the maternal abdomen longitudinally from the symphysis pubis to the uterine fundus and a similar distance laterally. For neonatal studies, a special cradle has been devised that can be attached to the SARA. The neonate is placed in the cradle and its head is rested on the SARA sensors to record the brain signals.

The neurological maturation of fetuses and neonates is traditionally assessed by evoked response study [7, 8]. Another modality for this purpose is the study of spontaneous brain activity (SBA). SBA contains characteristic patterns such as Tracé Alternant (TA), Trace Discontinu (TD), Continuous polyfrequency, etc [9]. These patterns and their frequency of occurrences change with gestational age. Thus, by studying these patterns it is possible to understand the neurological maturation of the neonates and fetuses.

Prior to a SARA study, ultrasound measurements are performed to locate the fetal head and this information is marked on the sensor domain. Based on this information, MEG from a large group of sensors overlaying this

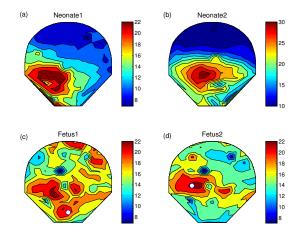


Fig. 1. Results of phase slip analysis of neonatal and fetal MEG. $\sigma(\Delta \tau)$ of the MEG data from the all the SARA sensors is displayed as a contour plot for (a), (b) neonate and (c),(d) for fetuses. White dots in (c) and (d) represent the fetal head position localized using ultrasound measurement.

region is used to study the SBA. The expert neurologists usually score the classical brain patterns by visual inspection. However, it is a tedious process considering the situation of analyzing data from a large group of sensors. Hence, an automated approach to identify the sensors that may contain the SBA would help the experts to restrict their inspection to those sensors and improve the capability to study the neurological maturation. In this work, we propose to use the Hilbert phase slip approach to identify the sensors containing SBA. In the case of neonates, the sensor over which the neonatal head is rested can be easily determined during the study (usually middle and lower sensors) and hence the SBA analysis can be restricted to those sensors. Thus, we can use the neonatal MEG as a test case for our approach and in the next step we apply this approach to the fetal MEG. In this study, we consider MEG datasets of two neonates and two fetuses. The neonatal data are recorded within two weeks after birth (conceptional age varying between 38-45 weeks) and the fetal datasets are recorded during 33 weeks and 36 weeks of gestation (for the details of the data acquisition we refer to [7]). Further, we bandpass filter the data between 1-25 Hz using Butterworth filter with zerophase distortion. Each data is recorded for a period of six minute duration with the sampling rate of 312.5 Hz. The interfering cardiac signals are attenuated offline by signal space projection technique [7]. In some cases, a few (partially attenuated) cardiac traces remain in the data and these are considered as artifacts in the data interpretation. For each data, we compute $\sigma(\Delta \tau)$ for the MEG from all the 151 sensors and present the results in Figure 1 as a contour diagram on the sensor array. Neonates discussed here are mostly asleep during a SARA study. Therefore the MEG signals will be more stationary compared to the fetus (see below). Based on this discussion, one would expect the brain signals to be more localized in the sensors where the neonatal head is positioned and the rest of the sensors being populated by sensor noise. In addition, as the neonatal brain signals are band limited process [10], the sensors containing these signals exhibit higher $\sigma(\Delta \tau)$ compared to the other sensors and it is observed in the results shown in Figure 1(a, b). The region localized by this approach overlaps very well with the sensor region over which the neonatal head rested during the study.

During pregnancy, the fetus tends to move inside the uterus and the fMEG data recorded are prone to be spread across more sensors than localized as shown in the neonates. Figure 1c shows an example of a fetus at 33wk with a larger dispersion in the fMEG signals. The movement in the above fetus is also confirmed from the acceleration patterns in the heart rate. On the other hand, the fetal data shown in Figure 1d corresponding to 36 wk of gestation had less fetal movement and this is evident in Figure 2d as the brain signals are localized over a few sensors. The fMEG signals are also shown to be a band limited process [11], hence one would expect the sensors containing the brain signals to display higher $\sigma(\Delta \tau)$ values compared to the other sensors and is observed in the results shown in Figures 1(c,d). In addition, the fMEG signals localized using this approach are in close agreement with the fetal head position marked using ultrasound measurement (shown as white dots in Figures 1 c, d).

IV. SPATIAL FILTER AND RECONSTRUCTION OF MEG

In this work, we introduce a spatial filtering approach to reconstruct the SBA. The traditional source analysis techniques such as beamformer, will assume a standard model (usually spherical model) and will try to identify the spatial locations that can maximally explain the signals observed in the sensor domain. However, the approach proposed here is entirely based on the sensor data and the information about the source cannot be obtained. In this preliminary study we assume that there is only a single source generating the brain signals but the forward model is unknown. For this purpose we consider the MEG from the top five sensors based on the $\sigma(\Delta \tau)$ values and denote their indexes as κ_i , (i = 1 to 5). The source can be reconstructed by linearly 1 = 1 + 1 + 1 = 1combining the data from these MEG sensors by weighting each one by its corresponding $\sigma(\Delta \tau)$. However, in this case the polarity of the original signals will not be preserved and in effect the features present in the original data may not be found in the reconstructed data. In order to correctly reconstruct the data so as to preserve the polarity, we do the following: Out of these five sensors we select the sensor that displayed highest $\sigma(\Delta \tau)$ and use it as a reference to adjust the polarity of the other four signals. We compute the correlation coefficient (ρ) between the reference and the other four sensors and multiply the $\sigma(\Delta \tau)$ by the sign of the corresponding ρ . In this process, we assign a positive sign for the reference sensor. We use these polarityadjusted $\sigma(\Delta \tau)$ values to construct the weight matrix w, which is a column matrix with n rows (same as the number of MEG sensors). This matrix is initially populated with zeros. The elements corresponding to the indexes in κ are replaced by the modified $\sigma(\Delta \tau)$. To this end we normalize w_i as follows:

$$z_i = w_i / \sum_i^n |w_i|$$

and reconstruct the MEG as S = Xz, where X is a matrix containing the raw MEG data.

Using this procedure we reconstruct the MEG for all four datasets studied in this work and present the results in Figure 2. If the whole reconstructed data is presented, it may not be possible to observe the distinct patterns in them. The raw MEG data is presented to the neurologist to score for the presence or absence of continuous and discontinuous patterns in the data and here we present some of these instances in the reconstructed data. In Figure 2, we present instances of reconstructed MEG containing (Discontinuous) TA and continuous patterns for Neonate1 and Fetus2. TA is characterized by a burst activity interleaved by relative quiescence and the continuous pattern is characterized by the mixture of slow and high frequency waves representing the background activity. The traces from Neonate1 (Figure 2a) and Fetus2 (Figure 2c) exhibit the features of TA and the traces shown in Figure 2(b)and (c) exhibit the features of continuous activity. Thus the signal reconstruction approach proposed preserves the features in the original data.

One can also use the spectral power in a suitable band (e.g. 1-25 Hz) to localize the sensors containing brain signals and thereby to reconstruct the MEG data. Since, it is more sensitive to the amplitude changes,

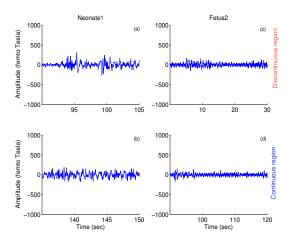


Fig. 2. Traces of reconstructed MEG of Neonate1 and Fetus2. A portion of the reconstructed data containing the TA patterns and continuous data is shown in (a) and (b) for Neonate1 and (c) and (d) for Fetus2, respectively. Due to the longer inter-burst duration in fetus, 30 sec duration of data is presented in (c) and (d).

it cannot distinguish between the partially attenuated cardiac signals and the brain signals and hence it may not be suitable for this purpose. On the other hand, the Hilbert phase is robust to the amplitude changes in the signal and hence it can correctly identify the brain signals.

V. CONCLUSION

A novel approach based on Hilbert phase is proposed to characterize the signal. The feasibility of this approach to identify the brain signals embedded in 151-dimensional MEG data is demonstrated. Based on the Hilbert phase approach, a novel spatial filter is proposed to reconstruct the MEG signal. Currently we are working on the development of a computer based automatic detection of the brain patterns. The MEG reconstruction approach proposed here will be used in the detection scheme to identify the brain patterns.

VI. ACKNOWLEDGMENTS

We would like to thank Dr. Jiri Vrba and Dr. Douglas F. Rose for useful discussions. This work was supported by the NIH grants R01-EB007826 and 5R01-NS-36277. We thank Ms. Jessica Temple for reading the manuscript.

REFERENCES

 P. Tass, M. G. Rosenblum, J. Weule, J. Kurths, A. Pikovsky, J. Volksmann, A. Schnitzler, and H.-J. Freund, Detection of n:m phase licking from noisy data: Application to magnetoencephalography, Phys. Rev. Lett., vol. 81, pp. 3291-3294, 1998.

- [2] J. Gross, P. A. Tass, S. Salenius, R. Hari, H. J. Freund, and A. Schnitzler, Cortico-muscular synchronization during isometric muscle contraction in humans as revealed by magnetoencephalography, J Physiol, vol. 527, pp. 623-31, 2000.
- [3] M. Palus and A. Stefanovska, Direction of coupling from phases of interacting oscillators: an information-theoretic approach, Phys Rev E, vol. 67, pp. 055201, 2003.
- [4] D. Rybski, S. Havlin, and A. Bunde, Phase synchronization in temperature and precipitation records, Physica A, vol. 320, pp. 601-610, 2003.
- [5] R. B. Govindan, S. Vairavan, J. D. Wilson, H. Preissl, J. Vrba, C. L. Lowery and H. Eswaran, Understanding dynamics of the system using Hilbert phases: An application to study neonatal and fetal brain signals. (under review: Phys. Rev. E).
- [6] H. Eswaran, H. Preissl, J. D. Wilson, P. Murphy, S. E. Robinson, and C. L. Lowery, First magnetomyographic recordings of uterine activity with spatial-temporal information with a 151-channel sensor array, Am J Obstet Gynecol, vol. 187, pp. 145-51, 2002.
- [7] M. Holst, H. Eswaran, C. Lowery, P. Murphy, J. Norton, and H. Preissl, Development of auditory evoked fields in human fetuses and newborns: a longitudinal MEG study, Clin Neurophysiol, vol. 116, pp. 1949-55, 2005.
- [8] E. Schleussner, U. Schneider, S. Kausch, C. Kahler, J. Haueisen, and H. J. Seewald, Fetal magnetoencephalography: a non-invasive method for the assessment of fetal neuronal maturation, Br J Obstet Gynaecol, vol. 108, pp. 1291-4, 2001.
- [9] E. M. Mizrahi, R. A. Hrachovy, and P. Kellaway, Atlas of neonatal electroencephalography Philadelphia, PA, Lipincott/Williams & Wilkins, 2004.
- [10] N. Haddad, B. Shihabuddin, H. Preissl, M. Holst, C. L. Lowery, and H. Eswaran, Magnetoencephalography in healthy neonates, Clin Neurophysiol, vol. 117, pp. 289-94, 2006.
- [11] H. Eswaran, N. I. Haddad, B. S. Shihabuddin, H. Preissl, E. R. Siegel, P. Murphy, and C. L. Lowery, Non-invasive detection and identification of brain activity patterns in the developing fetus, Clin Neurophysiol, vol. 118, pp. 1940-6, 2007.