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# Detection of Discontinuous Patterns in Spontaneous Brain Activity of Neonates and Fetuses

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## Abstract

The discontinuous patterns in neonatal magnetoencephalographic (MEG) data are quantified with a novel Hilbert phase (HP) based approach. The expert neurologists' scores were used as the gold standard. The performance of this approach was analyzed using a receiver operating characteristic (ROC) curve, and it was compared with two other approaches, namely spectral ratio (SR) and discrete wavelet transform (DWT) that have been proposed for the detection of discontinuous patterns in neonatal EEG. The area under the ROC curve (AUC) was used as a performance measure. AUCs obtained for SR, HP, and DWT were 0.87, 0.80, and 0.56, respectively. Although the performance of HP was lower than SR, it carries information about the frequency content of the signal that helps to distinguish brain patterns from artifacts such as cardiac residuals. Based on this property, the HP approach was extended to fetal MEG data. Further, using the frequency property of the HP approach,



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burst duration and interburst interval were computed for the discontinuous patterns detected and they are in agreement with reported values.

**Keywords**

Burst duration; fetuses; full-wave rectification; Hilbert phase (HP); interburst interval (IBI); magnetoencephalography (MEG); neonates; tracé alternant (TA); wavelet

## I. Introduction

NEUROPHYSIOLOGIC assessments of neonates and fetuses can offer clinicians important information concerning the presence, severity, and persistence of brain disorders. EEG recordings have been used traditionally in neonates to detect cerebral dysfunction from their characteristic patterns [1]. They are also used to study the neurological maturation based on the evolution of discontinuous brain patterns, namely, tracé discontinue (TD) or tracé alternant (TA) and continuous brain patterns. The percentages of continuous and discontinuous EEG tracings in preterm neonates have been studied by several researchers [2] and references therein. Each reported a decrease in the percentage of discontinuous tracings and an increase in the percentage of continuous tracings with increasing gestational age (GA) or conceptional age (CA). The discontinuous patterns are characterized by the occurrence of bursts of EEG activity alternating with periods of EEG quiescence, namely, interburst interval (IBI). The IBI and the duration of the burst (BD) were also studied [2] as a possible neurological maturational index, and an increase in BD and a decrease in IBI were observed across increasing GA. These studies underline the significance of the detection of discontinuous brain patterns, which can shed light in the assessment of neurological maturation in neonates.

Besides EEG, magnetoencephalography (MEG) was established over the last decades for the recording of human brain activity. This technique is noninvasive and records the magnetic fields corresponding to the electric currents generated by neurons in the brain. Based on the MEG technology, a first-of-a-kind device named SQUID Array for Reproductive Assessment (SARA) was designed and installed at the University of Arkansas for Medical Sciences specifically to study the maternal–fetal electrophysiology. Information about SARA and the recording procedure to acquire neonatal and fetal brain signals can be found in [3] and [4].

Recently, the MEG patterns of healthy neonates were studied, and the classical neonatal EEG patterns, namely, TA, continuous polyfrequency, and continuous slow activity were also observed in the neonatal MEG [3]. The occurrence of discontinuous and continuous brain patterns, similar to EEG studies of preterm neonates at comparable post-CA, was also observed in fetal MEG recordings [4].

Traditionally, neurologists score EEG and MEG brain patterns by visual inspection, which can be a laborious task considering the situations of lengthy and numerous recordings. In the case of fetal MEG, the neurologists are presented with a task of identifying discontinuous patterns of low signal strength, which sometimes might be corrupted with interfering cardiac (maternal or fetal origin) residuals and low-frequency maternal–fetal breathing artifacts. Thus, a computerized procedure capable of detecting discontinuous brain patterns in such an environment would aid the neurologists with an objective assessment of the percentage of their occurrences across GA and enable them to study the neurological maturation. To date, two different approaches have been proposed for the detection of discontinuous patterns in neonatal EEG recordings: 1) spectral ratio (SR) of a full-wave rectified signal to quantify the bursts of activity in discontinuous segments [5] and 2) the use of discrete wavelet transform (DWT)

based time–frequency analysis [6]. However, these approaches have not been tested in MEG datasets.

This paper proposes the use of a Hilbert phase (HP) based approach to detect discontinuous MEG patterns in neonates. The performance of this approach is compared with the other two existing discontinuous pattern detection approaches. To our knowledge, this is the first detailed report on a computerized procedure for the identification of discontinuous patterns in neonatal MEG data together with the statistical validation by comparison with the expert score. Further, the ability of the HP approach to provide the local frequency of the short segments analyzed enables it to clearly distinguish TA bursts from artifacts and to investigate the BD and IBI.

The neonatal brain can be functionally evaluated with EEG; however, fetal EEG is difficult to obtain [4]. Spontaneous MEG recordings are easier to perform, monitor, and interpret in the neonate than at a fetal stage in utero. Neonatal MEG findings can be validated with simultaneous EEG recording, which is not feasible with the fetus. For these reasons, the automated detection algorithm is first tested in a cohort of neonates with the aim of expanding its use to the fetal MEG recordings. Potential benefits of such an algorithm in fetal MEG studies will include the establishment of a maturational index based on the percentage of discontinuous patterns and their corresponding burst- and interburst durations throughout the GAs in utero. Deviations from the normal maturational indexes may serve as an early warning for fetal neurological distress.

## II. Methods

### A. Data Acquisition and Preprocessing

A total of 12 neonatal recordings (used in [3]) and two fetal recordings (used in [4]), each of 6 min duration, were considered for the current study. All neonatal MEG recordings were performed within four weeks after birth with CA ranging from 38 to 45 weeks and the two fetal recordings correspond to 33 and 36 weeks of GA [3], [4]. This study was approved by the local Institutional Review Board. For additional details about the data collection, see [3] and [4].

The interfering cardiac signals were attenuated offline by signal space projection technique [3], [4], and the data was bandpass filtered between 1 and 25 Hz for further analysis. In some cases, a few (partially attenuated) cardiac traces remained in the data and these were considered as artifacts in the data interpretation.

Two board-certified clinical neurophysiologists independently reviewed the spontaneous neonatal and fetal MEG data for discontinuous segments. The best five channels roughly overlaying the neonatal and fetal head region were presented to the neurologists to score for the discontinuous patterns. The scoring procedure employed by the two reviewers involved visual inspection of MEG data in nonoverlapping windows of 15 s (neonatal recordings) and 30 s (fetal recordings) duration for the presence or absence of discontinuous patterns. A larger investigation window was chosen for fetal MEG data to account for the longer IBI in fetal brain activity at earlier GAs [7]. The score for each window was set to 1 if either of the scorers identified a discontinuous pattern while others were set to 0. The scored data were then used for standardizing the automated discontinuous pattern detection algorithm, which was then applied to the entire neonatal and fetal MEG record.

The data from each of these channels were then divided into nonoverlapping windows in order to be consistent with the manual scoring procedure. As mentioned before, the discontinuous patterns are characterized by burst activity intermixed with quiescent periods. Full-wave

rectification approach is used to enhance the high-frequency TA burst activity and facilitate the quantification of TA [8].

In our calculations, the full-wave rectification procedure encompasses a two-step process involving the difference between the successive time points of the data as an equivalent to applying high-pass filter to the data, and followed by the computation of its absolute value. This filter alters the amplitude of the signal. As the primary objective is to detect the bursts, the amplitude reduction in the rectified data will not have an effect on the detection procedure. To this end, the HP-based approach is used to detect the discontinuous MEG patterns.

### B. HP-Based Discontinuous Pattern Detection Algorithm

For a signal $x(t)$, the Hilbert transform $h(t)$ is defined by the following convolution integral:

$$h(t) = (1/\pi)\,\mathrm{P.V.}\int_{-\infty}^{\infty} [x(\tau)/(t-\tau)]\,d\tau$$

where P.V. denotes Cauchy's principal value. The signal together with its Hilbert transform can be represented as a complex analytic signal $a(t) = x(t) + ih(t)$. Using the complex signal $a(t)$, the HP is defined as $\phi(t) = a\tan\{h(t)/x(t)\}$, and thus, the Hilbert transform allows one to study the instantaneous phase of the signal. The HP exhibits slips when the magnitude of their successive phase differences $|\phi(t_{i+1}) - \phi(t_i|$ exceeds $\pi$. The time difference between the successive HP slips ($\Delta\tau$) is characteristic of a system [9]. In the case of periodic signals, $\Delta\tau$ defines the signal's periodicity and standard deviation of $\Delta\tau$, $\sigma(\Delta\tau)$, is zero in such cases. A histogram of $\Delta\tau$ sheds light on the spectral content of the signal and this has been attempted in earlier work to quantify the spectral property of atmospheric variables [10]. In each nonoverlapping window, $\sigma(\Delta\tau)$ is computed for a window of 4 s with 2-s overlap. This procedure was applied to all five channels, which were also used for manual scoring. The presence of the specific pattern quantified by an optimal threshold in two or more channels was considered as a possible TA region. In order to define an optimal threshold, the algorithm was run across 12 neonatal MEG data for several thresholds. For each threshold, the sensitivity and specificity are calculated using the neurologists' scores as the gold standard. A receiver operating characteristic (ROC) curve is constructed and the threshold that has the maximum deviation from the diagonal line is defined as the optimal threshold (see Fig. 3). Fig. 1 shows an example of a neonatal TA and non-TA regions detected by the algorithm.

### C. BD and IBI Calculation

As mentioned before, the HP approach provides information about the frequency content of a signal, and this information is used for the calculation of BD and IBI. A step-by-step procedure for the detection of BD and IBI in the segments identified as a discontinuous pattern is given as follows: 1) the full-wave rectified data were smoothed using a moving average filter with a window of 0.5 s duration; 2) in this data, the time windows corresponding to the local minima of $\sigma(\Delta\tau)$ are located, and the median value of the data corresponding to the time windows is calculated; 3) a baseline is defined as the mean of all the median values; and 4) the signal content above the baseline is investigated for the calculation of the burst durations. Fig. 2 shows examples of BD and IBI calculation for neonatal and fetal discontinuous region.

The signal content above the baseline resembling cardiac residues can be identified based on the duration of the burst. For instance, in Fig. 2, the third column (Fetus IIa) and fourth column (Fetus IIb) show examples of fetal MEG data with a trace of cardiac residue at about 325 and 336 s mark, respectively, in the recording. The signal duration around this region is <1 s, and this can be differentiated from real burst activity located at about 305 and 350 s, respectively.

The baseline definition by $\sigma(\Delta\tau)$ plays an important role in the identification of real bursts against artifacts such as cardiac residues.

On an average, a cardiac residue is usually characterized by a sharp spike with a duration <1 s. Based on this, a limiting threshold of 1 s is used to avoid spurious detection of cardiac residues in the fetal datasets. As the proposed approach analyzes the data in nonoverlapping windows, the BD computed might be hindered if the burst occurs at the beginning or at the end of the analyzed data segment. In order to account for such scenarios, the data in the neighboring windows are also analyzed for BD calculations based on the baseline defined for the current window of investigation. Further, a limiting threshold of a maximum IBI proposed by Scher [11] was used for the IBI calculations.

### D. Performance Comparison

The performance of the HP approach in discontinuous pattern detection is compared with the other two approaches, namely, SR and DWT. A brief description of the other two approaches is given next.

**1) Spectral Ratio—**In this approach, as a first step, the MEG data for each nonoverlapping window are full-wave rectified [5], [8]. The power spectrum of this signal is then computed. In neonates, the number of bursts in TA activity varies from 2 to 12 per minute, which is equivalent to a frequency distribution of 0.03–0.2 Hz. To quantify the TA burst, an SR of the low-frequency (0.03–0.2 Hz, signal floor) to high-frequency (12–25 Hz, noise floor) region is computed as a delineating factor to detect the discontinuous patterns in neonates [5]. The presence of the specific pattern quantified by an optimal threshold (see Fig. 3) in two or more channels of the selected five channels was considered as a possible TA region.

**2) Discrete Wavelet Transform—**The MEG data corresponding to each nonoverlapping window is resampled to 64 Hz so as to wavelet-decompose the signal into the desired frequency bands [6]. The DWT is then applied to the MEG data, which decomposes signals into successive diadic frequency intervals, namely, 32–64, 16–32, 8–16, 4–8, 2–4, 1–2, and <1 Hz. The MEG data corresponding to different frequency bands are then reconstructed using the wavelet detailed coefficients, and spectral estimates of each band are calculated. The spectral estimates of each band in each nonoverlapping window are then normalized by the maximum value of the spectral estimates for all the different frequency bands. This normalized spectral estimate in each nonoverlapping window, which encompasses all the five-channel information, is used for the detection of discontinuous patterns. The normalized spectral estimates in the 4–8 Hz frequency band are investigated across an optimal threshold (see Fig. 3) for the identification of discontinuous patterns.

## III. Results and Discussion

As mentioned before, the proposed algorithm was standardized based on the scores of expert EEG/MEG readers. In order to compare the performance of the three approaches discussed before, an ROC curve analysis was performed across all 12 neonatal datasets.

Fig. 3 shows the ROC curve for the three different approaches. The sensitivity and 1-specificity values corresponding to the threshold that has the maximum deviation from the diagonal line are extracted from the ROC curve and are displayed (black dot) in Fig. 3. The area under the ROC curve (AUC) corresponding to the three approaches, namely, SR, HP and DWT, are 0.87, 0.80, and 0.56, respectively.

It can be seen from Fig. 3 that the HP approach has the highest specificity compared to the other two approaches. This gives an indication that the HP approach more closely resembles the neurologists' scores compared to the other two approaches.

Since the HP approach inherently contains information about the temporal location of bursts, it is possible to easily discriminate the (cardiac) artifacts from TA bursts by means of secondary analysis. This fact makes this algorithm better suited for the detection of discontinuous patterns in the fetal MEG environment. However, in the other two approaches, additional analysis is required to track the temporal location of the bursts. As a part of our initial testing, two fetal datasets corresponding to 33 and 36 weeks of GA were chosen. Considering the small sample size of the fetal datasets, the ROC analysis as computed for the neonatal study was not performed.

The discontinuous segments detected by the HP algorithm in the 12 neonatal and two fetal MEG data were further investigated for the burst- and interburst durations. Among the 12 neonatal datasets, the proposed algorithm did not find any discontinuous regions in four of them. The mean ± standard deviation of the BD and IBI for the remaining eight neonatal and two fetal MEG datasets are shown in Fig. 4. The IBI for the fetal MEG data (33 and 36 week) is significantly longer and it gets shorter with maturation for the neonates, which is evident in the negative correlation across the datasets ($r = -0.27$; $p < 0.01$) [2].

The validation of the algorithm with neonatal MEG data, as shown here, is a crucial step before performing large-scale testing on more challenging fetal MEG signals as the EEG technique cannot be applied during the prenatal period. Our initial application of the automated detection algorithm to fetal datasets has demonstrated the feasibility of extending this algorithm to fetal MEG. The preliminary results with the two fetal datasets were encouraging and should be validated with a larger population to study the neurological maturation.

## IV. Conclusion

An HP-based computerized procedure for the detection of discontinuous MEG patterns in neonates has been presented. The performance of this novel procedure is compared with that of the other two existing procedures, namely, SR and DWT. The feasibility of the HP approach in the detection of discontinuous patterns in fetal MEG data has also been presented. In future work, this approach will be applied to a larger population of fetal MEG data to detect the discontinuous patterns and understand the neurological maturation of the fetus.

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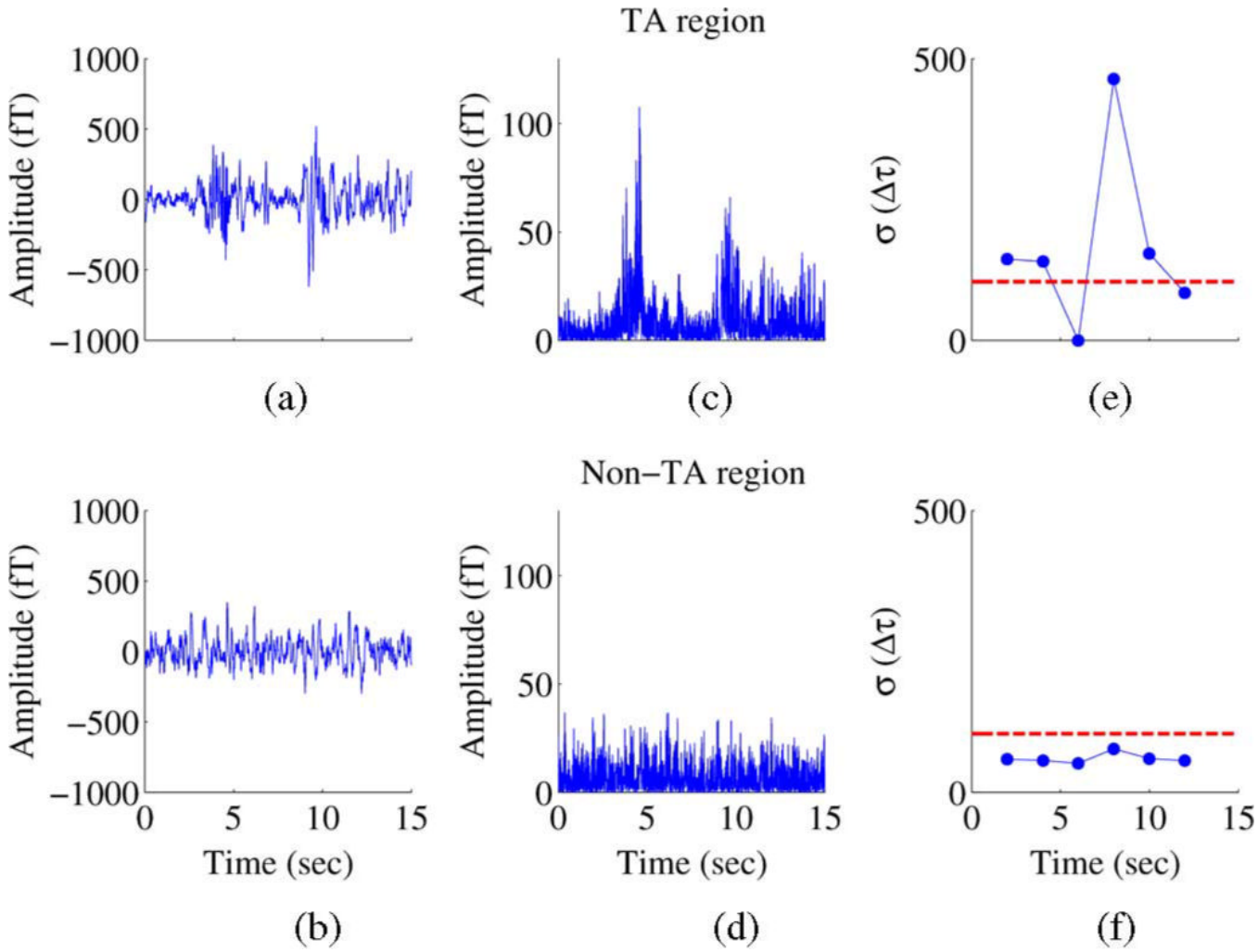


**Fig. 1.**

Representative examples of (a) TA and (b) non-TA regions detected by the algorithm in neonatal MEG data. (c) and (d) Full-wave rectified MEG data. (e) and (f) Corresponding σ (Δτ) and an optimal threshold (see Fig. 3) defined by the dotted line.

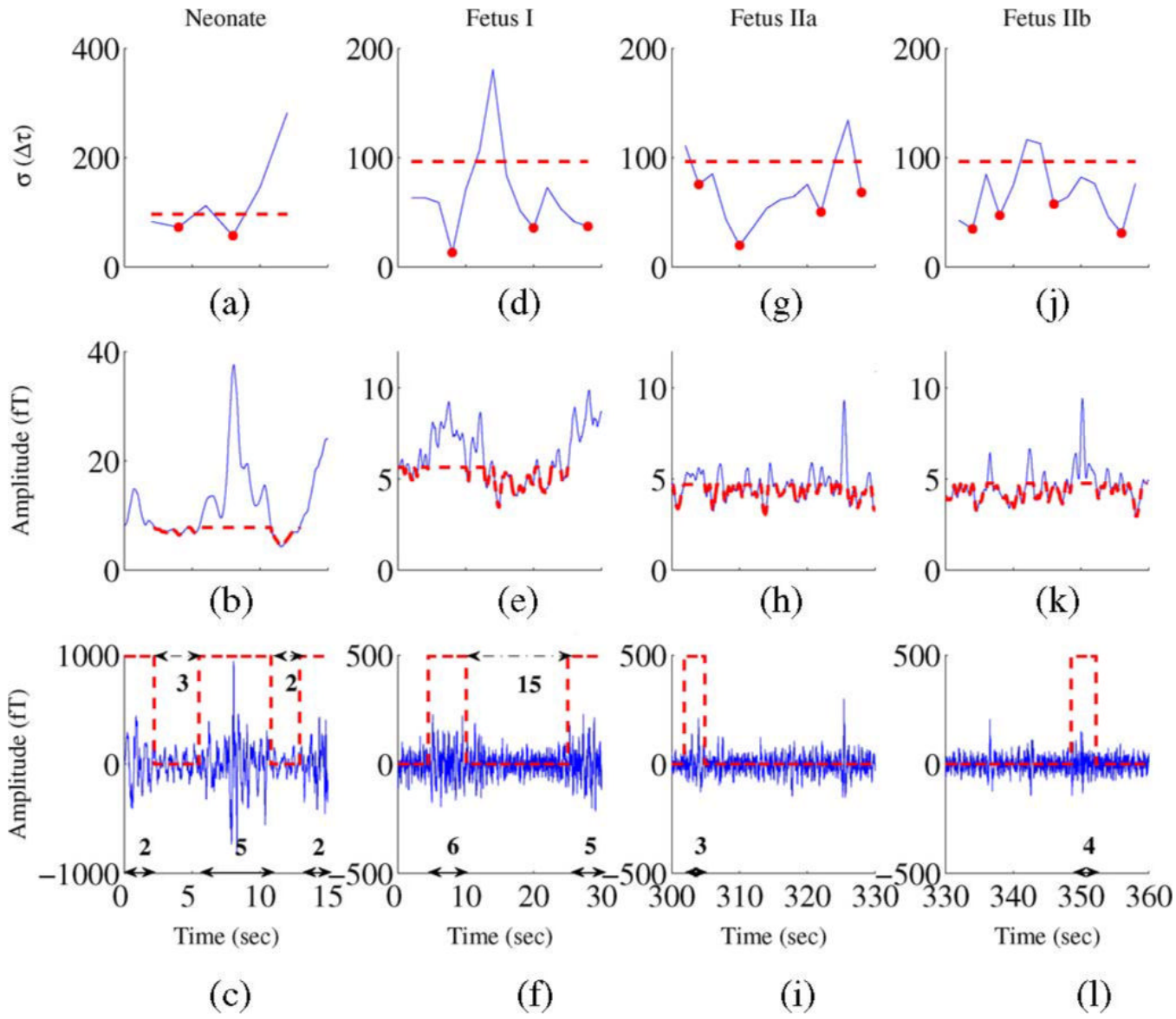


**Fig. 2.**

Detection of BD and IBI in neonatal and fetal discontinuous region. (a) σ(Δτ) computed from full-wave rectified MEG data and the original MEG data is shown in (c) and an optimal threshold (see Fig. 3), defined by the dotted line and local minima marked as dots. (b) Smoothed full-wave rectified MEG data with baseline marked as dotted line. (c) MEG data with highlighted BD and IBI. (d)–(l) Same quantities as plotted in (a)–(c) but for the fetuses. In fetal datasets, the threshold that closely matched with the neurologists' scores in the detection of discontinuous brain patterns is considered as an optimal threshold.

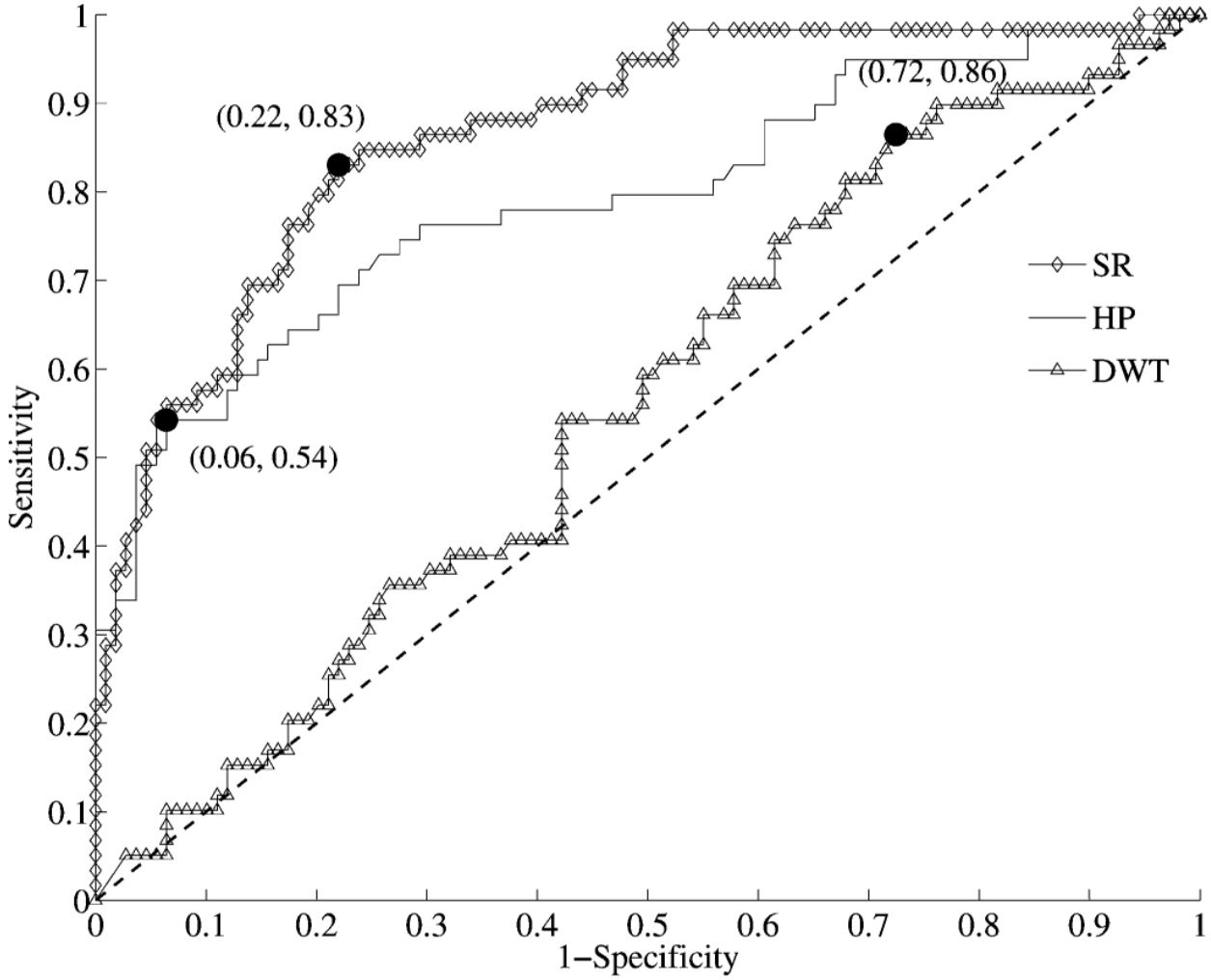


**Fig. 3.**

ROC curve obtained by sweeping the threshold for the different values. The maximum deviation from the diagonal line is marked as a black dot. The threshold corresponding to the black dot in each ROC curve defines the corresponding optimal threshold used in the detection of discontinuous regions in neonatal datasets.

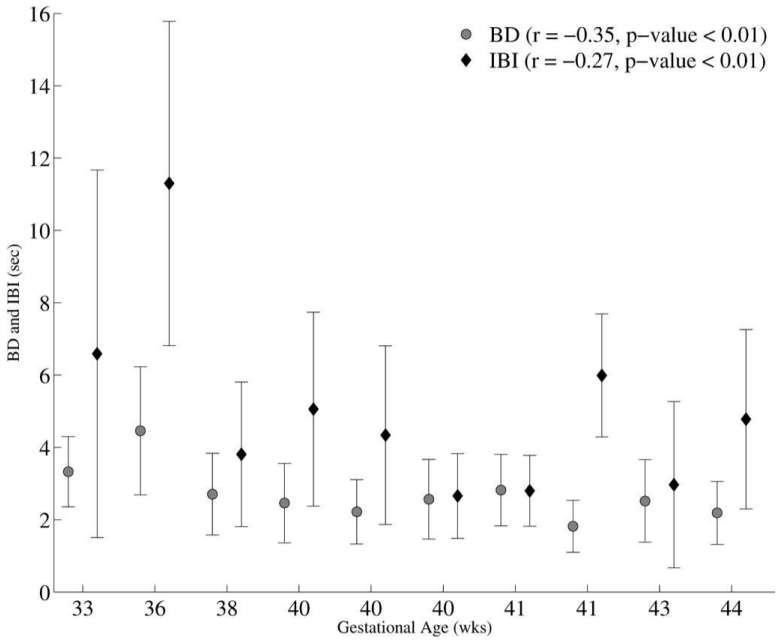


**Fig. 4.**
BD and IBI calculations for neonatal and fetal discontinuous regions.