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TIME-FREQUENCY ANALYSIS OF CTG SIGNALS

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Abstract

Monitoring foetal health is a very important task in clinical practice to appropriately plan pregnancy management and delivery. In the third trimester of pregnancy, cardiotocography (CTG) is the most employed diagnostic technique. In CTG monitoring, foetal heart rate (FHR) and uterine contractions (UC) signals are simultaneously recorded and analysed in order to ascertain foetal health. In particular, indexes related to variability of FHR (FHRV) are usually utilised, which enrich information provided by CTG. FHRV is acknowledged as an important parameter for the evaluation of foetal well-being. Moreover, HR fluctuations analysis allows for a non-invasive estimation of both the sympathetic and parasympathetic branches of the autonomic nervous system (ANS). Hence, one can observe all of the FHRV frequency components and their modifications by applying a time-frequency approach. Time dependent spectrum analysis, in fact, allows for a distinct understanding of the spectral components during dynamic or active foetal states and their change over time. This work aims to show some specific very useful examples of FHRV time-frequency analysis purposes. Furthermore, the necessity of a data pre-processing before FHRV signal processing is considered here. Obtained results showed important modifications of power spectral density (PSD) correlated to different foetal conditions. Hence they confirmed that FHRV provides extremely

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significant information concerning the cardiac and ANS activities. Our results showed also that some important clinical parameters related to PSD of FHRV (such as sympatho-vagal balance) can be erroneously estimated due to a not appropriate storage rate of CTG data.

Introduction

Cardiotocography

Cardiotocography (CTG) is one of the most diffused, non-invasive pre-natal diagnostic techniques, in clinical practice, to monitor foetal health, both in antepartum and intrapartum period. In some countries, it is a medical report with legal value. CTG monitoring has been proved to be useful, especially in antepartum period; since its introduction in the 1960s, electronic foetal monitoring led to a considerable reduction of perinatal morbidity and mortality. It can be used from the 24th week of gestation to delivery. However, in clinical routine, it is generally used from the 35th week. In CTG monitoring, foetal heart rate (FHR) and uterine contractions (UC) are simultaneously recorded by means of two probes placed on the maternal abdomen (a US Doppler probe for FHR signal and a pressure transducer for UC signal) [3].

Cardiotocographic data provides physicians information about healthy foetal development. To assess foetal health and reactivity, gynaecologists and obstetrics evaluate specific clinical signs (average value of FHR, number and kind of accelerations and decelerations in FHR signal, number and intensity of UC and their correlation with FHR modifications, etc.). Interpretation of CTG is generally based on eye inspection of the clinicians. The validity of this diagnostic procedure is still limited by the lack of objectivity and reproducibility. Moreover, important physiological mechanisms, like thermoregulatory oscillations, maturational changes with advancing gestational age, foetal behavioural states and maternal drugs can influence FHR. An incorrect evaluation of foetal status is of course very dangerous. On one hand a falsely diagnosed foetal distress may lead to an unnecessary intervention; on the other hand, an incorrect diagnosis of foetal well-being may deny the necessary care [43].

Therefore, more detailed information about the foetal status are necessary and can be particularly useful during the last period of gestation. To achieve this aim, several analysis methodologies have been proposed in recent years (FHR variability analysis, non-linear methodologies, automatic software, etc. [8, 23, 35, 40]).

Great interest has been dedicated to the variability of the FHR around its baseline, named FHR variability (FHRV), which, like so for adults, could be a base for a more powerful, detailed and objective analysis, both in antepartum and in intrapartum period [2, 9, 33, 34, 39].

FHRV can be analysed both in time domain and in frequency domain. However, the power spectral density (PSD) seems to be the index that best recovers all the information present in the HR series [17]. In particular, due to non-stationary nature of FHR, the time-frequency analysis of the FHRV is generally employed.

As it is well known, time-frequency analysis is a very useful tool, since it allows for a study of all signal frequency components and their modifications over time. In the non-stationary case, the PSD consists of a function that represents the energy content of a series in the time-frequency domain. There exist several methods to estimate it and the method best suited for the PSD evaluation depends on the particular application (often an empirical approach is followed for method choice) [30]. Among most commonly employed methods, parametric and non-parametric, we can mention Short-Time Fourier Transform (STFT); Auto Regressive methods (AR); Fast Recursive Least Square algorithms (RLS) [2, 30, 33, 34].

FHRV time-frequency analysis

In foetal monitoring field, time-frequency analysis is often adopted as a simple, non-invasive tool for investigating the functional state of the autonomic nervous system (ANS) and specifically the autonomic control of the cardiovascular system [14, 47]. For example, foetal HRV response to stimuli can reveal precious information about ANS reaction and compensation, which in turn depends on foetal well-being status. Studies of both term and pre-term infants suggest that new information may be obtained from accurate beat-to-beat HRV analysis.

The aim of this work is to show some very useful examples of FHR time-frequency analysis purposes. Indeed, time-frequency analysis of FHRV has been proved to be a good indicator for the evaluation of foetal well-being and reactivity in non-stress conditions. Foetal reactivity is considered as a very important CTG characteristic to diagnose foetal health or distress but its interpretation is still somewhat uncertain. An improvement can be accomplished characterising foetal reactivity proposing new FHRV frequency domain parameters to distinguish between reactive and non-reactive foetuses and therefore support a more exhaustive CTG analysis [34].

In foetal monitoring, furthermore, as above mentioned, it can be worth investigating eventual FHRV time-frequency modifications of PSD, which reflect foetal ANS activities in response to stimuli.

In particular, spectral analysis provides a tool for quantifying rather small changes in FHRV that may remain undetected if only visual interpretation of FHR tracings is used. Changes in FHR control, elicited by the ANS in response to foetal hypoxia, were for example reported in literature [40, 43].

A UC is a strong compressive stimulus; it provokes an acute hypoxic stress to the foetus and generally elicits reactions in the FHR. It is well known that a FHR deceleration usually follows a UC and this sign is of great interest for physicians. Interest in studying UC reactions is also outlined by recent studies in which UC were elicited by an oxitocin challenge test to explore the consequent blood flow changes [12, 18, 33]. In conclusion, it is worth investigating eventual FHRV spectral modifications, which reflect foetal ANS reactions to UC.

Pre-processing

Before FHR signal processing, it is worth mentioning that FHR signals are intrinsically uneven series; each FHR value is computed as inverse of the time between two consecutive R waves, so that FHR values are available only when new heartbeats occur.

In general, to obtain evenly sampled series, commercial cardiotocographs (e.g., HP-135x) use a zero-order interpolation, that is each sample is held constant until the next heartbeat occurs. Hence, with reference to FHR, if no new foetal beat is detected within a sampling interval (250 ms in HP cardiotocographs, corresponding to a storage rate of 4 Hz), the previous value is held (zero-order interpolation) [13]. This simple process provides FHR data at fixed sampling time instants (i.e., in the same time instants when UC values are recorded), by delaying some samples and adding some duplicates (in the case of missed or undetected heartbeats). This is an efficient solution for FHR time domain or other rough analyses, e.g., to compute classical parameters, such as baseline, accelerations and decelerations, but it is not suitable for frequency analyses because interpolation introduces alterations in the FHR power spectrum [17]. In particular, this interpolation process produces possible artifacts and an attenuation of the high frequency components of the PSD that, for example, affects the estimation of the sympatho-vagal balance (estimated as low frequency/high frequency power ratio), which represents an important clinical parameter [45, 46, 47].

Furthermore, some commercial software, employed for semi-automatic CTG analysis, in order to reduce required space memory and computational time, records CTG data at a lower storage rate (for example, 2 Hz) involving data missing [3].

In order to eliminate the spectrum alterations due to zero order interpolation, and, more generally, to recover the true (unevenly spaced) FHR series from CTG data, the duplicated samples cannot be simply deleted, since duplicated samples can arise by equal subsequent beat-to-beat intervals, so a pre-processing algorithm was developed for this goal.

Materials and Methods

Data collection

CTG were recorded during daily routine foetal monitoring in clinical environments from women between 31st and 41st week amenorrhea, who were in normal course of singleton pregnancy and had taken no drugs; patients laid down in a rest position. At birth, neonatal parameters such as Apgar score, new-born weight, kind of delivery (spontaneous or caesarean), eventual maternal pathologies, etc. had been also collected for eventual further analysis.

Cardiotocographic signals were acquired using HP-135x or Sonicaid cardiotocographs equipped with an ultrasound Doppler probe to detect FHR signal and a pressure transducer to record UC signal.

In HP cardiotocographs, FHR and UC signals are internally stored at 4 Hz (corresponding to a sampling interval of 250 ms), and then transferred to the output serial port of the device that was connected to a laptop PC through a serial (RS232) connection. On the contrary, in Sonicaid cardiotocograph, FHR and UC signals are unevenly stored. Both devices provide a three-level signal which indicates the ‘quality’ of the received Doppler signal, which can result optimal, acceptable or insufficient (the latter corresponding to signal loss).

CTG signals lasting less than 20 min or excessively noisy signals were excluded from our database (at the moment populated by about 600 CTG).

Pre-processing

Real CTG recordings were pre-processed, by means of an algorithm previously developed by the authors, in order to select reliable FHR segments, to eliminate possible artifacts related to the Doppler technique and to get rid of the zero-order interpolation [4, 36].

Summarising, the developed pre-processing algorithm, considering mathematical rules related to the relationship between the possible, real number of duplicate betas and the elapsed recording time recovers the true unevenly spaced FHR series (original beat-to-beat sequence) out of the digital CTG series provided by the device. Moreover, an opportune procedure removes possible cardiac arrhythmia. Next, just for time domain analysis, it replaces unreliable signal tracts lasting less than 4 s using linearly interpolated values. Finally, FHR processed data are uniformly re-sampled at 4 Hz and aligned with UC (within 0.25 s).

Simulation of FHR signals

Synthetic FHR signals were also artificially generated, via software, using a slightly modified version of a method proposed for adults by other authors [5, 24] and already employed in a previous work of the authors [4]. Following that procedure, an artificial R-R tachogram with specific power spectrum characteristics was generated. Considering that in foetal HRV different relationships between the LF and HF bands are present, the following model parameters were adapted to resemble real foetal cases. LF and HF bands of the FHRV power spectrum were considered to lie between 0.04 and 0.2 Hz, and 0.2-1 Hz, respectively. LF/HF power ratio was fixed to 5 and Standard Deviation (SD) of HF band to 0.03. Mean FHR was initially set at 140 bpm (within the range of normality, 120-160 bpm); other values were chosen in the range 80-200 bpm. Finally, a SD was considered superimposed to FHR signal, it was heuristically set at 2 (for more details of the algorithm, please refer to the previous publication [4]).

All simulated FHR signals had duration of 25 minutes.

To simulate commercial devices output, another algorithm was employed, developed for a previous work, to provide a zero-order interpolated version of the artificial series, with a storage rate of 4 Hz (usually employed by the HP cardiotocographs) and their decimated version with storage rate of 2 Hz [3].

FHRV time-frequency analysis

Since FHRV, as for adult, shows a lobed spectrum (in which each component corresponds to a FHR control elicited by the two branches of the ANS - sympathetic and parasympathetic or vagal), we considered FHR power spectrum mainly composed of a DC component (average of the FHR); a very low frequency (VLF) band (0-0.03 Hz), which shows a 1/f characteristic shape; an explicit lobe centred at about 0.1 Hz within low frequency (LF) band (0.03-0.2 Hz), reflecting mainly

sympathetic regulation; and relatively much littler lobes within high frequency (HF) band (0.2-1 Hz), linked to sporadic, transient activities regarding vagal activity [20, 28, 40] (values of frequency bands were adapted from [2, 23, 28, 40, 47]).

DC and VLF represent slow fluctuations of the FHR, related to very slow controls mechanisms (thermal and humoral) and, for a short-term analysis, are better represented in time domain (i.e., baseline and floating-line—running mean and median line of the FHR signal).

To filter out these components from the FHR signals, the baseline and the floating-line [21, 22] were computed (by a smoothing cubic spline) and then subtracted from the FHR signal. Actually, this operation corresponds to a high-pass filtering (about 0.03 Hz) of the signal. By removing such components, the FHRV signals were obtained. We did not consider the VLF band, very slow rhythms, since it is generally necessary to use long recordings (even up to 24 h recordings) to provide sufficient resolution [2].

Because of the non-stationary behaviour of the FHRV signal, a time-varying frequency analysis by means of Short Time Fourier Transform (STFT) had been carried out considering sliding Hamming windows of 128 samples (corresponding to 32 s) and using 99% overlap (window length was chosen accordingly to literature [15]).

Foetal reactivity

We assessed foetal reactivity, in antepartum period, by evaluating PSD characteristics of FHRV extracted from signals recorded in clinical environment. Once the FHR signals were pre-processed, 3 expert clinicians were asked to divide the selected CTG signals into two categories: reactive foetuses (RF) and non-reactive foetuses (NRF). A foetus is defined as reactive if two or more accelerations (an increase in the FHR of 15 bpm during at least 15 s) are identified within a 20 min CTG [25, 37]. The foetus is declared non-reactive if the variability of the FHR is very tiny (less than 5 bpm) even in presence of foetal movements (detected as short, small spikes superimposed onto UC signal). The clinicians classified 75 CTGs as corresponding to RF and 20 to NRF.

According to literature and previous works [22, 35, 44], the FHRV frequency analysis was carried out for each signal using only a 3 min segment (we decided not to use longer portions in order to collect a large number of comparable segments). Our target was to emphasise eventual specific spectrum characteristics only related

to steady physiological mechanisms and not to particular external or internal stimuli. Therefore, the 3 min segment was selected in absence of large FHR alterations (e.g., accelerations and/or decelerations) and other phenomena such as uterine contractions and/or foetal movements; segments were always corresponding to periods of low FHR variability.

After, the PSD grand averages relative to the two categories (RF and NRF) were evaluated. For each category, PSD peak values (expressed in $\mathrm{bpm}^2/\mathrm{Hz}$) and their frequency positions were computed in LF and HF bands. For each frequency range, the mean power (expressed in bpm^2), with SD of the powers corresponding to the different signals, was also evaluated.

PSD modifications corresponding to UC

In research concerning FHR reactions to UC, we also analysed CTG recorded in clinical environment. FHRV time-varying PSD was estimated by means of STFT. Moreover, to concisely describe spectral modifications against time, the power associated with LF and HF bands was computed, for each time instant, $P_{LF}(t)$ and $P_{HF}(t)$, as expressed by:

$$P_{LF}(t) = \frac{1}{T}\int_{0.03}^{0.2} |S(f,t)|^2 df,$$

$$P_{HF}(t) = \frac{1}{T}\int_{0.2}^{1} |S(f,t)|^2 df, \quad (1)$$

where $S(f,t)$ represents the time-varying spectral estimation of the FHRV signal and T is the time interval considered [33].

A synchronised grand-average of the power responses to 127 manifest UC was also computed. In other words, an average of all the LF and HF power signals was performed by aligning these signals with respect to the start of the segments. The average was computed for two kinds of segments, UC segments and reference segments (chosen before the UC onset in absence of stimuli, analogously to methodology described for foetal reactivity analysis). The aim of this operation was to try to highlight a common foetal ANS reaction to UC in a physiological situation.

Finally, we carried out a preliminary analysis to evaluate the maximum frequency contained in the time-frequency spectrum array of FHRV. To this aim, we used the "Modified Crossing Threshold Method", based on D'Alessio's algorithm

[6, 26]. The method considers that the tail of the spectrum gives information on the level of the noise present in the signal, since white noise is equally spread over all frequencies. An estimation of the noise made in the tail of the spectrum is then used for setting a threshold. The magnitude of each bin of the spectrum is compared with the threshold and when the magnitudes of two successive bins are higher than the threshold, the first bin is considered as the maximum frequency bin. We evaluated the noise level using the bins from 25 to 32 of a 128 FFT array (corresponding about to the frequency range .8-1 Hz). The selected frequency range to evaluate the noise depends on the method used in evaluating the FHR and its spectrum array [26], which could substantially modify the far tail of the spectrum. The algorithm threshold is computed multiplying this estimation of noise for an integer factor; we choose a value of 5, which means that the probability value for which a sample crosses the threshold is less than 1% in presence of only noise [6].

PSD alterations due to different CTG storage rates

To quantitatively evaluate distortion of FHRV spectrum due to different CTG storage rates (please, refer to a previous work of the authors for storage rate definition [2]), we employed Lomb method for PSD estimation [17]. In this case, we preferred to consider FHR simulated signals in order to have known, fixed characteristics.

The Lomb method can be used for any transform estimation on unevenly sampled signals.

When dealing with evenly sampled signals its formalism becomes its discrete counterpart, which in the case of the Fourier domain is well studied as the discrete time Fourier transform (DTFT), the discretely evaluated version (DFT) and the associated fast algorithm (FFT) used to compute it. When the signal is accessible only at unevenly spaced samples at t_n instants, the solution has generally been to reduce it to an evenly sampled signal through sampling interpolation. However, as stated above, this process introduces some distortion in the spectrum (or transform). To avoid this problem, Lomb proposed to estimate the Fourier spectra of an unevenly sampled signal by adjusting the model:

$$x(t_n) + \varepsilon_n = a\cos(2\pi f_i t_n) + b\sin(2\pi f_i t_n)$$

in such a way that the mean squared error is minimized with the proper a and b parameters.

About simulated signals, for each mean value of FHR, a set of 90 different FHR signals was generated. FHR signals were grouped in subsets of 30 signals; in particular, 30 uneven FHR signals (for simplicity, here also named series at 0 Hz) and 30 even FHR signals for each storage rate (4 Hz and 2 Hz).

As mentioned, the sympatho-vagal balance (SVB) is a useful clinical parameter, besides, it can be also a helpful index to assess significant differences between PSD estimates. Hence, according to literature [5], we decided to evaluate SVB variations in order to estimate PSD alterations. With regard to SVB computing, LF and HF powers were computed using equations (1), where, of course, $S(f, t)$ represents now the Lomb periodogram. Then, in order to highlight its common trend, we computed mean and standard deviation of all the SVB values, belonging to the same FHR signals subset.

Statistic analysis

A Student's *t*-test was employed to check the statistic separation between the analysed FHRV spectral power populations (for example, between RF and NRF categories in antepartum analysis and UC-segments and the reference-segments spectral power populations in intrapartum analysis; levels of statistical significance were set, respectively, at p value < 0.05 and < 0.01).

The test was carried out separately for both LF and HF bands.

Results

For sake of clearness, we decided to present results in different paragraphs concerning each research goal.

Pre-processing

The developed algorithm was tested using as input sets of 100 different FHR series, lasting 25 minutes, obtained by zero-order re-sampling of the artificially generated series.

Furthermore, to simulate extreme situations, such as severe tachycardia and bradycardia, other sets of 100 artificial FHR series were generated with the mean FHR value set respectively to 200 bpm and to 90 bpm. In addition, to obtain signals resembling other physiological conditions, we simulated also accelerations and decelerations (we adopted the classical definition: accelerations are transient increases of the FHR from the baseline of at least 15 bpm for at least 15 bpm whereas

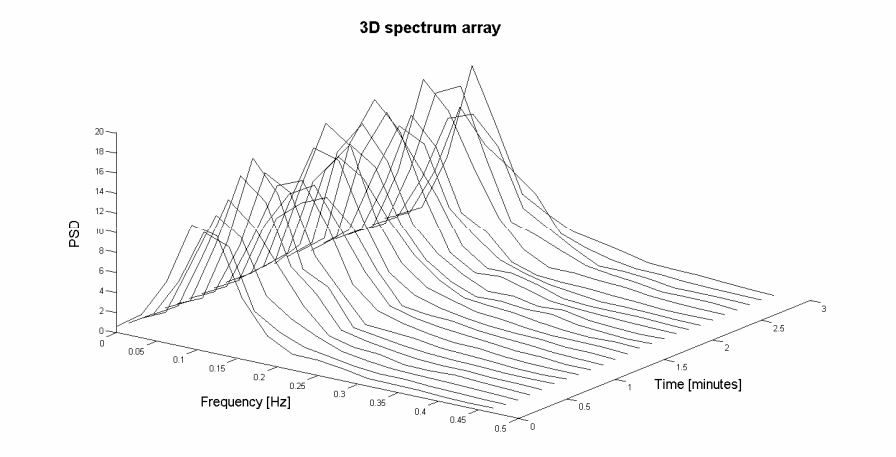
decelerations are transient decrease of the FHR below the baseline level of at least 15 bpm and lasting 15 s or more [10, 22, 42]) by using Gaussian-like signal tracts (with σ heuristically chosen equal to 0.2 and 0.3).

The output recovered series were compared to the artificial FHR series to evaluate existing differences in samples. In all the trials, the algorithm exactly recovered the uneven FHR series, that is no difference, between samples of the artificial and the recovered FHR series, was detected.

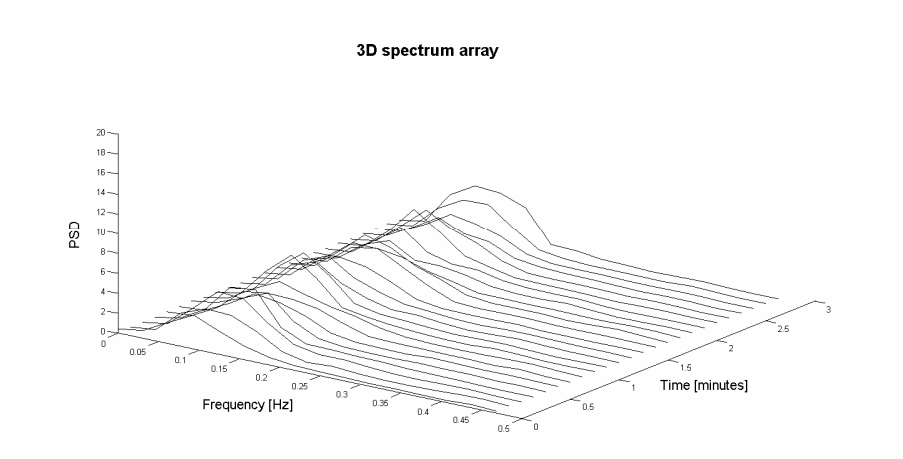
Foetal reactivity

Characteristics of the average PSD of FHRV resulted strongly different between RF and NRF categories, confirming the usefulness of the frequency analysis as a support in distinguishing foetal reactivity. The amplitude of the average PSD related to RF, its peak value and mean power resulted higher than those related to NRF, for each of the analysed frequency ranges (see Figures 1(a) and 1(b) and Table 1 for results relative to LF band). No significant difference was observed in the frequency peak position.

The populations of the average powers of the two categories (RF and NRF), computed in the LF band, resulted not completely separated, but partially overlapped. However, RF population resulted significantly different (*t*-test) compared with NRF population.



(a)



(b)

Figure 1. (a) Average PSD estimated on 75 FHR signals corresponding to reactive foetuses (PSD of RF). (b) Average PSD estimated on 20 FHR signals corresponding to non-reactive foetuses (PSD of NRF). Both PSDs were computed on 3-minutes signal tracts.

Table 1. PSD parameters evaluated for the LF band of FHRV relative to the two signal subsets (RF and NRF)

LF band					
	M = Maximum amplitude of PSD [bpm^2/Hz]	Peak frequency [Hz]	Average power (AP) [bpm^2]	SD of AP	Number of segments
RF	17,920	0,125	1,553	1,140	75
NRF	5,780	0,125	0,412	0,177	20

The average PSD was also computed, for each frequency range, in each week's gestation in the range 37-40. For each week's gestation, in the LF band, the PSD average corresponding to RF was higher than the PSD average corresponding to NRF (see Table 2).

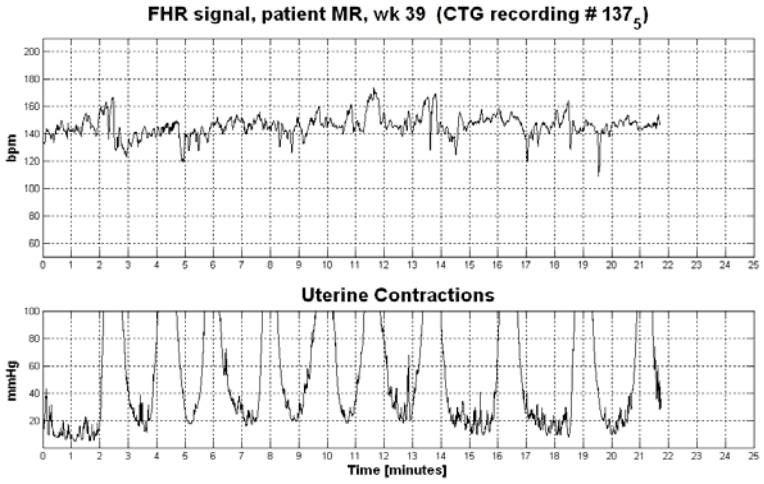
Moreover, the average power shows a slight increase going from 37th to 38th week of gestation and then a slight decrease, both for RF and NRF categories. This result suites with previous literature findings [28].

Table 2. PSD parameters evaluated for the LF band of FHRV relative to the two signal subsets (RF and NRF) and in each week's gestation. Total number of segments is different from that reported in Table 1 since some CTG involved in the average analysis were recorded in weeks of gestation not considered in this analysis

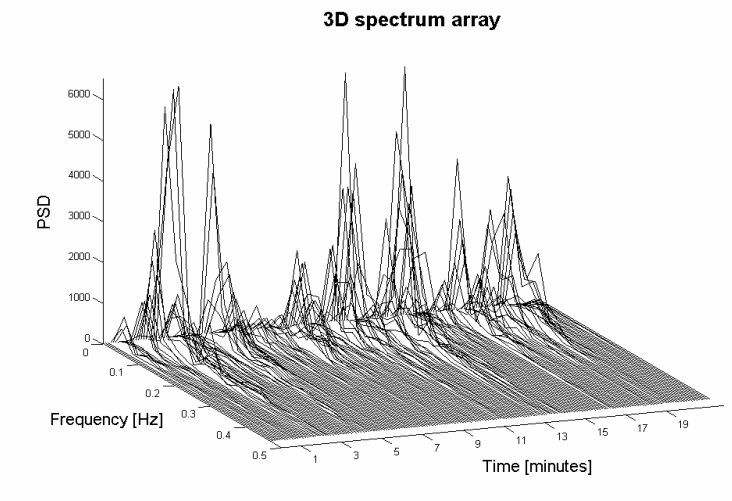
	LF band			
	M = Maximum amplitude of PSD [bpm^2/Hz]	Average power (AP) [bpm^2]	SD of AP	Number of segments
RF – 37th WG	30,510	1,532	1,014	16
NRF – 37th	11,828	0,434	0,177	3
RF – 38th WG	28,772	1,715	1,439	15
NRF – 38th	8,592	0,501	0,188	6
RF – 39th WG	24,342	1,609	1,387	15
NRF – 39th	9,188	0,364	0,266	3
RF – 40th WG	14,144	1,138	0,704	9
NRF – 40th	6,785	0,318	0,043	2

PSD modifications corresponding to UC

As an example, Figure 2 reports a FHRV time-frequency distribution obtained by STFT method (Figure 2(b)) together with the corresponding CTG signal (Figure 2(a)).



(a)



(b)

Figure 2. (a) Example of CTG recording (FHR and UC signals) obtained during delivery at the 39th week of gestation. (b) 3D representation of the time-frequency matrix estimated by means of STFT for the FHR signal shown on the top of Figure 2(a).

As illustrated by Figure 2(b), generally, the maximum amplitude of the LF lobe increases in correspondence of UC.

It is worth noting that the LF power, at about the 8th minute, shows a modification, even if there is not a correspondent clear modification of the floating-line.

Furthermore, to present concise results, obtained average powers of LF band of FHRV power spectrum, estimated both for selected UC segments and reference segments, are reported in Table 3 (for more detailed results, please refer to the previous paper of the authors [33]).

Table 3. Average powers in bpm^2 of LF band computed for the 127 reference and UC segments

	Average LF Power [bpm^2]
Ref. segments	164.86
UC segments	373.75

It is possible to note that average power corresponding to UC-segments is about

twice as value as average power corresponding to reference-segments. Moreover, UC-segments population resulted significantly different compared with reference-segments population for both FHRV power spectrum bands (*t*-test).

Finally, preliminary results obtained by means of Modified Crossing Threshold Method highlighted that an enlargement of the band (shift to a higher value of signal maximum frequency) corresponds to the power increase of FHRV PSD. The following Figure 3 shows an example of obtained results about the comparison between the power increase and the correspondent shift of signal maximum frequency.

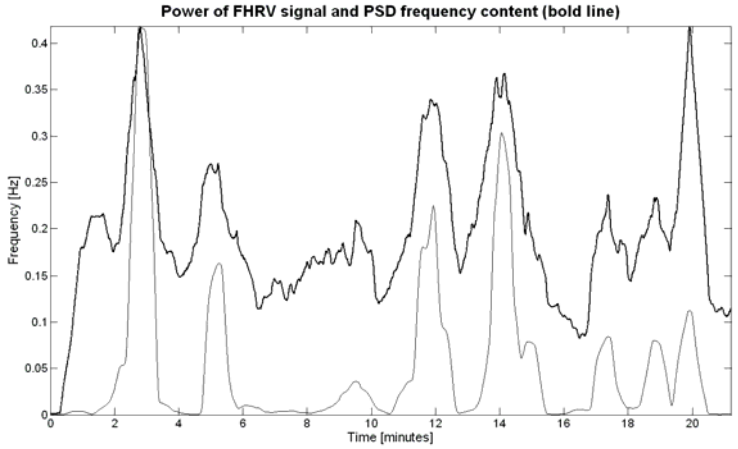
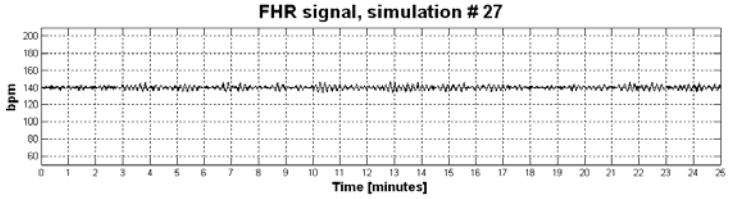


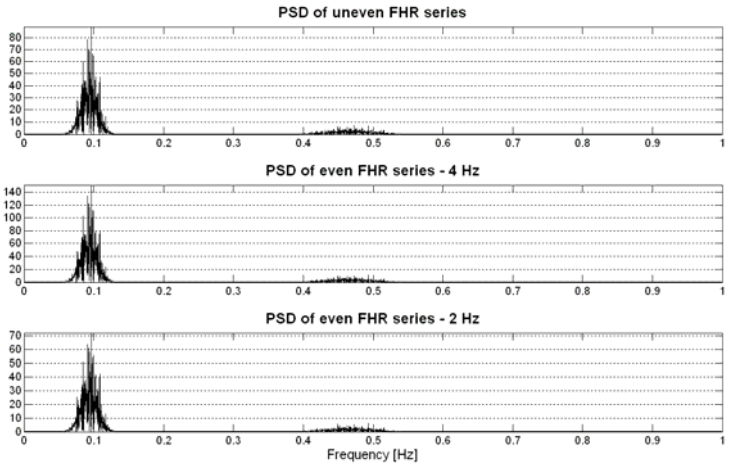
Figure 3. Power of FHRV signal relative to CTG recording #137_5 is here represented in arbitrary units. In correspondence of a power increase a higher value of the signal maximum frequency (bold line), represented in Hz, can be observed.

PSD alterations due to different CTG storage rates

Obtained results showed that different CTG storage rates, employed for the same FHR signal, involved different PSD estimations, as illustrated by the example shown in Figure 4.



(a)



(b)

Figure 4. (a) Simulated FHR signal # 27 (internal numbering of our database). (b) From the top, PSD estimations, by means of Lomb method, of simulated FHR signal #27, its evenly spaced version at 4 Hz and its evenly spaced version at 2 Hz. Amplitude differences are clearly visible in both LF and HF bands.

About SVB assessment, results are concisely presented reporting average SVB values obtained by using the FHR simulated signals and different storage rates. Average score and standard deviation obtained on subset of 30 synthetic signals are reported for each storage rate in Table 4. Just for sake of brevity, only results relative to some different FHR mean value are reported.

Table 4. Average score ± standard deviation, obtained on subset of 30 synthetic signals. Results are reported for each analysed storage rate and for 3 different FHR mean values

SVB values		
FHR mean = 80 *bpm*		
0 Hz	4 Hz	2 Hz
4.73 ± 0.01	5.45 ± 0.01	4.77 ± 0.03

FHR mean = 100 *bpm*		
0 Hz	4 Hz	2 Hz
4.96 ± 0.02	5.46 ± 0.05	4.96 ± 0.04
FHR mean = 140 *bpm*		
0 Hz	4 Hz	2 Hz
4.97 ± 0.02	5.53 ± 0.03	5.16 ± 0.11
FHR mean = 180 *bpm*		
0 Hz	4 Hz	2 Hz
4.94 ± 0.05	5.33 ± 0.07	4.85 ± 0.06
FHR mean = 200 *bpm*		
0 Hz	4 Hz	2 Hz
4.93 ± 0.04	5.42 ± 0.1	4.99 ± 0.2

Discussion

Cardiotocography is an established part of daily obstetric practice, to monitor foetal health, mostly in the last weeks of gestation. Its usefulness is undoubted; nevertheless, there is, still nowadays, substantial intra- and inter-observer variation in the assessment of FHR patterns, related mainly to the visual inspection of CTG, which can lead to intervention when it is not required or lack of intervention when it is. Several analysis methodologies (in time domain, in frequency domain, with semi-automatic software which compute specific time domain parameters, etc.) were proposed in recent years to improve its reliability and objectivity [3, 40].

This is still insufficient to certainly identify suspect or ambiguous conditions. So, great interest was dedicated to the FHRV. It is commonly accepted that the use of a convenient technique for measuring and displaying beat to beat fluctuations is of value for estimating the maturation of ANS and the integrity of the nervous control of heart rate [7]. In particular, frequency analysis of FHRV could be a useful, additional tool [2, 23, 28].

This work presents some applications of FHRV time-frequency analysis which can result very useful in further support foetal health diagnosis.

About foetal reactivity in antepartum period, this work presents a study for

improving the understanding and the interpretation of cardiotocographic data, by means of analysis of PSD characteristics. Sometimes, the foetus is in a healthy status but the CTG does not show, in time domain, characteristics corresponding to the definition of RF. In these situations, clinicians base their diagnosis almost exclusively on their experience. Therefore, it should be advantageous to have a new tool to support diagnosis in such doubtful cases. Preliminary results are satisfying, because they seem to indicate a certain differentiation between RF and NRF categories in frequency domain. This information could be useful to improve the knowledge of foetal condition. However, these results must be confirmed by a more extensive analysis.

Careful monitoring has to be also dedicated to intrapartum period; in fact, while labour is of short duration in comparison to pregnancy, this period is of great risk for the foetus [19]. Therefore, clinicians regularly check FHR and UC to try to identify foetal distress symptoms and adapt the extracting procedure for signs of at-risk. In particular, FHR alterations in correspondence to UC are evaluated, to assess foetal reactivity. However, it is well known that there is still controversy over the interpretation of different FHR patterns, objective clinical criteria to recognise foetal distress by CTG data are still poorly defined, especially during labour [1] and no clear conclusion is still available. Positive predictive value of abnormal intrapartum FHR patterns for foetal acidemia is only around 30% [43], whereas detection of foetal distress, early in labour, may significantly improve newborn's health. Therefore, it is important to try to obtain more reliable and objective methods for CTG interpretation and for neonatal outcome prediction [12, 16, 18, 29, 32, 38, 48]. Besides, literature regarding intrapartum CTG is much less rich than that about antepartum CTG, mainly due to registration difficulties.

In this scenario, analysis of FHRV can provide additional, useful information related to the foetal ANS control of the heart and its compensation capability. Analogously as for adults, specific stimuli can alter heart autonomic regulation and in turn generate specific modifications in the HR, particularly evident in frequency domain. Indeed, a UC is a strong compressive stimulus [11] (intra-uterine pressure can become four times stronger than basal pressure) that severely solicits the immature foetal ANS. This stress causes reactions in the FHR; one of the most evident is a FHR deceleration that usually follows a UC, which is an important sign for physicians. Therefore, a more detailed study of the reaction of foetal ANS to UC such as FHRV spectral analysis may help in the understanding of specific foetal reactivity, capability and modality of foetal compensation to hypoxic stress.

Some researchers groups examined changes in FHRV during UC but the reported results are not in agreement. Some studies, in fact, found that increase in uterine activity is associated with a decrease in FHRV [48]; whereas other studies reported an increase in short-term FHRV during UC [9].

This work presents a study to investigate spectral modifications of the FHRV in response to the external stimulus represented by UC, for healthy foetuses, in order to improve the understanding of foetal ANS reactions to this natural stress and to find possible predictive information about risky foetal conditions.

It is well known that gestational age (related to ANS maturation) considerably affects the foetal hemodynamic responses to stimuli and distress; nevertheless, weeks of gestation were similar in all our recordings so that it is possible to disregard this factor as an additional cause of FHR changes [27, 31].

Our results showed a significant increase of the average power (*t*-test) during UC-segments with respect to the reference-segments.

Moreover, we observed a shift to higher values of the maximum frequency contained in the signal in correspondence of the power increase. So that, we can conclude that the power increase is not due to a specific band enlargement but is spread over all frequencies.

However, these issues deserve a more detailed and exhaustive analysis, for example, involving also cases of foetal distress and aiming to recognise characteristic patterns to distinguish foetal well-being and foetal distress in order to propose such methodology in daily clinical practice.

In spite of the great importance of obtained results in field of FHRV spectral analysis, it is worth stressing that spectral analysis of FHRV often employs methods (such as, for example, the Fast Fourier Transform (FFT)), which require an evenly sampled time series. Instead, the FHRV series is computed from the variations in the beat-to-beat interval timing of the cardiac cycle, R-R series, which is determined at R-wave moments and so intrinsically involves non-equidistant samples. Therefore, in order to achieve an evenly sampled time series from the R-R series, an interpolation and re-sampling is usually adopted. This technique results in unwanted effects in the power spectrum [5, 45] and then alters the results of frequency analyses [17]. To avoid this problem, some researchers proposed the Lomb-Scargle (LS) periodogram as a more appropriate spectral estimation technique for unevenly sampled time series. It is shown to provide a superior PSD estimate respect to FFT

or AR estimate with linear or cubic interpolation and uses only the original data [5, 17].

In foetal monitoring, as more and more times mentioned, the cardiotocography is the most commonly technique employed in clinical routine. Cardiotocographs store FHR signals as evenly spaced series and a zero-order interpolation has usually engaged for this purpose. Moreover, in order to reduce needed space memory and computational time, some commercial software employs a reduced storage rate.

Zero-order interpolation can produce significant errors in the PSD estimation, which can be greater then the errors produced using higher order interpolation [17, 20]. Moreover, the real, uneven FHR series is not available for suitable, satisfactory spectral analysis methodologies (such as LS).

Our results confirmed the assumption that using zero-order interpolation, or other storage rates, generates not neglect errors in PSD estimation and in turn, for example, in sympatho-vagal balance value.

In particular, from achieved results, it is possible to observe that considering SVB value (computed by means of Lomb method) obtained for series stored at 0 Hz (uneven FHR series) as reference, the zero-order interpolation, necessary to obtain series stored at 4 Hz, involves an overestimation of SVB for each FHR mean; whereas, the storage rate at 2 Hz produces an unforeseeable behaviour and when average values are comparable with the reference, there results a significant increase in the standard deviation.

Conclusion

The variability of the foetal heart rate around its baseline provides extremely significant information concerning the cardiac and ANS activities and their functional development during pregnancy up to labour. Our results demonstrated important modifications of PSD related to different foetal conditions. Therefore, FHRV time-frequency analysis could be very useful for a more objective evaluation of the foetal status and capability to react to stress situations. However, FHR signals from cardiotocographic data are often subjected to a zero-order interpolation or other pre-processing steps, which affect the frequency content of the signal. To eliminate the FHR spectrum alterations related to these signal analysis and then for accurate analyses and further researches onto FHR recorded in clinical environment, it can be useful for a pre-processing data tool to recover the true unevenly spaced FHR series from the CTG data, as that developed from the authors [4] and summarised here.

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