Linear and Nonlinear Parameters for the Analysis of Fetal Heart Rate Signal From Cardiotocographic Recordings

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***Abstract*—Antepartum fetal monitoring based on the classical cardiotocography (CTG) is a noninvasive and simple tool for checking fetal status. Its introduction in the clinical routine limited the occurrence of fetal problems leading to a reduction of the precocious child mortality. Nevertheless, very poor indications on fetal pathologies can be inferred from the even automatic CTG analysis methods, which are actually employed. The feeling is that fetal heart rate (FHR) signals and uterine contractions carry much more information on fetal state than is usually extracted by classical analysis methods. In particular, FHR signal contains indications about the neural development of the fetus. However, the methods actually adopted for judging a CTG trace as "abnormal" give weak predictive indications about fetal dangers. We propose a new methodological approach for the CTG monitoring, based on a multiparametric FHR analysis, which includes spectral parameters from autoregressive models and nonlinear algorithms (approximate entropy). This preliminary study considers 14 normal fetuses, eight cases of gestational (maternal) diabetes, and 13 intrauterine growth retarded fetuses. A comparison with the traditional time domain analysis is also included. This paper shows that the proposed new parameters are able to separate normal from pathological fetuses. Results constitute the first step for realizing a new clinical classification system for the early diagnosis of most common fetal pathologies.**

***Index Terms*—Cardiotocography (CTG), fetal heart rate (FHR), fetal pathologies, nonlinear parameters, spectral analysis.**

I. Introduction

HEART RATE (HR) is known to contain reliable indications about the synergic activity of the autonomic nervous system (ANS), which regulates the heartbeat dynamics [1]. A huge number of experimental studies in large populations, both in physiologic and in pathologic conditions, underlined the powerfulness of HR analysis in the noninvasive but quantitative monitoring of cardiovascular control systems [2]. At the same time, parameters from HR signal really differentiate pathological states, providing interesting hints about the generation of the disease conditions.

These HR properties could be particularly useful in monitoring the fetal wellbeing. The analysis of a fetal HR (FHR) signal represents a noninvasive fundamental tool for checking fetal conditions in the antepartum period [3], [4]. As a matter of fact, a major portion of unfavorable fetal outcomes seems due to events occurring before the labor onset [5]. As other studies demonstrate, the FHR signal could provide reliable indications on fetal status: several conditions such as hypoxia, acidemia, and drug induction produce noticeable variations of FHR values, both in the time and in the frequency domain [6], [7]. Moreover, HR measurements and analysis provide a quantitative tool for evaluating the synergetic control activity performed by the sympathetic and parasympathetic branches of the ANS. They represent a powerful method for establishing the development of the nervous system of the fetus during the last period of pregnancy, starting from the 25th week of gestation [8].

Literature results underline that fetal distress that can be preceded by alterations in interbeat intervals before any appreciable change occurs in HR itself [9]. In addition, recent studies on HR signals of adult and newborn subjects emphasize that both linear and nonlinear effects contribute to the signal generation pattern [10], [11]. If observed over long periods of time, the series obtained from the HR values are highly irregular, typical of nonlinear system behavior.

All these results lead to think that FHR regulation mechanisms show an intrinsic nonlinear behavior, i.e., FHR values can highly oscillate in time and not always tend to an equilibrium state or to a sinusal rhythm (or a baseline). Thus, FHR variation contains information on the neural events controlling fetal heart, although the technological and methodological tools used up to now for clinical diagnosis do not extract reliable quantitative indexes linking FHR signal patterns with patho-physiological fetal states.

As far as the technology for FHR recording is concerned with, two main approaches allow the noninvasive measurement of the fetal heart rate signal antepartum. The first one detects both the maternal and fetal electrocardiograms (ECGs) through abdominal leads. Signals are separated through appropriate digital filtering and RR intervals of the fetal ECG are recognized [12]; the second one records the movement of the fetal heart which is externally detected through an abdominal probe via the ultrasound (US)-Doppler method [13].

The first approach presents the disadvantage that sometime it is impossible to extract the fetal ECG from the recording and,

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in any case, the maternal and fetal ECG must be separated offline. However, it allows an accurate although time-consuming identification of fetal RR intervals with better performances in terms of signal-to-noise ratio [12].

The second one is certainly the most diffused technology in the clinical practice. The recent, commercially available fetal monitors use an ultrasound pulse-Doppler method. A pulse, typically consisting of several cycles of 1–2-MHz sinusoids, is transmitted toward the fetal heart. The reflected pulse, slightly shifted in frequency (Doppler shift) by contractions of the fetal heart, is compared with the transmitted pulse (demodulation).

In earlier fetal monitors, beat-to-beat fetal heart rate was calculated using peak detection of the demodulated signal (time T from highest peak in a heart beat to highest peak in the successive heart beat). Since the two heartbeats can have similar multiple peaks, several different time intervals and, consequently, several different FHR values are possible. Moreover peak-to-peak detection lacked in accuracy due to "jitter" (artificial variability) affecting the beat-to-beat FHR. With the introduction of the autocorrelation method, successive heart signals are compared and tested for their similarity. Thus, not one point in time within a heart action, but the total waveform complex, is compared to the following one. The autocorrelation has led the US technology to closely approach the "gold standard" of the direct ECG in detecting the FHR signal [14], [15]. Even with the autocorrelation method, slight movements of the fetus, of the mother, and other sources can change the detected Doppler signal and the obtained FHR signal is often noisy and may contain artifacts, spurious maternal HR and periods with loss of the signal itself. However, although not accurate as the abdominal ECG, this approach guarantees to obtain a FHR signal in almost all conditions and, thus, it provides a recording in most prenatal clinical monitoring sessions.

The US Doppler method, coupled with the recording of uterine activity through an external pressure transducer, is commonly known as "cardiotocography" (CTG). Since its introduction in the clinical routine, the Cardiotocographic (CTG) monitoring has led to a drastic reduction of intrapartum and precocious child mortality [16]. However, although the CTG represents the most widely used noninvasive approach to monitor antepartum fetal conditions, it rarely detects emergencies of fetal pathologies as it has been pointed out by several clinical studies [17]. There are still many problems, which are related to inter and intraindividual variability in reading the CTG tracings and to the methodology employed for judging them. Despite the presence of the International Federation of Gynecology and Obstetrics (FIGO) guidelines, the actual CTG analysis has demonstrated a low predictive value for the fetal danger and very poor indications about fetus/newborn illness [5], [18].

One of the reasons is that obstetric clinicians consider the FHR as composed by a baseline (mean HR) on which the frequency control mechanisms act by provoking some irregularities called accelerations and decelerations [19], [20]. So far, the detection and classification of accelerations and decelerations represent the core of CTG record analysis as changes of that hypothetical FHR base value are supposed to reveal fetal sufferance status. Then, even automatic classifiers try to replicate the criteria adopted by clinicians.

The few existing computerized CTG systems perform also a quantitative assessment of the short-term variability (STV) and long-term irregularity (LTI) together with the calculation of a set of parameters, which evaluate morphologic characteristic of the signal and its changes in the time domain [21], [22]. Results of this implemented algorithmic approach only led to a reduction of inter and intraobserver variability. A previous work, focused on testing the only commercially available system at that time (Sonicaid System 8000) with an initial multitrial research [23], did not show significant clinical improvements from the traditional analysis by eye inspection only. Even important risky conditions for fetal compromise as *intrauterine growth retardation (IUGR)* due to uteroplacental insufficiency and *maternal type I diabetes* did not found an appreciable classification starting from the traditional analysis.

For achieving a reliable classification of FHR patterns, it seems then necessary to adopt new methodological tools considering new indexes more responsive to normal and pathological fetal conditions. In this paper, we propose to introduce few parameters, which are typical of frequency domain and of nonlinear analysis approaches, to improve the diagnostic ability of the traditional time domain cardiotocographic FHR analysis. These parameters allow obtaining a quantitative evaluation of both linear and nonlinear contributions to the FHR generation.

The final goal is to realize a new CTG software for monitoring fetal condition antepartum, based on a multiparametric analysis of FHR, with potential applications to a computerized system of clinical decision making support, in the field of prenatal monitoring.

II. Methods

A. Data Collection

1) Hardware and Software Setup: Because of its great diffusion in clinical prenatal fetal monitoring, we decided to adopt CTG for our FHR analysis, despite its possible lack of accuracy in detecting RR intervals. As explained in the following, the fetal monitor we used was setup in order to achieve a good compromise in terms of heart rate variability (HRV) bandwidth and accuracy.

FHR signals have been recorded by means of a Hewlett Packard M1351A CTG fetal monitor, linked with a PC computer through a RS-232 serial port. The US transducer transmits 998.4-kHz ultrasound bursts. The burst widths are controlled by software with a repetition rate of 3.2 kHz and the received echo is amplified by a high-frequency amplifier with a gain of 120. The demodulator is controlled by software in its receive window. The demodulated signal is bandpass filtered (100–500 Hz) and it is amplified by a software-controlled gain.

The series HP-135x fetal monitors use an autocorrelation technique to compare the demodulated Doppler signal of a heartbeat with the next one. Each Doppler signal is sampled at 200 Hz (5 ms). The time window over which the autocorrelation function (ACF) is computed is 1.2 s, corresponding to a FHR lower bound of 50 beats per minute (bpm). A peak-detection

software then determines the heart period (the equivalent of RR period) from the ACF. With a peak position interpolation algorithm, the effective resolution is better than 2 ms [24]. The resulting heart period is then converted into a heart frequency as soon as a new heart event is detected and accepted.

Due to historical reasons, almost all commercially available fetal CTG monitors display only the FHR expressed in number of bpm, and do not offer the series of interbeat intervals, usually employed in HRV analysis.

The HP 1351A produces a new FHR value in bpm every 250 ms and stores it in a buffer. In the commercially available system, the PC reads ten consecutive values of the buffer every 2.5 s and determines the actual FHR as the average of the ten values (corresponding to a sampling frequency of 0.4 Hz). We modified the software in order to read the FHR from the buffer at 2 Hz (every 0.5 s). This allows increasing the FHR Nyquist frequency up to 1 Hz. The disadvantage is the noise amount also increases. Nevertheless, the choice of reading the FHR values each 0.5 sec represents a reasonable compromise to achieve an enough large bandwidth and an acceptable accuracy of the FHR signal.

2) Experimental Protocol: We considered FHR signals from cardiotocographic recordings of 35 pregnant women: 14 normal, 13 IUGR, and eight maternal diabetes (MD), from the 33rd to the 38th week of gestation.

An expert clinician made the reported classification by considering different clinical examinations. The clinician has previously examined the CTG tracings but he was unable to identify possible pathological states on that basis only. Afterwards, the diagnosis of the physician at delivery (weight, type of delivery, Apgar score) has also been collected as a further indication and control.

All recordings were obtained in a controlled clinical environment, with the mothers lying on a bed in a relaxed condition. The recording time for each case was always longer than 1 h, in order to guarantee at least one alternance between the two most important behavioral states which can be observed in the fetus: the activity and the quiet condition [25].

Data are a consistent preliminary subset (same duration, same FHR sampling frequency, same CTG monitor) belonging to a database collected at the Clinica Ostetrica, Università di Roma "Tor Vergata," Rome, Italy, in recent years.

3) Preprocessing of FHR Signal: A good quality CTG recording requires the ultrasound beam be correctly oriented toward the fetal heart: this condition may be hard to achieve and to maintain during the whole observation time. Many other factors may also worsen the accuracy of FHR detection and the CTG signal often appears corrupted by a large amount of noise, artifacts, or even signal loss as the example in Fig. 1(a) shows.

In the HP-M1351A, a quality index quantifies three different levels of the FHR signal: optimal (green), acceptable quality (yellow), and insufficient quality and/or signal unavailable (red). The evaluation is based on the output of the autocorrelation procedure upon which the recording of FHR signal is based [15].

Each FHR recording has been divided in subintervals of 360 points each (3 min) after the isolated red-quality points have been corrected. Through a moving average procedure we substitute such values with the average of the nearest five FHR points. If part of the FHR signal contains more than five consecutive red-quality points and the corresponding subinterval includes more than 5% of red quality values, the subinterval is not considered for the analysis. Fig. 1(b) shows the FHR after the filtering procedure has been completed.

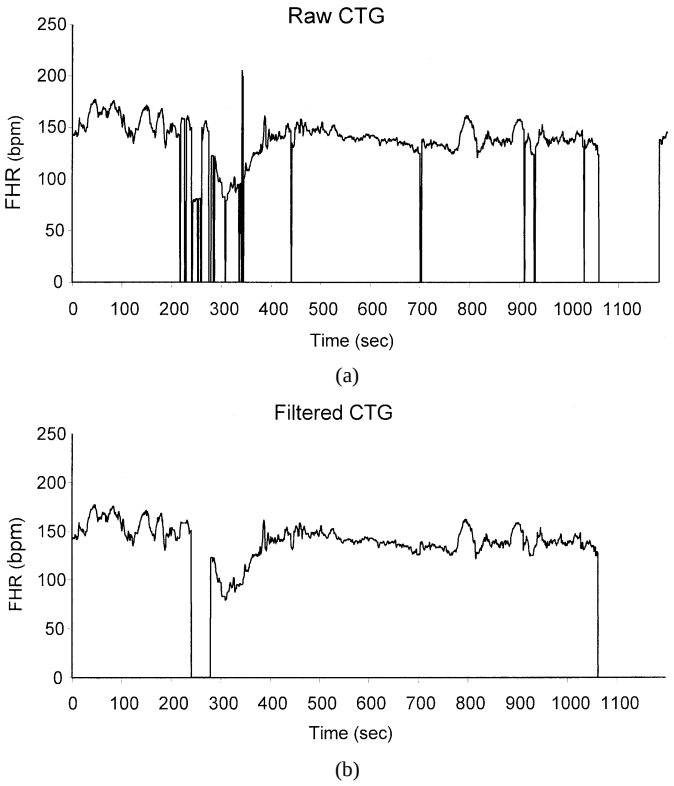


Fig. 1. An example of CTG signal (a) before and (b) after the moving average filtering procedure. Sampling frequency is 2 Hz.

Moreover, if compared with standard RR Holter recordings, the buffering procedure described in the hardware subsection highly reduces the precision of the RR sequence as generated by inverting the FHR signal (60 000/FHR ms). Besides, it is possible that the CTG device erroneously locks on the slower maternal fetal beat, even if the autocorrelation method is employed. This leads to an abrupt decrease into the FHR signal and it influences the evaluation of variability indexes. Therefore, we developed and then employed an artifact detection technique, which relays on the work of van Geijn *et al.*. [26]. The main concept is that an acceleration of heart rate develops more slowly than a deceleration does, thus, the limit for the acceptance of the point $S(i+1)$ differs according to whether $S(i+1)$ is smaller or greater then S(i).

Once the FHR signals have passed these preprocessing stages, an expert clinician identified, on the printed tracings, the presence of different patterns that are associated to activity and quiet epochs. Activity patterns are characterized by rapid and sudden FHR variations with body and eye movements of the fetus [25], [27] whereas quiet states are associated with non-REM sleep, showing an apparent sinusal rhythm of the FHR. In the following we will refer to A period as Activity and Q period as Quiet.

B. Parameter Computation

The investigation of the mechanisms controlling the FHR variability requires the use of both linear and nonlinear modeling approaches as the mechanisms responsible for signal generation show complex interactions [28]–[30].

We evaluate the FHR characteristics by calculating FHR mean and variance, parameters based on the estimation of the power spectral density (PSD) and by extracting regularity indexes based on nonlinear approaches such as approximate entropy (ApEn) [31]. We evaluated also some classical CTG parameters for comparison, starting from the identification of the baseline (computed following the Mantel's approach [19]), as defined in [32]: the number of accelerations, the STV, the LTI, and the interval index (II). We neglected the number of decelerations for two reasons. The first one is because their number strongly depend on the number of uterine contractions and our recordings antepartum present very few and occasional contractions. The number of decelerations was then poorly significant and biased by the status of the mother (presence or not of uterine contractions). Second, although the importance of FHR decelerations is universally recognized intrapartum, our purpose was to investigate fetal HRV in nonstress conditions, which basically means to exclude the effects of mechanical actions or stimulations on the fetus.

1) PSD Analysis: Each FHR interval of sufficient quality has been submitted to a parametric spectral analysis based on the estimation of an autoregressive (AR) modeling. The PSD analysis provides quantitative measurement of the activity performed by the ANS, which controls the physiologic variability of the heartbeats. Pathological states modify the HR patterns as it has been demonstrated in several HR signal conditions [2]. The AR modeling of the signal $RR_{360}(n)$ (3-min length of FHR corresponding to 360 points) is viewed as

$$RR_{360}(n) = \sum_{i=1}^{p} a_i\, RR_{360}(n-i) + w_n \tag{1}$$

where $w_n \sim \mathrm{WGN}(0, \sigma^2)$ (white Gaussian noise), p is the model order, and a_i are the model parameters.

Identification has been made through the estimation of the Autocorrelation function after the mean value Δ has been subtracted from the signal RR_{360} (biased estimation). Model parameters are calculated recursively through the Levinson–Durbin algorithm [33]. The choice of the model order p considers values in the range of 8–20, avoiding both under- and over-fitting problems. In this range, the minimum p of the Akaike figure of merit is identified as the possible optimal model order p^O

$$AIC(k) = \frac{2k}{N} + \log \sigma_k^2. \tag{2}$$

For $p = p^{\mathrm{O}}$, if the prediction error ε_{p^O} satisfies the whiteness Anderson test, p^{O} is identified as the correct model order, otherwise p is increased until the test is verified [34].

Once the proper model order is obtained, the PSD of the AR process is

$$\begin{aligned}\mathrm{PSD}(f) &= \frac{\sigma^2\Delta}{\left|1 - \sum_{k=1}^{p} a_k e^{-j2\pi k f \Delta}\right|^2} \\ &= \frac{\sigma^2\Delta}{A(e^{j2\pi f\Delta})A^*(e^{j2\pi f\Delta})} \\ &= \left.\frac{\sigma^2\Delta}{A(z)A^*\left(\frac{1}{z^*}\right)}\right|_{z=\exp(j2\pi f\Delta)}\end{aligned} \tag{3}$$

where Δ is the mean value of RR_{360} in s and $A(z)$ is the z-transform of the transfer function of the process (1).

The total power $\sigma^2{}_{RR_{360}}$ can be written as [see (3)]

$$\begin{aligned}\sigma^2{}_{RR_{360}} &= \int_{-\frac{1}{[2\Delta]}}^{\frac{1}{[2\Delta]}} \frac{\sigma^2\Delta}{A(e^{j2\pi f\Delta})A(e^{-j2\pi f\Delta})} df \\ &= \frac{\sigma^2}{j2\pi}\int_{|z|=1} \frac{z^{-1}}{A(z)A(z^{-1})} dz.\end{aligned} \tag{4}$$

The integral can be calculated as the sum of the residuals γ_k relevant to each pole of the function to be integrated, inside the unit circle. If b_k (modulus < 1) is one of the p poles of $H(z) = A(z)A(z^{-1})$

$$\sigma^2{}_{RR_{360}} = \sigma^2 \sum_{k=1}^{p} \gamma_k = \sigma^2 \sum_{k=1}^{p} \frac{1}{\prod_{i=1\neq k}^{p}(1 - b_i b_k{}^{-1}) \prod_{i=1}^{p}(1 - b_i b_k)}. \tag{5}$$

The presence of a complex conjugate couple of poles $(p_i, p_i{}^*)$ produces a real component of the ACF. By computing the frequency associated to each pole $f(b_k) = \arg(b_k)/(2\,\pi\,\Delta)$, it is possible to assign the residual of the pole itself (i.e. its contribution to the total power) to the frequency band containing it [35].

Through the proposed parametric approach, the FHR signal undergoes an automatic decomposition into a sum of sinusoidal contributions each one identified by its central frequency and the associated amount of power [36].

As it is well known from the literature a strong relationship can be established between the presence of spectral components and the activity of neural cardiovascular control systems [37].

Differently from what one can observe in a PSD of an adult subject [2], in the FHR spectrum we identify four contributions: the very low frequency (VLF: 0–0.03 Hz) is related to long period and nonlinear contributions, the low frequency (LF: 0.03–0.15 Hz) is mainly correlated with neural sympathetic activity, whereas high frequency (HF: 0.5–1 Hz) marks the presence of fetal breathing. The movement frequency (MF: 0.15–0.5 Hz) depends on fetal movements and maternal breathing and it is typical of the FHR spectrum. Evidence of this component in presence of fetal movements (basically of the trunk) is also reported in [38] and [39].

Parameters include FHR mean and variance values and the LF/(HF + MF) ratio, which quantify the autonomic balance between neural control mechanisms from different origin (in accordance with the LF/HF ratio normally calculated in adults).

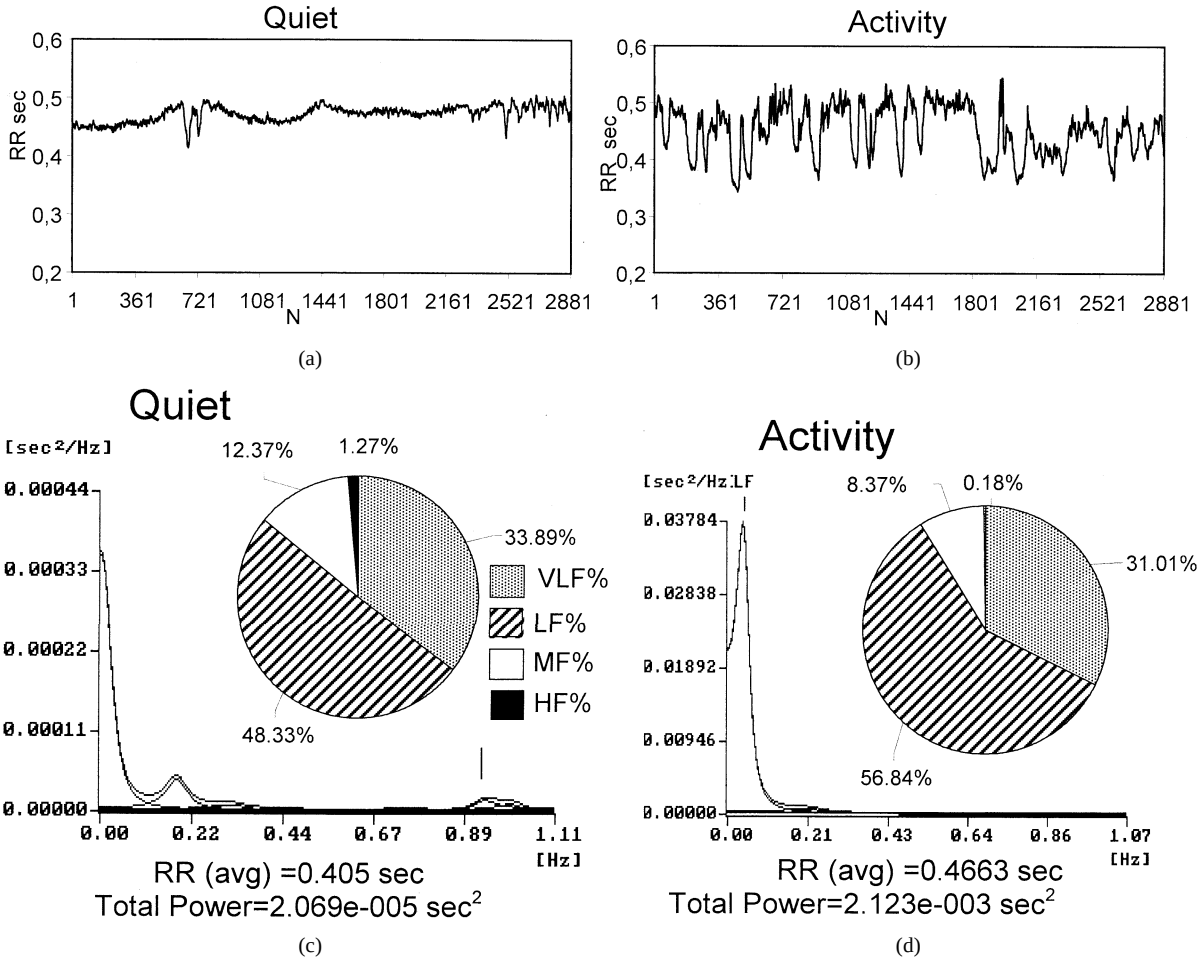


Fig. 2. CTG signals in (a) activity and in (b) quiet epochs from the same recording with the relevant PSD [(c) and (d)] obtained by AR modeling approach (N = 360 corresponding to 180 s). The pie graphs associated with the PSDs represent the contributions in percentage of the four frequency bands (VLF, LF, MF, and HF) to the total power spectrum.

An approach attempting to obtain at the same time, both the time and the frequency information about the FHR signal, considers the temporal evolution in the frequency content of the FHR. The method consists of evaluating the power spectrum on successive signal windows (overlapped or not) covering the whole trace length. Spectral modifications are shown in compressed spectral array (CSA) representation, providing the time evolution of the frequency response of the fetal heart.

2) Approximate Entropy: ApEn is a family of statistical indexes. ApEn measures regularity and ultimately correlation and persistence of a signal. A time series containing many repetitive patterns has a relatively small ApEn, a less predictable process has a higher ApEn. In this paper, we refer to the original definition by Pincus [40]. The estimator, which has been used for the calculation, is [41]

$$\begin{aligned}\mathrm{ApEn}(m,r) &= \frac{\sum_{i=1}^{N-m+1}\log C_i(m,r)}{N-m+1} \\ &\quad - \frac{\sum_{i=1}^{N-m}\log C_i(m+1,r)}{N-m} \\ &= -\,\mathrm{mean_i}\left[\log\frac{C_i(m+1,r)}{C_i(m,r)}\right] \qquad (6)\end{aligned}$$

where m is a natural number, r is a positive real, and N = 720.

The parameter m determines the lengths of the vectors that are compared. By increasing m it increases the degree of detail for the signal analysis.

The r parameter represents the filtering level or, in other words, the tolerance level with respect to signal outliers: differences between two vectors smaller than r, in absolute value, are considered not relevant. r is usually expressed as a fraction of one standard deviation of $RR_{720}(i)$.

ApEn has been proposed for the application to a wide variety of relatively short (>100 values) and noisy time series data. It classifies both deterministic and stochastic signals and it is robust against noise contamination [31].

The number of input data points N ranges typically between 75 and 5000. Both theoretical analysis and clinical applications concluded that $m = 1, 2$ and r between 0.1 and 0.25 Std of the input data produce good statistical validity of ApEn (m, r, N). Six ApEn values have been calculated on FHR time windows consisting of N = 720 values (360 overlapping). The six ApEn values resulted from the computation with $m = 1,\ 2$ and $r = 0.1\sigma,\ 0.15\sigma,\ 0.2\sigma$, where $\sigma = \mathrm{Std}[RR_{720}(i)]$.

At the end of the analysis process, the estimated parameters have been also related to the conditions of the baby at delivery

as they have been assessed by the obstetric personnel and by the measurement of the Apgar Score [42].

III. Results

The multiparametric analysis previously described has been applied to the 35 selected FHR signals.

As a first step, the PSD has been calculated both during activity and quiet epochs. Fig. 2(a) and (b) shows FHR signals during quiet Fig. 2(a) and activity Fig. 2(b) periods together with the relevant PSD [Fig. 2(c) and (d)] in a normal fetus of 34 weeks. Spectral components are more concentrated in LF and MF bands during Activity as HF components are visible during quiet epochs.

All estimated parameters have been submitted to a statistical t-test for paired data (comparison A versus Q epochs in the same group of subjects). In the normal population, FHR variance decreases, passing from 614±394 (A period) to 240 ± 134 ms^2 (Q period) ($p < 0.05$). Even spectral components in LF and MF bands are less evident. LF in normal subjects, in A epoch, is 324 ± 174 ms^2 versus 123 ± 95 ms^2 in Q epoch, ($p < 0.0005$). MF component is 28 ± 26 ms^2 versus 16 ± 9 ms^2 ($p < 0.005$).

Despite the fact that in activity periods total power, VLF and LF spectral components are higher, the contribution of MF and HF components in percentage to the total power are higher in Q epochs, as shown in the pie-graphs in Fig. 2(c) and (d). These last results are related to the presence of fetal breathing activity, which is more evident in quiet epochs, as it happens in sleeping adult subjects with respect to wake.

Values of the spectral parameters change as different fetal conditions occur (activity or quiet sleep), confirming their usefulness in the classification of fetal states. Spectra during quiet period show a LF/(MF + HF) ratio <1 as it happens when the respiratory activity is prevalent. Moreover, spectral decomposition shows the presence of MF and HF contributions that can be attributed to the maternal respiration activity, which can influence the FHR variability in a reflex way, and to the spontaneous "fetal respiration" activity, respectively. In particular, HF component is mainly related to the respiratory training activity of the fetus, which periodically ingests and emits the amniotic liquid. We quantify fetal movements and the influence of maternal breathing through the MF spectral component, which has been introduced to better discriminate physiological mechanisms that control the FHR.

What has been observed in a single FHR interval is confirmed by the calculation of PSD in a sequence during more than one hour recording. Fig. 3 shows the successive 3-min spectra in the form of CSA or the same recording. Different patterns, corresponding to Q (central part of the plot) and A epoch (first and last parts of the plot) can be observed in the registration. What is physiologically expected is enhanced by patterns obtained through the application of the spectral analysis to the FHR signal.

In particular, the quiet period shows a reduced variability, as LF components are clearly observable in the activity epoch. In the example of Fig. 3, the spectral component related to the fetal breathing is not visible as the fetus does its respiration activity only seldom during the FHR recording.

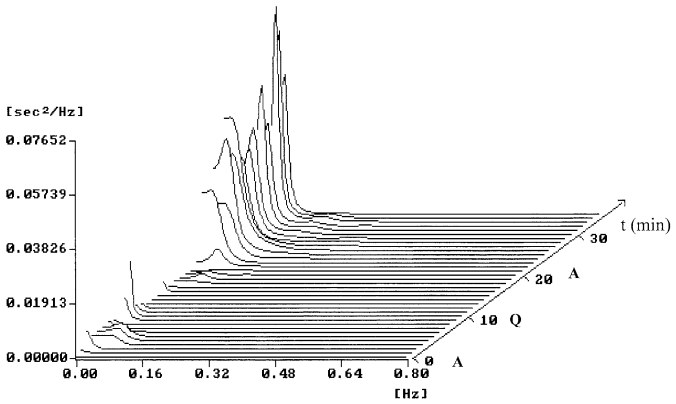
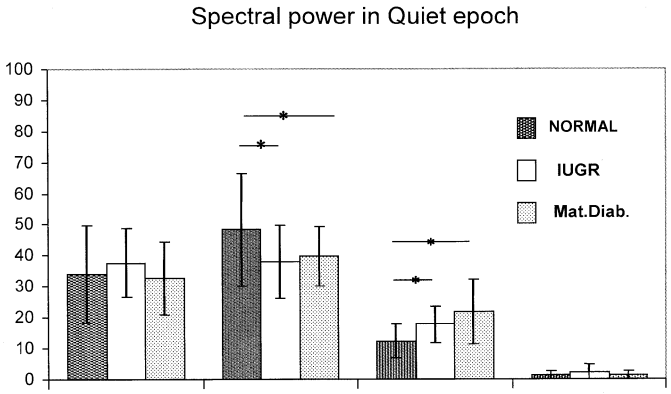


Fig. 3. PSD of the FHR signal during a whole CTG recording showing alternation of activity and quiet epochs. Representation by CSA allows following spectral parameters and their changes in time as it can be noticed in the plot. Each spectrum covers a 3-min time window.



	Tot. Pow.(ms²)		VLF%		LF%		MF%		HF%	
	avg	std	avg	std	avg	std	avg	std	avg	std
NORMAL	240	134	33.9	15.7	48.3	18.1	12.4	5.6	1.27	1.31
IUGR	168	89	37.6	11.2	37.8	11.8	17.8	5.9	2.34	2.50
Mat.Diab.	132	68	32.6	11.7	39.6	9.5	21.7	10.5	1.30	1.30

Fig. 4. Distribution of power spectral components in IUGR and MD fetuses in quiet epochs. Bars represent avg±std of VLF, LF, MF, and HF components in % in respect to the amount of the total power ($^* = p < 0.05$ t-test for unpaired data). The associated table in the lower part of the figure reports the numerical values, including also the total power in ms^2.

When we compared Normal with the two pathological groups in both A and Q periods, it was possible to observe significant differences only in the Q periods because of the great variability of the different fetuses in the activity states.

Parameter values have been submitted to a statistical t-test for unpaired data (comparison of normal versus pathological subjects) and are summarized in Fig. 4 for Normal, IUGR, and MD fetuses.

LF component in % differs in Normal versus IUGR and in Normal versus MD fetuses ($p<0.05$). The same ability to separate normal and pathological fetuses has been observed in the MF% component ($p < 0.05$).

The AEn stimator follows the fetal behavior annotated by clinicians during CTG monitoring. In normal fetuses, the highest sensitivity to the transition from quiet to activity is found for m = 1 and r = 0.20, as shown in Fig. 5. Despite the signal variability, ApEn is significantly higher in quiet periods

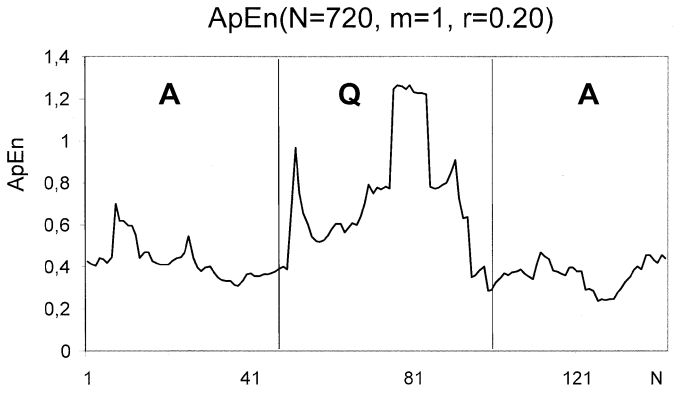
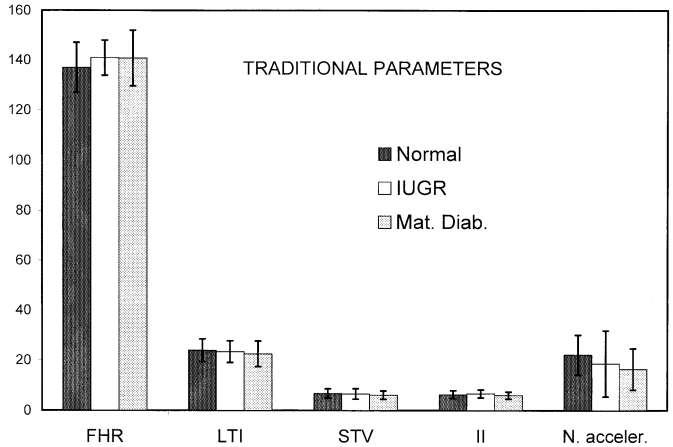


Fig. 5. Example of ApEn (N = 720, m = 1, r = 0.20) computed in a single FHR recording. Activity (A) and quiet (Q) periods are separated by the dotted lines.



	FHR(bpm)		LTI(ms)		STV(ms)		II		N. Acceler.	
	avg	std	avg	std	avg	std	avg	std	avg	std
NORMAL	137	10.0	23.9	4.5	6.7	1.8	6.3	1.5	22.1	7.9
IUGR	140.8	7.0	23.3	4.3	6.5	2.0	6.6	1.5	18.6	13.1
Mat.Diab	140.7	11.1	22.5	5.0	6.0	1.6	5.9	1.4	16.3	8.2

Fig. 6. Distribution of traditional parameters values in normal, IUGR and MD fetuses. Bars represent avg±std of FHR average (bpm), LTI, STV, II, and number of accelerations. The associated table in the lower part of the figure reports the numerical values. For all possible comparisons, t-test for unpaired data is not significant.

($p<0.05$) for the whole normal population. In order to compare the normal fetuses with IUGR and MD ones, only the quiet periods have been considered, because of the great variability within the active conditions.

Values of ApEn (N = 720, m = 1, r = 0,20) evidence differences between Normal and IUGR (0.68±0.14 versus 0.81±0.22; $p < 0.05$) and between Normal and MD (0.68±0.14 versus 0.82±0.12; $p < 0.05$).

For comparison, traditional indexes have been measured in the time domain, after the recordings have been submitted to the same preprocessing procedure. Fig. 6 reports both the bar graphs and the numerical values in Normal, IUGR, and MD population, expressed in avg±std, of LTI, STV, II, and the number of accelerations together with the FHR average value. Possible differences inside the groups have been investigated by a statistical t-test for unpaired data, which compared Normal fetuses with IUGR and MD, respectively. Test results did not evidence

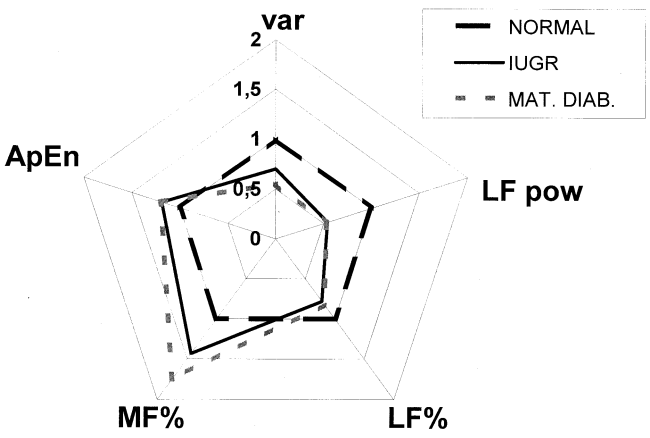


Fig. 7. Radar graph representation of the five parameters that better separate normal from pathological fetuses. Values in each radius are normalized with respect to the average value of the normal population. The black dashed line corresponds to Normal, the continuous black line to IUGR and the gray dotted line to fetuses from diabetic mothers (MAT. DIAB.).

any significant difference between groups (t – test = ns for all comparisons).

The radar graph in Fig. 7 summarizes the most significant results of the comparison among groups. In order to compare parameters having different scales, the radar graph has been normalized for each parameter with the average value of the Normal population. Normal fetuses show higher values of variance, spectral power in the LF band both in absolute and in % values. Pathological subjects instead show higher values of MF power component (in %) and ApEn.

IV. Discussion

The existing CTG automatic analysis tools base their expertise on scoring procedures that try to reproduce the time domain criteria used by the clinicians, although in a quantitative way, in order to decide if the fetus is in a "risky" condition. Often this "risky" condition does not represent pathology, but may lead the fetus to pathology in the remaining time of the pregnancy. This is the case for IUGR and MD, which are not pathologies, although they represent a danger for the fetus, and are very difficult to identify through a standard antepartum CTG monitoring. The possibility to early identify them could represent a noticeable step toward the prediction of fetal outcome. However "the proposed step, included in all the existing scoring systems, i.e., to calculate figures and to relate these figures to fetal outcome, is a step to far," as declared in [5].

In our opinion this gap can be filled by two successive steps: first, by introducing new indexes closely related to the physiology of the neural control of FHR, presenting high sensitivity with respect to normal and potential pathological fetal states and second, by finding "smart" classifiers able to distinguish normal and "risky" CTG tracings.

The original goal of this study was to face the first step by improving the cardiotocographic analysis through a multiparametric analysis based on linear and nonlinear signal processing techniques.

Our set of 35 recordings shows that neither the eye inspection analysis by the clinician nor the computation of traditional

parameters can identify IUGRs and MD from normal fetuses, while PSD indexes and ApEn could.

In the analysis of FHR signal, the accurate recording and preprocessing phases are of extreme importance in the fulfilment of consistent results.

As a first indication, the analysis by AR spectral estimation and ApEn has shown significant differences in quiet versus activity period inside the same group of subjects. Comparison of quiet versus activity period of Normal subjects shows that the total power of the FHR signal is higher in activity epoch, as we could have expected because activity implies higher variability of FHR. Even Spectral power in VLF, LF, and MF bands (in absolute value) is higher as also the LF power in %.

The fact that MF and HF power in % are higher in quiet period means a different distribution among the frequency bands. The MF band is more influenced by maternal breathing and fetal body movements. HF band reflects the contribution of fetal breathing movements, which are more present in quiet. ApEn too is higher in quiet periods, in accordance with what happens in adult healthy subjects, who have ApEn values higher during night.

Spectral parameters establish significant differences between normal and pathological subjects. In particular, the observed decrease of LF power component (in %) could be attributed to a decrease in the contribution of the neural sympathetic control.

Quiet periods of pathological groups exhibits a different pattern with respect to Normal fetuses. The significant increase of MF power (%) could be an index that fetuses at risk may be characterized by a different behavior, which could be identified as "disturbed" quiet status. Although they seem to exhibit the same FHR patterns as normal, from the morphological point of view, spectral analysis is able to evidence differences in power distribution.

In this way, the corresponding significant increase of ApEn value (meaning the FHR pattern is more irregular with respect to normal fetuses) requires a deeper investigation to better understand in which way the signal regularity is influenced by pathological condition of the fetus. This observation underlines the difference between signal variability and regularity. As a matter of fact the increase of ApEn in potential pathological conditions corresponds to a significant decrease in FHR variance with respect to normal healthy conditions.

V. Conclusion

CTG has shown up to now a low predictive power when only the traditional time domain techniques were employed. Our work seems to evidence that the weakness of prediction is not due to the US technique itself, although it is less precise than abdominal ECG, but to the lack of reliable methodological tools that have been used to extract information from the FHR signal. As a matter of fact, the new indexes we introduced are significantly different between normal and potential pathological fetuses, while traditional parameters are not. Our opinion is that the US-CTG monitoring should receive a significant improvement by including the most significant parameters that have been provided by the current analysis into a nonlinear multivariate classifier (either an expert system, a neural network or a classifier based on fuzzy logic techniques). By coupling physiology related indexes and nonlinear classifiers, it should be possible to enhance the reliability and robustness of fetal well-being nonstress monitoring in the antepartum period. This work could represent a first step toward an early detection of fetal risk in pregnancy and toward a prediction of fetal outcome based on noninvasive and standard technology.

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References

[1] M. V. Kamath and E. L. Fallen, "Power spectral analysis of heart rate variability: a noninvasive signature of cardiac autonomic function," *Crit. Rev. Biomed. Eng.*, vol. 21, no. 3, pp. 245–311, 1993.

[2] "Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology," *Eur. Heart J.*, vol. 17, no. 3, pp. 354–381, 1996.

[3] S. Cerutti, S. Civardi, A. Bianchi, M. G. Signorini, E. Ferrazzi, and G. Pardi, "Spectral analysis of antepartum heart rate variability," *Clin. Phys. Physiol. Meas.*, vol. 10, Suppl. B, pp. 27–31, 1989.

[4] E. E. van Woerden, H. P. van Geijn, F. J. Caron, and R. Mantel, "Spectral analysis of fetal heart rhythm in relation to fetal regular mouthing," *Int. J. Biomed. Comput.*, vol. 25, no. 4, pp. 253–260, 1990.

[5] H. P. van Geijn, "Developments in CTG analysis," *Baillieres Clin. Obstet. Gynaecol.*, vol. 10, no. 2, pp. 185–209, 1996.

[6] J. H. Smith, K. J. Anand, P. M. Cotes, G. S. Dawes, R. A. Harkness, T. A. Howlett, L. H. Rees, and C. W. Redman, "Antenatal fetal heart rate variation in relation to the respiratory and metabolic status of the compromised human fetus," *Brit. J. Obstet. Gynaecol.*, vol. 95, no. 10, pp. 980–989, 1988.

[7] K. Lindecrantz, S. Cerutti, S. Civardi, K. H. Hokegard, H. Lilja, K. G. Rosen, M. G. Signorini, and C. Widmark, "Power spectrum analysis of the fetal heart rate during noradrenaline infusion and acute hypoxemia in the chronic fetal lamb preparation," *Int. J. Biomed. Comput.*, vol. 33, no. 3–4, pp. 199–207, 1993.

[8] J. P. Lecanuetand and B. Schaal, "Fetal sensory competencies," *Eur. J. Obstet. Gynecol. Reprod. Biol.*, vol. 68, no. 1–2, pp. 1–23, 1996.

[9] E. H. Hon and S. T. Lee, "Electronic evaluation of the fetal heart rate patterns preceding fetal death: further observations," *Amer. J. Obstet. Gynecol.*, vol. 8, no. 7, pp. 814–826, 1965.

[10] G. Sugihara, W. Allan, D. Sobel, and K. D. Allan, "Nonlinear control of heart rate variability in human infants," *Proc. Nat. Acad. Sci.*, vol. 93, pp. 2608–2613, 1996.

[11] M. G. Signorini, R. Sassi, and S. Cerutti, "Assessment of nonlinear dynamics in heart rate variability signal," in *Nonlinear Biomedical Signal Processing*, 1 ed, M. Akay, Ed. Piscataway, NJ: IEEE Press, 2000, vol. II, pp. 263–281.

[12] S. Cerutti, G. Baselli, S. Civardi, E. Ferrazzi, A. M. Marconi, M. Pagani, and G. Pardi, "Variability analysis of fetal heart rate signals as obtained from abdominal electrocardiographic recordings," *J. Perinat. Med.*, vol. 14, no. 6, pp. 445–452, 1986.

[13] G. S. Dawes, M. Moulden, and C. W. Redman, "The advantages of computerized fetal heart rate analysis," *J. Perinat. Med.*, vol. 19, no. 1–2, pp. 39–45, 1991.

[14] *Fetal Monitor Test—A Brief Summary*, Hewlett-Packard, Boeblingen, Germany, 1995, pp. 1–6.

[15] G. W. Lawson, R. Belcher, G. S. Dawes, and C. W. Redman, "A comparison of ultrasound (with autocorrelation) and direct electrocardiogram fetal heart rate detector systems," *Amer. J. Obstet. Gynecol.*, vol. 147, no. 6, pp. 721–722, 1983.

[16] H. P. van Geijn, "The European community project "Perinatal monitoring"," *J. Perinat. Med.*, vol. 15, no. 4, pp. 367–368, 1987.

[17] H. P. van Geijn, A. M. Lachmeijer, and F. J. Copray, "European multicentre studies in the field of obstetrics," *Eur. J. Obstet. Gynecol. Reprod. Biol.*, vol. 50, no. 1, pp. 5–23, 1993.

[18] G. S. Dawes, M. Moulden, and C. W. Redman, "Computerized analysis of antepartum fetal heart rate," *Amer. J. Obstet. Gynecol.*, vol. 173, no. 4, pp. 1353–1354, 1995.
[19] R. Mantel, H. P. van Geijn, F. J. Caron, J. M. Swartjes, E. E. van Woerden, and H. W. Jongsma, "Computer analysis of antepartum fetal heart rate: 1. Baseline determination," *Int. J. Biomed. Comput.*, vol. 25, no. 4, pp. 261–272, 1990.
[20] ——, "Computer analysis of antepartum fetal heart rate: 2. Detection of accelerations and decelerations," *Int. J. Biomed. Comput.*, vol. 25, no. 4, pp. 273–286, 1990.
[21] J. De Haan, J. H. Vam Bemmel, B. Versteeg, A. F. L. Veth, L. A. M. Stolte, J. Janssens, and T. K. A. B. Eskes, "Quantitative evaluation of fetal heart rate. i. processing methods," *Eur. J. Obstet. Gynecol.*, vol. 3, pp. 95–103, 1971.
[22] D. Arduini and G. Rizzo, "Quantitative analysis of fetal rate: its application in antepartum clinical monitoring and behavioral pattern recognition," *Int. J. Biomed. Comput.*, vol. 25, no. 4, pp. 247–252, 1990.
[23] R. Mantel, H. P. van Geijn, I. A. Ververs, and F. J. Copray, "Automated analysis of near-term antepartum fetal heart rate in relation to fetal behavioral states: the Sonicaid System 8000," *Amer. J. Obstet. Gynecol.*, vol. 165, no. 1, pp. 57–65, 1991.
[24] *HP Series M135 x Technical Reference*, Hewlett-Packard, Boeblingen, Germany, 1994.
[25] J. G. Nijhuis, H. F. Prechtl, C. B. Martin Jr., and R. S. Bots, "Are there behavioral states in the human fetus?," *Early Human Dev.*, vol. 6, no. 2, pp. 177–195, 1982.
[26] H. P. van Geijn, H. W. Jongsma, J. De Haan, and T. K. Eskes, "Analysis of heart rate and beat-to-beat variability: Interval difference index," *Amer. J. Obstet. Gynecol.*, vol. 138, no. 3, pp. 246–252, 1980.
[27] R. Mantel, H. P. van Geijn, I. A. Ververs, G. J. Colenbrander, and P. J. Kostense, "Automated analysis of antepartum fetal heart rate in relation to fetal rest-activity states: a longitudinal study of uncomplicated pregnancies using the Sonicaid System 8000," *Eur. J. Obstet. Gynecol. Reprod. Biol.*, vol. 71, no. 1, pp. 41–51, 1997.
[28] L. Glass and M. C. Mackey, *From Clock to Chaos: The Rhythms of Life*. Princeton, NJ: Princeton Univ. Press, 1988.
[29] A. L. Goldberger, "Non-linear dynamics for clinicians: chaos theory, fractals and complexity at the bedside," *Lancet*, vol. 34, no. 7, pp. 1312–1314, 1996.
[30] P. van Leeuwen, S. Lange, H. Bettermann, D. Gronemeyer, and W. Hatzmann, "Fetal heart rate variability and complexity in the course of pregnancy," *Early Human Dev.*, vol. 54, no. 3, pp. 259–269, 1999.
[31] S. M. Pincus, "Approximated entropy (ApEn) as a complexity measure," *Chaos*, vol. 5, pp. 110–117, 1995.
[32] G. Magenes, M. G. Signorini, and D. Arduini, "Classification of cardiotocographic record by neural networks," in *Proc. IEEE-INNS-ENNS Int. Joint Conf.*, 2002, pp. 637–641.
[33] S. M. Kay and S. L. Marple, "Spectrum analysis: a modern perspective," *Proc. IEEE*, vol. 6, pp. 1380–1418, Sept. 1981.
[34] A. Cohen, *Biomedical Signal Processing*. Boca Raton, FL: CRC, 1986, p. 298.
[35] L. H. Zetterberg, "Estimation of parameters for a linear difference equation with application to ECG analysis," *Math. Biosci.*, vol. 5, pp. 227–275, 1969.
[36] G. Baselli, S. Cerutti, S. Civardi, D. Liberati, F. Lombardi, A. Malliani, and M. Pagani, "Spectral and cross-spectral analysis of heart rate and arterial blood pressure variability signals," *Comput. Biomed. Res.*, vol. 19, pp. 520–534, 1986.
[37] A. Malliani, M. Pagani, F. Lombardi, and S. Cerutti, "Cardiovascular neural regulation explored in the frequency domain," *Circulation*, vol. 84, no. 2, pp. 482–492, 1991.
[38] O. Sibony, J. P. Fouillot, M. Benaoudia, A. Benhalla, J. F. Oury, C. Sureau, and P. Blot, "Quantification of the fetal heart rate variability by spectral analysis of fetal well-being and fetal distress," *Eur. J. Obstet. Gynecol. Reprod. Biol.*, vol. 54, no. 2, pp. 103–108, 1994.
[39] G. Breborowicz, J. Moczko, and J. Gadzinowski, "Analysis of fetal heart rate in frequency domain," in *A Critical Appraisal of Fetal Surveillance Amsterdam*, H. P. van Geijn and F. J. Copray, Eds. New York: Elsevier, 1998, pp. 325–332.
[40] S. M. Pincus, "Approximated entropy as a measure of system complexity," *Proc. Nat. Acad. Sci.*, vol. 8, pp. 2297–2311, 1991.
[41] S. M. Pincus and W. M. Huang, "Approximate entropy: statistical properties and applications," *Commun. Stat. Theory Meth.*, vol. 21, pp. 3061–3070, 1992.
[42] J. Bernardes, D. Ayres-de-Campos, A. Costa-Pereira, L. Pereira-Leite, and A. Garrido, "Objective computerized fetal heart rate analysis," *Int. J. Gynaecol. Obstet.*, vol. 62, no. 2, pp. 141–147, 1998.

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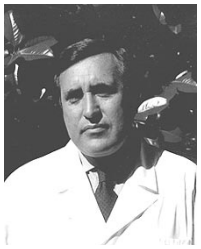

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