NON-LINEAR ANALYSIS OF FETAL HEART RATE IN CARDIOTOCOGRAPHY USING SAMPLE ENTROPY

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Abstract: The complex system of mother and foetus interacting during pregnancy contains both dependent and independent subsystems and it is unlikely that it can be studied using only linear techniques. Considering this, the conventional medical analysis of Fetal Heart Rate (FHR) based on Cardiotocography (CTG) traces can be expanded considering nonlinear approaches. This work presents the use of Sample Entropy (SampEn) as a measure of system complexity, using a 5 minutes window of FHR signal (1200 samples), using values for parameters *m* and *r* based on literature to analyse the signal complexity behaviour in time. The database is comprised of 22 pre-classified intrapartum exams, expected to have a high degree of time domain dynamics. The analysis shows that severe FHR decelerations result in small values of SampEn, reflecting a low level of complexity. On the other hand, a set of high level transient FHR accelerations also causes the same effect. The occurrences of repetitive patterns (similar to sinusoidal waves, which are pathological) cause a drop of SampEn values. The results encourage us to consider SampEn as one viable parameter for nonlinear FHR signal analysis.

1 INTRODUCTION

The CTG examination is the simultaneous and continuous recording of the FHR, fetal movements and uterine contractions. The analysis of these signals can help diagnose a large set of fetal diseases or health problems (Ingemarsson, Ingemarsson, & Spencer, 1993).

A partial CTG trace with FHR and the uterine tonus monitoring is shown in Figure 1. The occurrence of uterine contractions usually indicates the *intrapartum* period. The diagnostic based on these two signals provides early detection of fetal health problems.

The fetal heart rate and the interval between the beats change periodically and non-periodically in time and this variability is normally considered as a health indicator.

The fetal cardiac rhythm is influenced by many different subsystems, such as the heart, brain and neural system development, fetal oxygen supply and also the maternal conditions (such as fever or high blood pressure). This complex scenario suggests the presence of nonlinear behaviour and characteristics in FHR.

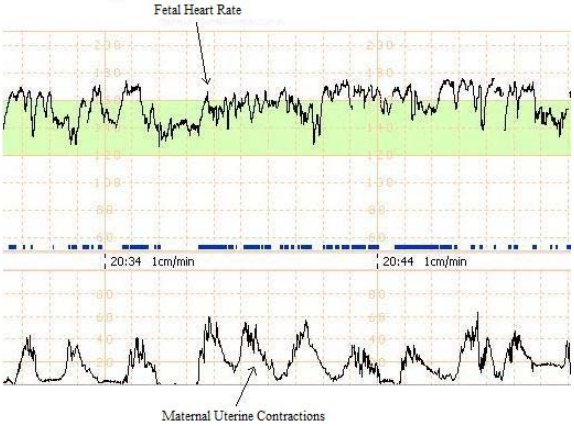

Figure 1: FHR and uterine contractions signals in a CTG.

According to Savi, from the point of view of mathematical modelling, the description of biological phenomena could be more realistically modelled with nonlinear analysis rather than with linear analysis. Surrogate data obtained from the

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analyzed time series can be used to present evidences of nonlinear components in the signal (Kantz & Schreiber, 1997).

Nonlinear approaches to calculate biological time series complexity can be obtained using nonlinear entropy measures such as Approximate Entropy (Pincus, 1991); Lempel-Ziv complexity (Doganaksoy & Gölogluu, 2009) and Sample Entropy (Richman & Moorman, 2000).

The Sample Entropy is a metric based on Approximate Entropy that has been already applied to evaluate the complexity in cardiovascular time series (Richman & Moorman, 2000).

This work presents a nonlinear analysis of FHR, which is the most significant signal monitored in a CTG, based on Sample Entropy (SampEn) behaviour in time.

2 MATERIALS AND METHODS

2.1 Sample Entropy

The *SampEn* of a time series is the negative natural logarithm of the probability that two similar sequences of *m* points remain similar at the next point. The polarization of self-matches is not considered. Low values of *SampEn* indicate lower complexity and more regularity in the time series.

For a better understanding of these definitions as a measure of system complexity, the mathematical foundations of its calculation is provided.

Given S_i as a time series with N samples $S_i = \{S_1, S_2, \ldots, S_N\}$ the first step to calculate $SampEn(S_i,m,r)$, is the determination of two input parameters *m* and *r*, where *m* is the length of a subset of S_i and *r* is the similarity criteria. Consider also that $p_m(i)$ is the subsequence or pattern of S_N beginning in sample *i* and with *m* samples of length.

Consider two patterns $p_m(i)$ and $p_m(j)$, beginning, at index *i* and *j* respectively. These patterns can be considered similar if the scalar distance between them, *i.e.*, the module of the difference between sample pairs is less than *r*. (1).

$$\left|S_{i+k} - S_{j+k}\right| < r \quad \text{for} \quad 0 < k < m. \tag{1}$$

Consider P_m as the set of all patterns from S_N with length *m*. The relation $C_{i,m}(r)$ can now be defined (2).

$$C_{i,m}(r) = \frac{n_{i,m}(r)}{N-m+1} \tag{2}$$

where $n_{i,m}(r)$ is the number of patterns similar to $p_m(i)$ in P_m. The parameter $C_m(r)$ must be calculated as the average of all $C_{i,m}(r)$ for the entire P_m set.

Finally, $SampEn(S_i,m,r)$ can be found (3).

$$SampEn(S_i, m, r) = \ln \frac{C_m(r)}{C_{m+1}(r)} \tag{3}$$

2.2 Development Environment and CTG Database

The development environment was based on the Matlab software, version 7.6.0.324 R2008a (Mathworks, 2009).

The results were obtained using a database from Trium GmBH, a project partner from Munich, Germany. This database was labelled as the CTG-I and contains 22 intrapartum exams (during labour and delivery), all classified by medical staff.

This database was chosen because of the high level of dynamics found during labour, especially when the influence of uterine contractions can be found in FHR signals.

2.3 Entropy Calculation Parameters

Sample entropy can be calculated for the whole FHR signal, providing a long term index or, alternatively, windows of samples can be used for short term nonlinear characteristics evaluation.

Data were submitted to many tests with different Δt_e window sizes and also changing *m* and *r* parameters.

In this paper, the FHR signal entropy calculations consider a subset of 1200 samples, which represents a 5 minute-long window. The aim is the monitoring of the signal entropy based on its time evolution. For example, the entropy behaviour during pathological FHR events, such as prolonged decelerations, could be a predictive tool for electronic fetal monitoring.

The *SampEn* input parameters used were $m=5$ and $r=0.2\sigma[FHR(t)]$, where $FHR(t)$ is the FHR signal and $\sigma[FHR(t)]$ is the standard deviation of the time series (Kaplan & Staffin, 2008).

3 RESULTS AND DISCUSSION

In this section, the general results obtained with the CTG-I database are presented with some illustrative examples of high and low values of *SampEn* and the correspondent visualization of FHR trace in time.

Several physiological changes occur in the perinatal period and fetal signals are expected to have high dynamics, hence, high values of entropy are usually expected in these time series. The presence of low values should be investigated.

The FHR and *SampEn(FHR,m,r)* plots for the *ctg20040215-0803261* examination are presented on Figure 2. Notice that the *SampEn* is calculated only for the specified windows of 1200 samples.

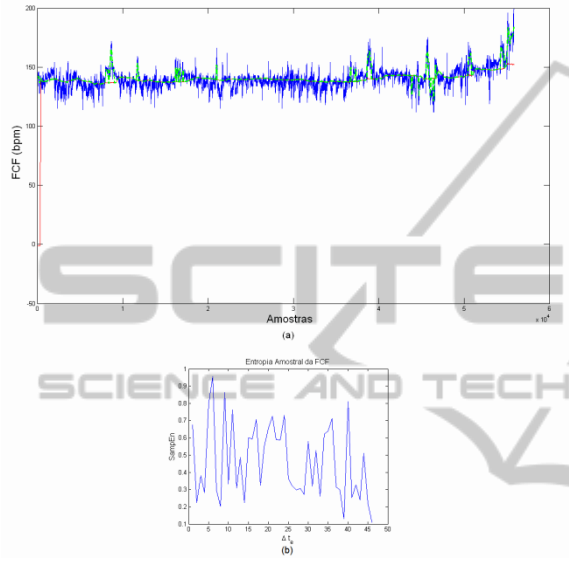

Figure 2: Exam *ctg20040215-0803261* (a) FHR plot and (b) SampEn calculation using the specified window.

As mentioned before, for a more clear interpretation of the entropy behaviour, some specific time intervals are analysed.

The first analysis is a zoom at the $18<\Delta t_e<24$ interval, where we can find high values of sample entropy. In a closer look of the FHR signal in Figure 3, one can see that there are many oscillations.

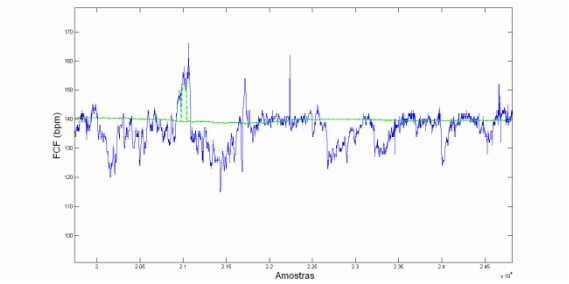

Figure 3: Extracted trace from *ctg20040215-0803261* exam with high values of SampEn.

During the same exam, right after the trace shown in Figure 3, during the interval $25<\Delta t_e<29$, we can find low values of *SampEn*, even when the trace apparently shows that the signal is oscillating and high values of sample entropy could be expected. The reason for that can be seen in Figure 4. Actually, the signal complexity decreases because the trace shows a periodic repetitive pattern identified by the region S1. A sinusoidal behaviour of FHR is considered as pathological in visual CTG classification (Ingemarsson, Ingemarsson, & Spencer, 1993). This encouraged us to consider low values of *SampEn* as a possible index to predict fetal health problems.

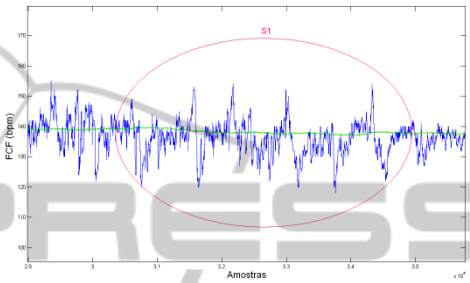

Figure 4: Trace extracted from *ctg20040215-0803261* exam with low values of SampEn (repetitive pattern).

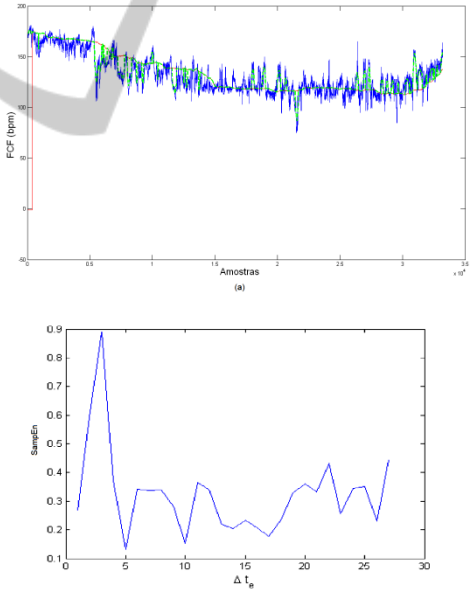

Figure 5: Exam *ctg20011218-2348371* (a) FHR with low variability and a drop of the baseline and (b) decreasing SampEn values .

The ctg20011218-2348371 exam presented in Figure 5 was previously classified as pathological, with low values of short-term variability and also because of the FHR baseline behaviour (Marques, Cortez, & Madeiro, 2010). At the beginning there can be seen a tachycardia, followed by the decrease of the signal baseline. The *SampEn* trace shows high

values at the beginning also followed by low values, remaining at this level until the end of the examination.

In the next analysis, the FHR sample entropy can be used to indicate transient changes in the time series. The *ctg20040214-0722052* exam contains severe FHR decelerations, correspondingly to very low values of *SampEn*. For example, for the interval $36<\Delta t_e<40$, the entropy remains in the same level until the original signal returns to its baseline, as can be seen in Figure 6.

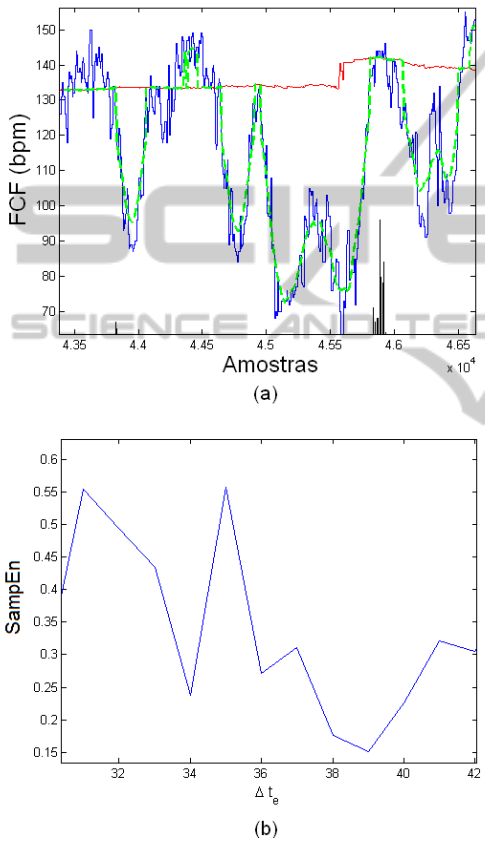

Figure 6: Exam *ctg20040214-0722052* (a) FHR with severe decelerations and (b) low values of SampEn.

On the other hand, during the *ctg20020124-1015523* examination, a set of transient accelerations of FHR can be found. These changes and the repetitive pattern presnt also result in low values of entropy. For example, during the interval $5<\Delta t_e<12$, the calculated sample entropy is very low, as shown in Figure 7.

The results presented here as a set of examples of FHR complexity in time were found on the entire set of the CTG-I database.

As can be seen, the sample entropy does not require a slow converging process, acting as a fast technique for detecting changes in FHR, for the considered set of windows.

For this kind of analysis, some complementary information, such as fetal HRV low and high frequency parameters, short-term and long-term variability and other nonlinear measures could be very useful for automatic or even visual analysis of CTG traces.

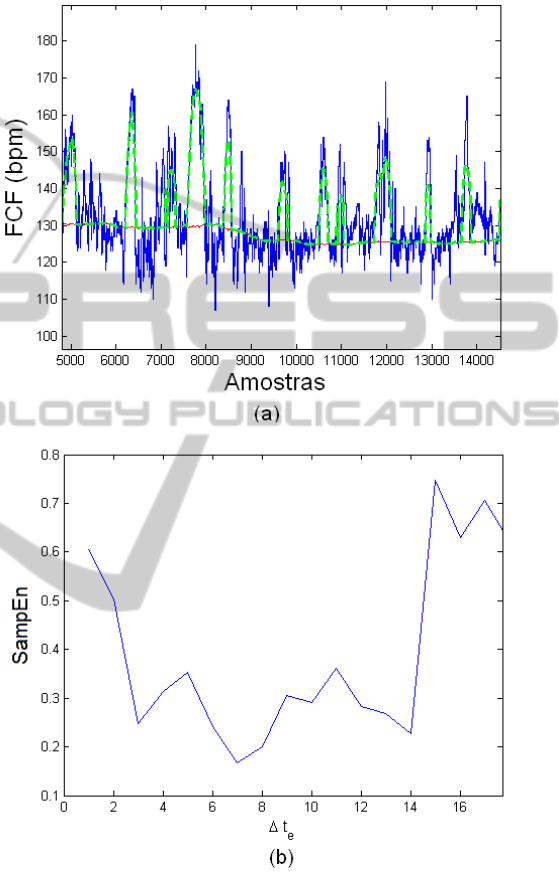

Figure 7: Exam *ctg20020124-1015523* (a) FHR with severe decelerations and (b) low values of SampEn.

Some physiological interpretations can be done from the SampEn calculation. First of all, it can be used as a normality indice of the FHR long term variability which is an important neural development estimator. Besides, low entropy values found in severe FHR accelerations and decelerations can provide a first level monitoring parameter for the detection of fetal distress.

Finally, as mentioned before, low entropy values may also indicate repetitive patterns around the FHR baseline which are not classified as accelerations or decelerations. These are usually suspicious or pathological and are difficult to detect with the visual inspection only.

4 CONCLUSIONS

Nonlinear measures of biological time series such as FHR are important tools to improve the conventional medical analysis. This work suggests the use of the Sample Entropy for 5 minutes windows datasets to visualize this nonlinear metric evolving in time.

One of the main conclusions is that repetitive patterns of FHR result on small values of SampEn. This agrees with usual medical interpretation and could detect pathological cases related to this condition, since high values of *SampEn* are usually expected for healthy fetuses.

In the same way, low short-term FHR variability also results in low levels of entropy. Another important result is that the presence of significant transient changes in FHR, such as decelerations and accelerations also caused SampEn to decrease.

We suggest that medical staff should consider the use of FHR SampEn as a measure of system complexity and a viable complementary tool to help measure fetal health.

Nonlinear surrogate FHR analysis is going to be presented in future works. Besides, other approaches can be considered, such as Approximate Entropy and Lempel-Ziv Complexity to compare the results.

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