Biocybernetics and Biomedical Engineering
2010, Volume 30, Number 2, pp. 67–72

Sensitivity Analysis of a Sample Entropy Estimator on its Parameters in Application to Electrohysterographical Signals

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An electrohysterographical signal (EHG) represents a bioelectrical activity of a pregnant uterus. The most frequently used method of analysis of EHG is based on entropy indexes, e.g. an approximate entropy or sample entropy index which are dependent on two parameters. Hitherto, these parameters were selected arbitrary apart from their influence on physiological meaning of the EHG signals. The aim of the presented paper was an evaluation of sensitivity of the sample entropy index on its parameters. Moreover, it was computed such value of these parameters which ensured prediction of an upcoming labor on basis on the EHG description by the sample entropy index.

K e y w o r d s: sensitivity analysis, nonlinear signal analysis, pregnancy monitoring

1. Introduction

Monitoring of a pregnancy and labor course as well as of fetus well-being is a pivotal problem of the reproductive medicine. Nowadays, technical instruments support obstetricians and midwives in a clinical practice. Despite of the fact that ultrasonography, cardiotocography and pulsoximetry are standard tools used by doctors, an identification and prevention of preterm labors and fetal hypoxia is still a serious challenge [1]. In particular, some authors stress that registration of spatial averaging mechanical uterine contractions by tocography makes impossible a prediction of a labor [2]. Therefore, alternative methods of uterine contractions monitoring are studied. One of them consists in measurement of an bioelectrical activity of an uterus basing on the fact that biopetential changes always anticipate a mechanical contraction.

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Received 07 November 2008; accepted 13 November 2009

A measurement method of an electrohysterographical signal (EHG) was in details described by Radomski et al. [3]. The sensor consists of two measuring electrodes and one reference electrode. The first measuring electrode is placed over the body of a pregnant uterus and the second one over the cervical part of the uterus. The reference electrode is localized on patient's thigh.

The aim of the EHG analysis is to find such model of the signal which enables to differentiate a physiological state of an uterus (i.e. puerperal vs. pregnant state). Two approaches of the analysis of the EHG signal are presented in literature. The first one obeys the EHG analysis in the frequency domain using Fourier or wavelet methods [4]. However, the obtained spectrums are very sensitive on measurement moments and inter-patients variability. Therefore, an application of these methods to prediction of preterm labor is questionable.

Theoretical analyzes of a physiological mechanism of uterine bioelectrical activities indicates that it is a highly nonlinear process. Although many indexes are used in nonlinear signal analysis only entropy based indexes well describe the signal regularity. Just the signal regularity seems to be the most predictive descriptor of EHG (Fig. 1).

The application of approximated entropy was proposed by Graczyk et al. [5]. Next, Radomski et al. showed usefulness of sample entropy which is an unbiased version of the approximated entropy [6]. However, these estimators are dependent on two parameters which can affect differential abilities.

The aim of the presented study was to perform a sensitivity analysis of a sample entropy estimator on its parameters in application to electrohysterographical signals.

2. Sample Entropy Estimation

The idea supporting application of the sample entropy to EHG analysis results from the observations that an electrical activity of an uterus becomes more regular when a labor is forthcoming [7]. This phenomena is shown in Fig. 1. During a labor we can observe regular complexes of bioelectrical burst. Instead, a bioelectrical activity of an unpregnant uterus looks like white noise because each muscular cell generates own potentials.

The sample entropy was estimated in similar way as the approximated entropy. The estimation procedure was conducted in the following manner. Let EHG signal will be represented by a time series denoting as $\{x(n)\}$. Let's create m vectors contained consecutive values of x_i, commencing at the i-th sample, i.e.

$$\mathbf{X}_m(i) = \begin{bmatrix} x(i) & x(i+1) & \ldots & x(i+m-1) \end{bmatrix} \quad \text{for } 1 \le i \le N - m + 1. \tag{1}$$

By $d\left[\mathbf{X}_m(i), \mathbf{X}_m(j)\right]$ is denoted the distance between two vectors $\mathbf{X}_m(i)\mathbf{X}_m(j)$ which is defined as:

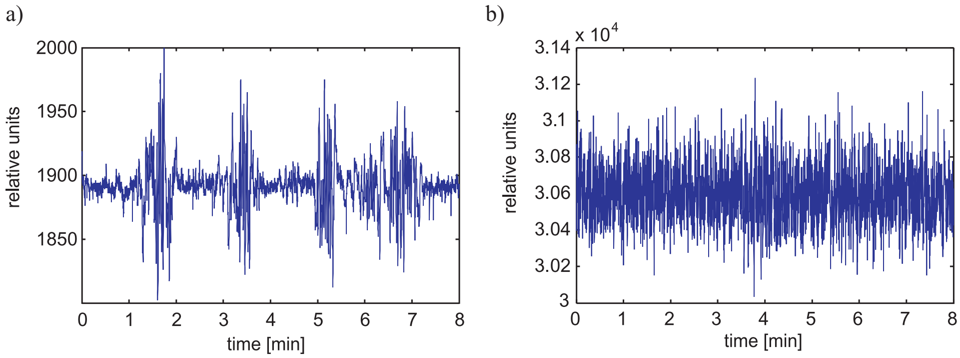

Fig. 1. An example of EHG signal a) during labor b) during puerperium. The voltage relative units relatively to the reference voltage

$$d\left[\mathbf{X}_m(i),\mathbf{X}_m(j)\right]=\max_k\left|x(i+k)-x(j+k)\right|. \tag{2}$$

The distance measure was used for counting of the number of the similar elements of the vectors $\mathbf{X}_m(i)$ and $\mathbf{X}_m(j)$.

Let introduce a set of such indexes which for this distance is not greater than r. This set is described by the following expression:

$$\mathrm{J}_m=\left\{j:d\left[\mathbf{X}_m(i),\mathbf{X}_m(j)\right]\le r\right\}. \tag{3}$$

For a given $\mathbf{X}_m$ and for $1 \le i \ne j \le N-m$ we can define the coefficient

$$B_i^m=\frac{\mathrm{card}\{\mathrm{J}_m\}}{N-m-1}. \tag{4}$$

Then, one can compute the number of the similar vector elements averaging over i in the following manner:

$$B^m=\tfrac{1}{N-m}\sum_{i=1}^{N-m}B_i^m. \tag{5}$$

It expresses the probability that two sequences coincide for m points. Analogically, such probability is computed for the vector $\mathbf{X}_{m+1}$. The estimator of the sample entropy is given by;

$$\mathrm{SamEn}(m,r)=-\ln\frac{B^{m+1}}{B^m}. \tag{6}$$

This estimator depends on two parameters m, r.

3. Sensitivity Analysis of a Sample Entropy Estimator

This estimator depends on two parameters *m,r*. Setting their values properly is still problematic. Some rules for this purpose were described in the literature [8]. The simplest rule states that the optimal values for the best sample entropy estimation are $m = 2$, $r = 0.2\sigma$, where σ is a standard deviation of a modeled signal. The more complicated rule was proposed by Richman et al. basing on the width of 95% confidential interval for sample entropy. This method was applied to analysis of neonatal heart variability [7]. Biological signals are characterized by large variability and specificity for a given biological process so the method applied for heart variability does not have to be sufficient for EHG. Moreover, the parameter's dependence could not be stable in relation to uterine physiological activities.

Thus, firstly we studied numerically the entropy sample variability in relation to *m* and *r* parameters in the three groups of EHG signals. The first group consisted of EHG signals registered from 49 women being before a labor. The second group contained EHG signals observed in 31 women during a labor and the third group – in 6 women during puerperium. The analyzed signals were registered from the electrode placed over the body of the uterus. The parameter *m* was equaled to 1, 2…7 while $r \in [0, 0, 25\sigma]$. This interval was discretisated with the discretisation step equal to 0.01. The obtained results were shown in Fig. 2.

The left and middle figures shows that the median of the SamEn estimator changes smoothly in relation to *m* and *r* values. This is not observed in the right figure where the sharp edges are seen. It is caused by small number of patients in the third group leading to the underestimated median.

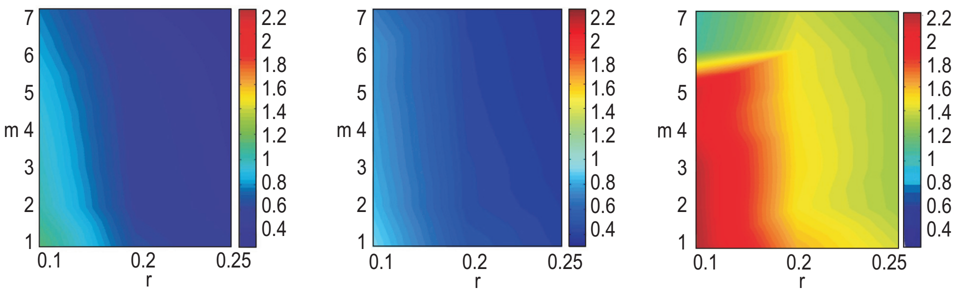

Fig. 2. The $m \times r$ space of median values of sample entropy estimated before a labor (left), during a labor (middle) and after a labor (right). The values of the median correspond to the colors legend

The performed analysis indicated that the sample entropy estimators were weekly dependent on *m* parameter while they were significantly dependent on *r* values. These relations were observed in the three groups. Moreover, the computational complexity becomes higher with increasing *m* values. Thus, in the further analysis the *m*-dependence could be neglected. Taking into account trade-off between this complexity and *m*-dependence of the sample entropy it was assumed $m = 2$.

According to the clinical goal of EHG modeling i.e. differentiation of a physiological state of an uterus the value of *r* parameter was computed in the following manner:

$$\hat{r} = \arg\max_{r>0.1} \frac{\sigma_{out}(r)}{\sigma_{in}(r)} \tag{7}$$

where $\sigma_{out}, \sigma_{in}$ were the inter- and intragroup variances of estimated values. Figure 3 presents these variances. To simplify the optimization procedure only two groups were taken into consideration, i.e. patients being in labor and patients being before labor. It was possible because the variances of the sample entropy for puerperium were significantly different from the variances for the remaining groups. However, the relations $\sigma_{out}(r), \sigma_{in}(r)$ are nonlinear and determined only implicitly.

Thus, the problem was solved numerically using the Broyden–Fletcher–Goldfarb–Shanno (BFGS) method. Optimization was performed only for pre-labor and labor states because the variances of the sample entropies computed for puerperium were higher for all *r* values (Fig. 3).

Different starting points were used to avoid local optimums. Moreover, the constrain $r > 0.1$ was introduced because too small value of *r* gives an overestimation of the sample entropy. The applied numerical procedure showed that $\hat{r} = 0.17$.

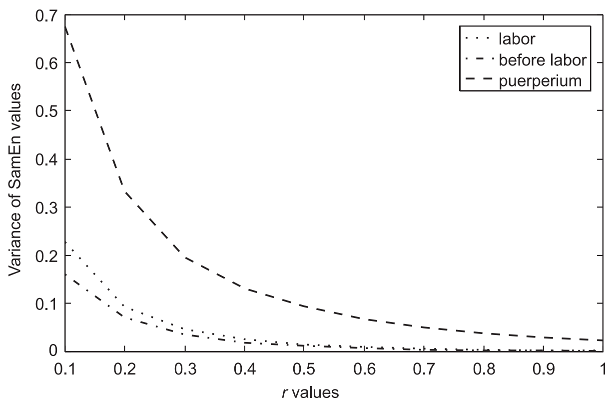

Fig. 3. The relationship between variances of SamEn values and r values. The variance of the SamEn for puerperium was significantly different from variances for the peri-labor period so the differentiation problem was considered only for two groups

4. Conclusion

Numerous publications suggest that a nonlinear analysis of biological signals can be suitable from clinically discriminating point of view. Our preview analysis showed that sample entropy gave better and more robust results than approximated entropy in relation to EHG signals. In this paper the selection of parameter values of sample entropy was considered. Our results confirmed that this estimator was weakly dependent on *m* values and significantly dependent on *r* values. Lastly, Lu et al. proposed a heuristic method of automatic adjustment of this parameter [9]. The method should be tested for EHG signals. However, this method could be sensitive to a noise because *r* values will be adapted for a given signal taking into account a short term variability of the signal. Moreover, differentiation of *r* values caused by adaptation could make comparison between physiological states of an uterus difficult. Thus, we proposed the method based on intra and inter-variability of sample entropy values. The method gave promising results. Its drawback is a need of proper estimation of these variances in a given women population. It seems that the problem of *r* values choice requires further investigations taking into account clinical application of an EHG model.

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