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Customization of Entropy Estimation Measures for Human Arterial Hypertension Records Segmentation

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***Abstract*— This paper describes a new application of the recently developed Coefficient of Sample Entropy (CosEn) measure. This entropy estimator is specially suited for cases where the length of the time series is extremely short. CosEn has already been used successfully to characterize and detect atrial fibrillation, using as few as 12 heartbeats.**

We have customized the methodology employed for heartbeat interval series to blood pressure hypertensive (BPHT) human records. Little can be found about BPHT records and its nonlinear regularity analysis. The method described in this paper provides a good segmentation between control and pathologic groups, based on the corresponding labeled BPHT records. The experimental dataset was drawn from the available records at the Hypertension Unit of the University Hospital of Mostoles, in Spain. The hypertension related variables studied were systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean blood pressure (MBP). The hypothesis test yielded the following results in each case: acceptance probability of 0 for SBP, 0.005 for DBP and 0 for MBP. The confidence intervals for the three variables were nonoverlapping.

I. INTRODUCTION

Biological systems can be considered a manifestation of complex and nonlinear processes. Such systems exhibit not only the readily observable stationary or periodic behavior, but they also usually have a nonpredictable, chaotic, nonlinear or nonstationary behavior [1]. Nonlinear methods based on entropy computations or data complexity statistics have become very popular recently in applications related to the analysis of biological signals due to their good results. Their capability to unveil hidden nonlinear information embedded in records has proven very powerful in signal class segmentation applications. Classical linear methods lack of robustness or characterization depth in most of these cases [2], [3].

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Blood pressure (BP) is considered to be a key parameter when evaluating the cardiovascular control system of a patient since essential hypertension (HT) is considered to be a trigger of a variety of mayor cardiovascular diseases, such as cerebral stroke or myocardial infarct [4]. BP has been widely characterized by traditional, linear methods, which assume a certain degree of stationarity. On the contrary, little can be found about BP studies with nonlinear entropy methods [1], [5], [6]. Most of this few studies are based on animal blood pressure hypertensive (BPHT) records. Additionally, usual nonlinear methods employed in these cases are correlation dimension (CD) [1], Lempel–Ziv (LZ) [5] and detrended fluctuation analysis (DFA) [6]. However, due to the specific features of BP records, these metrics do not properly fit to this BP analysis task since a large number of samples are needed in order to obtain a good entropy estimation [1]. Most of them require a number of samples in the order of several hundreds or thousands, whereas a long–term BP record may contain some 120 samples at most.

In this paper, our interest is focused on human BPHT records. These data series are usually noninvasively recorded by means of a digital sphygmomanometer. This technique termed sphygmomanometry is known to be the most accurate and noninvasive method for BP data acquisition, although it is quite uncomfortable for the patient. A cuff surrounding the arm should previously be inflated until its pressure is higher than the Systolic Blood Pressure (SBP), and then deinflated so as to take a measure. During the data acquisition it is convenient that the patient remains still in a steady state, such as sitting, relaxed, with the arm straight and immobile [4]. Owing to such uncomfortability and constraints, long or continuous BPHT records are not usually possible. Therefore, in order to enable a nonlinear analysis of such records, a more robust entropy measure is needed.

An increased BP variability in the different ways it can be recorded (ambulatory or home) implies a worse prognosis in several studies. However, as far as we know, a complexity analysis of these arterial BP measures and its correlation with a clinical prognosis has not been carried out yet.

Our previous research has proved that there is a progressive loss of complexity from a normality state to illness in thermo–regulation [7] and in glucoregulation [8], and such loss entails a worse prognosis. In other works, it has been observed that there is an inverse correlation between variability and complexity, and probably both phenomena are manifestations of the same deterioration process of the fine control physiological systems. However, a complexity

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analysis offers methods much more objective, sensitive, and accurate to quantify such deterioration.

A new regularity measure, named coefficient of Sample Entropy (CosEn), has been proposed recently to evaluate and detect atrial fibrillation (AF) on very short data records [9]. This measure provides good results over time series containing only 12 heartbeats. Because of the similar characteristics between the RR signals considered in [9], and the BPHT signals analyzed in this work (both signals are short and nonevenly sampled), the method in [9] was customized and used to characterize BPHT human records. Our objective was to assess the capability of CosEn to distinguish between healthy and pathologic subjects based on the regularity estimation computed from BP ambulatory records.

II. METHOD

CosEn is based on the estimation of SampEn. However, this measure depends largely on the value of its parameters r and m, which is critical specially when dealing with very short time series. The first step in the direction of reducing the influence of r was described in [10], where a new entropy estimate, termed Quadratic Sample Entropy (QSE), was introduced. This measure enables any r to be used, since the measured conditional probability is normalized by the volume of the matching region [9].

The tolerance parameter r can be optimized for each physiological record, for example, to guarantee that a minimum number of matches is obtained and therefore a confident entropy estimation is possible [9]. This optimization was achieved using a matches function (counts the number of matches below a threshold) to find the optimal r value for each possible number of them, termed M, and the corresponding ROC curves to estimate the optimal M.

A. QSE computation

QSE is a measure devised to solve the limitations and possible pitfalls in the computation and interpretation of Sample Entropy (SampEn), particularly for short data records where the number of matches found to compute the conditional probability is low and limited [10]. QSE is based on the transformation of this SampEn conditional probability [3] to a density. This is achieved by normalizing SampEn by the volume of the matching region, using a term given by $2r^m$. Thus, QSE is calculated as:

$$\mathrm{QSE} = \mathrm{SampEn}(N, m, r) + \log(2r) \tag{1}$$

where N denotes the record length, m and r are the classical SampEn input parameters, accounting for the embedded dimension and tolerance level, respectively. SampEn can be computed as described in [3] using the source code implementation available at [11].

B. Coefficient of Sample Entropy (CosEn) computation

Derived from QSE, CosEn, is another entropy estimate that was first devised and applied to the detection of AF from RR series. This application is based on the fact that the mean signal value was found to contribute significantly and independently to the diagnosis in AF detection. CosEn is computed similarly as QSE [9]:

$$\mathrm{CosEn} = \mathrm{SampEn}(N, m, r) - \log(2r) - \log(\mu_x) \tag{2}$$

where μ_x denotes the mean value of the input signal x, being the other terms in the expression the same as in (1).

The parameter m was set to 2 in our case, and r was obtained in terms of M for each signal independently. For each M, ROC curves were calculated, and the area under each curve was plotted against M. Optimum M for final CosEn computation was estimated as the one that maximized the ROC area curve, in order to yield the optimal segmentation. The details of this optimization process are described next.

1) Tolerance r estimation: The level r was estimated for each signal. Initially, M was varied from 2 to the maximum possible number of matches, $M_{\max}$. The input to the matches function [11] was the time series x and the run length m. The output of this function, modified accordingly to allocate this optimization process, was the optimal r value for each N_m. The rationale of this step is to reverse the usual functioning of matches functions, instead of counting the number of matches given a tolerance, find the unknown tolerance value that yields a predefined number of matches. Thus, r value was set according to:

$$r(M(n)) = d_{M(n)} + \epsilon \qquad n = 1, 2, ..., M_{\max} \tag{3}$$

where $d_{M(n)}$ denotes the dissimilarity value needed to achieve M matches, and ϵ accounts for the order of the smallest difference among dissimilarities:

$$\epsilon = 10^{\lfloor \log_{10}(d_{\min}) \rfloor} \tag{4}$$

$$d_{\min} = \min_{k, k \neq n} \{|d(n) - d(k)|\} \tag{5}$$

2) ROC curves: The ROC area curves obtained using the method described above are used to estimate the optimum M. However, these curves are relatively noisy, and some filtering is needed to obtain such optimum. To this end, moving average filters of different lengths were considered due to their simplicity and good results for this task. Specifically, the time–domain equation of the filter used is:

$$y(n) = \frac{1}{2L+1} \sum_{k=-L}^{L} y(n-k) \tag{6}$$

where L accounts for the length in samples of the filter. The filtering was computed for different lengths, ranging from 5 to 50 in steps of 5 samples.

3) Optimum M estimation: Finally, the local optimum M_L^{opt} for each filtered ROC area curve (RAC_L) was obtained as the argument that maximizes such area, namely:

$$M_L^{\text{opt}} = \arg\max_n \{\text{RAC}_L(n)\} \tag{7}$$

From all the M_L^{opt}, a global optimum M^{opt} had to be chosen. We used an statistical analysis based on median and Median Absolute Deviation (MAD) values of M_L^{opt} due to their robustness as statistical measures of data dispersion. M_L^{opt} optimal values fell within a narrow interval.

Let $\chi = \text{median}(M(k)_L)$, M^{opt} can be estimated as:

$$M^{\text{opt}} = \text{median}\left\{M_L^{\text{opt}} : M \in [\chi - \text{MAD}, \chi + \text{MAD}]\right\} \tag{8}$$

$$\text{MAD} = \text{median}\left\{|M(k)_L - \text{median}\left\{M(k)_L\right\}|\right\} \tag{9}$$

C. Statistical analysis

CosEn values estimated using (2) were first screened by means of the Shapiro–Wilks normality test (α=0.05). This test suits a low number of observations.

Then, if a normal distribution could be assumed, the Student T-Test was carried out in order to assess the segmentation capability between healthy and pathologic subjects. Otherwise, the Mann-Whitney U significance test was used for the same purpose, comparing medians instead.

Confidence intervals were estimated as:

$$CI = [\mu - 2\sigma_\mu, \mu + 2\sigma_\mu] \tag{10}$$

$$\sigma_\mu = \frac{\sqrt{\left(\frac{\sum_{i=1}^{n}(CosEn_i(x)-\mu)^2}{n}\right)}}{\sqrt{n}} = \frac{\sigma}{\sqrt{n}} \tag{11}$$

where μ accounts for the mean and σ_μ for the standardized mean error, if time series data were considered to be drawn from a normal distribution. If the normality test was not satisfied, these values account for the median and MAD, respectively. The standardized mean error σ_μ was computed as described in (11) and MAD as stated by (9). $CosEn_i$ denotes the estimated entropy value for signal i and n represents the total number of signals of each data group.

III. EXPERIMENTS AND RESULTS

A. Experimental dataset

The 24-hour Ambulatory BP Monitoring (ABPM) readings used in the experiments were provided by the Hypertension Unit, Hospital Universitario de Móstoles, Madrid (Spain). These data series were acquired and recorded using a SpaceLabs 90207 automated noninvasive oscillometric device. This device was programmed to register BP at 20–minute intervals during the daytime period and at 30–minute intervals during the nighttime period. These periods might change if a sample was considered invalid by the device, since an additional reading had then to be recorded automatically 5 minutes later.

Most of the records were acquired on working days. Patients were instructed to maintain their usual activities, and to keep their arm extended and immobile at the time of each cuff inflation to avoid outliers in the data.

However, a further screening of the records was conducted before being included in the experimental dataset. The noisy data points that despite the resampling function of the device and the patient care were present in the record, were removed. After this screening, the dataset contained signals with lengths ranging from 52 samples minimum to 63 samples maximum. For this study, the signal lengths were set to the maximum length of the shortest signal, 52 samples, removing the spare data at the end of the longer records.

The resulting experimental dataset contains 61 data records. Severe hypertensive patients account for 31 of these records. These patients were on anti–hypertensive drug treatment, and were attended regularly at the Hypertension Unit mentioned above. The remaining 30 data records correspond to subjects with a suspected diagnosis of essential hypertension. Since no drug-treatment was given to them, they were considered as control patients. Each record contains systolic BP (SBP), diastolic BP (DBP), mean BP (MBP) and cardiac frequency (F_c) information. Table I show mean and standard deviation for values for each variable and data group.

TABLE I

STATISTICAL CHARACTERISTICS ($\mu \pm 2\sigma$) OF THE DATABASE.

	SBP	DBP	MBP	F_C
Ctrl. (mmHg)	120.11 ± 32.04	73.26 ± 25.70	89.15 ± 25.12	72.15 ± 28.00
Patho. (mmHg)	148.16 ± 43.20	84.04 ± 36.86	106.66 ± 34.92	71.55 ± 26.02

B. Results

The algorithm introduced in Sec.II was assessed using the database described in sec.III-A. The segmentation results obtained in terms of CosEn CI are shown in Fig.1. The statistical segmentation results are shown in table II.

SBP, DBP and F_C come from normal distributions, as the Shapiro–Wilks p–Value was higher than 0.05 (the null hypothesis was accepted). MBPs p–Value indicated that MBP data can not be considered to match a normal distribution. Thus, MBP data had to be characterized by its median and MAD values instead of mean and mean standardized error.

Fig.1 shows that segmentation for SBP, DBP and MPB is straightforward, as the confidence intervals do not overlap, while no discrimination can be obtained between control and pathologic groups in terms of F_C. This visual results are quantitatively demonstrated with the results presented in table II. The T-test p–Value is lower than 0.05 for SBP, DBP and MBP but higher for F_c, thus leading to overlapping CI.

Finally, it can be observed that MBP regularity value seems more influenced by SBP rather than DBP, since they exhibit similar CI for both groups.

IV. DISCUSSION

Entropy metrics such as SampEn, Approximate Entropy (ApEn), and Detrended Fluctuation Analysis (DFA) were

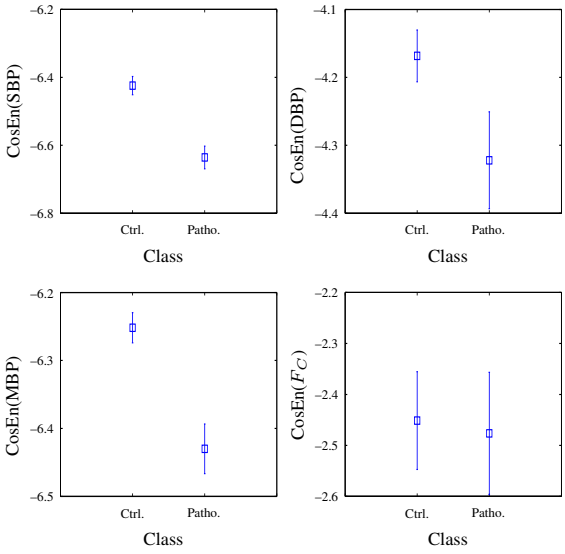

Fig. 1. Confidence intervals (CI) for systolic (SBP), diastolic (DBP), mean BP (MBP) and cardiac frequency (F_C) for both data groups, control (Ctrl.) and hypertensive (Patho.).

TABLE II

STATISTICAL RESULTS FOR COSEN SEGMENTATION.

	SBP	DBP	MBP	F_C
SW pValue	0.053	0.165	0.022	0.868
T-test pValue	0	0.005	0	0.749
CI Ctrl.	[–6.451, –6.397]	[–4.207, –4.130]	[–6.274, –6.230]	[–2.547, –2.355]
CI Patho.	[–6.669, –6.603]	[–4.393, –4.251]	[–6.467, –6.394]	[–2.596, –2.357]

computed over the experimental dataset described, but no confident segmentation results were obtained, not even with a parametrization study. Therefore, other measures had to be studied. These measures should cope with short record lengths and provide confident estimations when the number of samples in the records is very low. QSE and CosEn measures were considered because of their good results when using data records as short as 12 samples.

The CosEn method proposed in [9] was originally devised to detect AF on short RR data records. The RR records are known to be nonlinear, nonstationary, discrete and unevenly sampled data signals. Similarly, the BPHT data records used in this work are characterized by it nonstationarity, nonlinearity, short record length and unevenly sampled too, which enabled us to adapt and apply CosEn in this BP study.

The results confirmed that CosEn is a suitable entropy estimator for BPHT records. Graphical results depicted in Fig.1 show that SBP, DBP and MBP are relevant variables when referring to such records. CI are nonoverlapping in the three mentioned variables, being able then to distinguish between control and pathologic patient data. Graphical information is supported by the analytical results given in table II, where the nonoverlapping CI are quantified and the Student T-Test null hypothesis acceptance probability is lower than 0.05, which shows that there exists a difference between mean values of the distributions for each data group.

V. CONCLUSION

A method to detect AF from RR record analysis, described in [9], has been customized to study the segmentation and detection of chronic and non–well controlled essential hypertension, using human BPHT records.

Entropy computation from human BPHT records is a challenging task. Most entropy estimators require a relatively large number of samples to provide confident estimations. Recording long length BPHT signals is not possible using current ambulatory methods and devices due to the uncomfortable data acquisition procedure. Most of the work over BPHT records has been done with classical linear methods.

This paper proposes an extension of the CosEn method to analyze and discern among BPHT data records, based on the similarity between human BPHT records and RR signal records. The method proposed and optimized for AF detection over RR signals has been extended to segment and discern between control and pathologic data from 24h ambulatory BP records with a maximum length of 52 samples.

The resulting method has proven to be able to obtain a good segmentation between control and pathologic BPHT short data records, as it provides nonoverlapping CI and very low student T-test null hypothesis acceptance probability.

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