Characterization of Home-Acquired Blood Pressure Time Series Using Multiscale Entropy for Patients Treated Against Kidney Cancer

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Abstract. This study deals with the telemonitoring, with a connected tensiometer, of 16 patients treated for a kidney cancer. Each one of these patients recorded his/her blood pressure at home during 63 days and the data was sent to his/her medical doctor. At the same time they were treated with antihypertensive medication when necessary. In this work, our goal was to analyze the complexity of the blood pressure time series. For this purpose, we proposed to use the refined composite multiscale entropy (RCMSE) measures. Our results show that the patterns of RCMSE through temporal scales evolve with the antihypertensive medication. The later might therefore have an impact on home-acquired blood pressure complexity. RCMSE could therefore be an interesting information theory-based tool to study home-acquired physiological data.

Keywords: Telemonitoring · Connected tensiometer
Blood pressure · Time series · Multiscale entropy · Clustering
Irregularity · Complexity

1 Introduction

Kidney cancer is the 12th kind of cancer in terms of frequency in the world. It represents 338,000 new cases diagnosed in 2012 [1]. It can be treated by a VEGF[1] chemotherapy that consists in eliminating the capillaries of the tumor. However such a treatment can lead to blood pressure increases. This is why antihypertensive medication are often given to the patients. Our work deals with patients treated against a kidney cancer using a VEGF chemotherapy. During the treatment, patients recorded their blood pressure once a day at home using a

[1] Vascular Endothelial Growth Factor.

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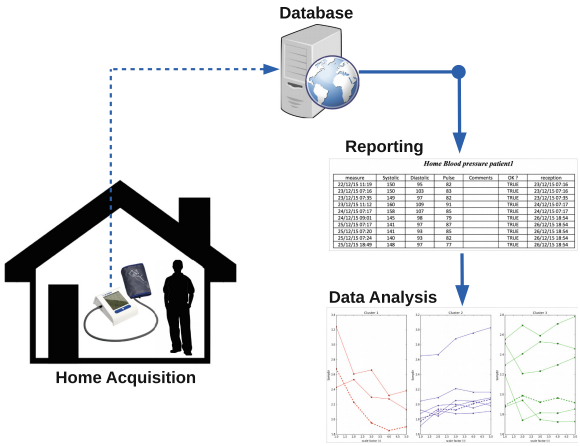

Fig. 1. Project overview

connected tensiometer (see Fig. 1). Such an IoT-based sensor [2,3] facilitates the following of blood pressure increases. Our goal herein is to study, with the refined composite multiscale entropy (RCMSE), the complexity of the blood pressure time series.

RCMSE is an improved version of the multiscale entropy (MSE). MSE relies on the sample entropy algorithm and on a coarse-graining procedure to study irregularity of time series at different time scales [4].

The paper is organized as follows: the MSE and RCMSE algorithms and the measurement procedure are introduced in Sect. 2. Our results are then detailed and discussed in Sect. 3. The paper ends with a Conclusion.

2 Materials and Methods

2.1 Sample Entropy

Pincus proposed to quantify the irregularity of time series with approximate entropy (ApEn) [5]. To overcome the limitation of ApEn, sample entropy has later been introduced [6]. Sample entropy is a conditional probability measure that quantifies the likehood that a sequence of m consecutive data points – that matches another sequence of the same length – will still match the other sequence when their length is increased by one sample $(m+1)$ [4]. Sample entropy is computed as:

$$SampEn(m, r, N) = -\ln \frac{A^m(r)}{B^m(r)}, \tag{1}$$

where r is the tolerance, m is the sample length, $A^m(r)$ and $B^m(r)$ are, respectively, the probability that two sequences will match for $m+1$ and m points.

2.2 Multiscale Entropy

MSE allows to quantify the complexity of time series by measuring its irregularity at different time scales [4,6].

The MSE algorithm is composed of three steps [7,8]

1. a coarse-graining procedure is used to derive a set of time series representing the system dynamics on different time scales. For a monovariate discrete signal x of length N, the coarse-grained time series y^τ is computed as:

$$y_j^{(\tau)} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} x_i, \tag{2}$$

   where τ is the scale factor and $1 \leqslant j \leqslant \frac{N}{\tau}$. The length of the coarse-grained time series is N/τ.
2. computation of the sample entropy for each coarse-grained times series.
3. plot of the sample entropy for each time scale τ.

2.3 Refined Composite Multiscale Entropy

MSE generates some undefined values for short time series [9]. When large scale factors τ are used, the coarse-grained time series may have a small number of samples. This may lead to undefined sample entropy values. This is why RCMSE has been introduced [9].

In RCMSE, the coarse-grained signal $y_k^{(\tau)}$ is computed for different values of a parameter k:

$$y_{k,j}^{(\tau)} = \frac{1}{\tau} \sum_{i=(j-1)\tau+k}^{j\tau+k-1} x_i, \tag{3}$$

where τ is the scale factor, x is the original signal, $1 \leqslant j \leqslant \frac{N}{\tau}$ and $1 \leqslant k \leqslant \tau$.

The RCMSE at scale τ is calculated using the following formulation:

$$RCMSE(x, \tau, m, r) = -\ln \frac{\sum_{k=1}^{\tau} n_{k,\tau}^{m+1}}{\sum_{k=1}^{\tau} n_{k,\tau}^{m}}, \tag{4}$$

where r is the tolerance, m is the sample length, $n_{k,\tau}^{m+1}$ and $n_{k,\tau}^{m}$ are the number of matched vector pairs (computed on $y_k^{(\tau)}$) for $m+1$ and m, respectively.

2.4 Measurement Procedure

The study was conducted on 16 patients (5 women, 11 men; 171 cm ± 9 cm; 87 kg ± 29 kg; 62 years ± 8 years). The 16 patients were daily monitored, during 63 days, using a connected tensiometer (Tel-O-Graph®, I.E.M. GmbH). Each recorded time series (Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) time series) had therefore 63 samples. In our work, $MBP(k)$

processed by RCMSE was defined as $MBP(k) = (SBP(k) + 2 \times DBP(k))/3$, $1 \leqslant k \leqslant 63$, where $SBP(k)$ is the systolic blood pressure at day k, $DBP(k)$ is the diastolic blood pressure at day k and $MBP(k)$ is the mean blood pressure at day k.

2.5 Parameters Used

To compute RCMSE, 3 parameters have to be set: m, r, and τ. It has been recommended that, to compute the sample entropy, the time series length has to be between 10^m and 20^m [6]. Our data have 63 samples. We therefore have chosen $m = 1$ and time scale $\tau \leqslant 5$. Moreover, we have chosen $r = 0.15 \times \sigma$ (where σ is the standard deviation of time series at scale factor $\tau = 1$) [8].

3 Results and Discussion

Figure 2 presents three examples of MBP time series. Figure 3 shows the corresponding RCMSE curves. By analyzing all the time series we observe 3 kinds of RCMSE patterns: global decreasing sample entropy with scales (cluster 1), global increasing sample entropy with scales (cluster 2), and non-monotonic sample entropy values with scales (cluster 3); see Fig. 4.

If sample entropy increases with scales, this means that the signal contains complex structures across multiple scales. If the sample entropy decreases with scales, this means that the signal has information only on the shortest scale (similarly to white noise [8]). In the undetermined case, no definite conclusion can be drawn.

We can observe that the signals of cluster 1 are similar to RCMSE of a white noise: the signal irregularity decreases with scale. Cluster 2 corresponds to an increase of the signal irregularity with scales. Cluster 3 corresponds to an intermediate situation.

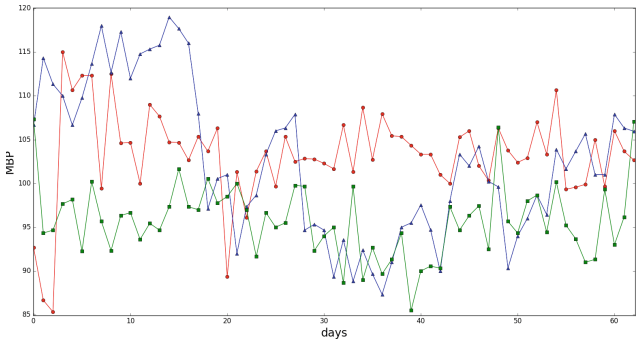

Fig. 2. Representative signals for each cluster (cluster 1: red — cluster 2: blue — cluster 3: green). (Color figure online)

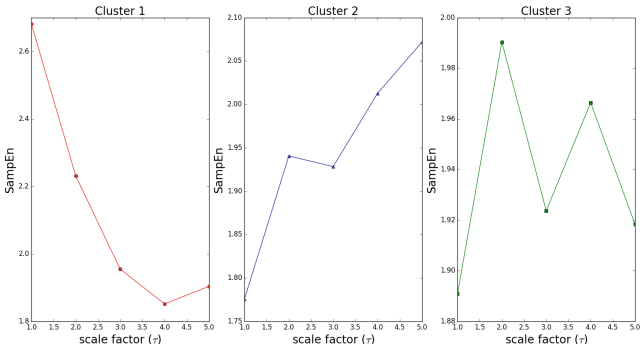

Fig. 3. RCMSE and clusters of representative signals shown in Fig. 2.

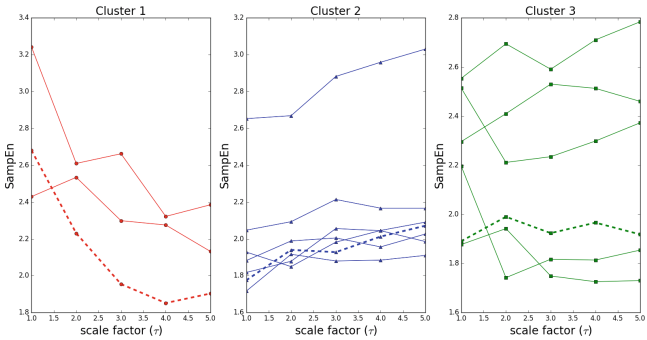

Fig. 4. RCMSE and clusters. Original signals leading to dotted RCMSE are represented in Fig. 2

Table 1. Clusters, RCMSE and #medication

Cluster	Cluster 1	Cluster 2	Cluster 3
RCMSE shape	Decrease	Increase	Undetermined
#patients	3	7	6
#medication	1	2	3

These clusters have been compared with the number of hypertensive medication taken by the patients. As reported in Table 1, for cluster 1, patients received only 1 antihypertensive treatment. For cluster 2, patients received 2 antihypertensive treatments. For cluster 3, patients received 3 antihypertensive treatments.

Anti-hypertensive medication may therefore play a role in the complexity of mean blood pressure time series.

4 Conclusion

In this work we studied the complexity of blood pressure time series with RCMSE. Further work is needed to apply the RCMSE algorithm on much more data. However, our work shows that antihypertensive medication might have an influence on mean blood pressure complexity. Our study shows that the complexity of data extracted by connected devices may be interesting for physiological purposes. Now, RCMSE could be applied to other IoT-based physiological time series. The next step of our work will consist in identifying patient profiles in order to personalize the telemonitoring.

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