

Artifacts in dependency structures of Portapres[®] signals

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Abstract— Portapres[®] is a unique device that reliably accomplishes a challenging task of continuous and non-invasive recording of blood pressure (BP) waveforms in moving subjects. The complex procedure of Portapres[®] signal acquisition includes periodic changes of cuffed fingers to avoid pain and stress, as well as the blood pressure correction due to the increasing and decreasing elevation of arm posture. Due to these procedures, the recorded waveforms are corrupted. The aim of this paper is to analyze the influence of inevitable artifacts on parameters obtained from the blood pressure waveforms. The analyzed waveforms are obtained from healthy volunteers at Bezanijska Kosa Hospital, Belgrade. The parameters include systolic blood pressure (SBP) and pulse interval (PI) extracted by Beatscope[®] software. The interrelationship of SBP and PI signals forms a major cardiovascular feedback – baroreflex. It can be analyzed using the sequence method for spontaneous baroreflex sensitivity, but the tools that reveal more profound dependency structures include cross-approximate and cross-sample entropy, as well as the copula structures. The influence of artifacts, inevitable in Portapres[®] signals, is the main goal of this study. The analyses revealed that automatic artifact correction induced no significant changes considering the statistical moments and the baroreflex sensitivity; the same applies to the copula density and rank tests. The entropy analysis, however, turned out to be extremely sensitive so its implementation in Portapres[®] signal analysis is not recommended.

Keywords- continuous non-invasive blood pressure monitoring; Portapres[®], cardiac parameters, dependency structures, copula, entropy, sequence analysis.

I. INTRODUCTION

The most reliable recording of the continuous blood pressure (BP) waveforms is performed by sensors implanted into the abdominal aorta with wired or (preferably) wireless connection to the remote A/D converter. Such recordings are highly invasive and could be performed during the surgery, or in experiments with laboratory animals. Completely non-invasive, cuff-less, recording is a subject of current extensive studies. In spite of the substantial progress that has been made [1]-[9], no reliable commercial device has been approved yet.

Semi-invasive ambulatory recording of continuous waveforms can be performed by Finapres[®] system that uses finger cuffs. The Portapres[®] is a Finapres[®]-based advanced technological solution that combines two golden clinical standards: a) 24-hour continuous, real-time recordings of arterial blood pressure in ambulatory subjects and b) recording the blood pressure in freely moving subjects. It is functional from 0 to 35 Celsius degrees and battery capacity provides 60 hours of recording in portable regime [10].

Embedded Beatscope[®] software allows online monitoring,

control, storage and offline review of the complete Portapres[®] data. Beatscope[®] extracts cardiac parameters, including systolic and diastolic blood pressure (SBP and DBP) and pulse interval (PI) [11]. The sampling frequency is equal to 100Hz, yielding a PI signal with a resolution of 10ms [11]. An important Portapres[®] feature that makes its uniqueness is the blood pressure correction, necessary due to increasing and decreasing elevation of finger cuffs [11].

Cardiac parameters (SBP, DBP, and PI) are extracted at beat-to-beat basis (cca 72 times per minute). For the sake of comparison, usual “pressure Holter” wearable devices yield one SBP signal per 10-15 minutes.

Yet, Portapres[®] still needs a finger cuff. In order to prevent the finger exhaustion during the long measurements, two cuffs at adjacent fingers are used [11]. The cuff functionality periodically changes, with a period of one or two minutes [11]. The periodical change of cuffs induces periodical artifacts in the recorded signal [11]. Artifacts are induced by elevation correction as well [11].

The aim of this paper is to analyze the effect of artifacts induced by cuff changes and elevation correction. Three types of analyses were considered: basic statistical analysis that is a standard in any ambulatory monitoring; baroreflex sensitivity based on classical sequence analysis; and, finally, dependency analysis based on Cross-Approximate entropy (*XApEn*), on Cross-Sample entropy (*XSampEn*), and on copula dependency structures. The signals for analysis are recorded at Bezanijska

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Kosa hospital, with the courtesy of prof. dr Branislav Milovanovic. To our best knowledge, this is the unique Portapres® in the Republic of Serbia.

II. MATERIALS AND METHODS

A. Experimental data

The signals were recorded from 25 healthy volunteers, according to the ethical protocol at Medical faculty, University of Belgrade, and ethical protocol of Bezanijska Kosa Hospital and with protocol permission signed by each subject. All signals were of the sufficient length for the sequence and statistical analysis. Copula and entropy analysis require longer signals, at least 10 minutes, so seven signals satisfied this criterion [11]. Blood pressure sampling interval was 10ms, which is sufficient for cardiac time series (although 1ms is a recommendation for ambulatory recording in sitting or lying patients) [11]. Time series extracted from BP waveforms were systolic blood pressure (SBP) obtained as local BP maxima and pulse interval (PI), obtained as an interval between the local maximal increasing gradients ($\Delta(\text{BP})/\Delta T$)_{max}, i.e. as the maximal pressure change (Δ)BP per sampling interval $\Delta T=10\text{ms}$.

B. Portapres®

Portapres® is a portable semi-invasive ambulatory device for 24-hours continuous blood pressure recording in moving subjects. Portapres® is shown in Fig. 1. It consists of the main unit which is placed on patient's waist and of the wrist unit which serves as an interface between the main unit and finger cuffs; its purpose is to supply finger cuffs with air. Finally, it comprises two cuffs placed around fingers; their activity is interchangeable to avoid the unpleasantness of the measurements that last several hours. Such measurements are based on clamp method and double cuff system [12]. The light source and detector are built in the finger cuffs, and blood pressure estimation is based on usual infrared photoplethysmographic (PPG) method [13]. Wrist unit equalizes the level of pressure in finger cuff with the PPG output. Pressure changes in the arteries are accompanied by changes in the external pressure of the cuff, which enables the maintenance of constant blood flow over time [14]. Clamp method was used by Finapres® system which is also implemented in Portapres® and TackForce Monitor® systems [15].

Portapres® also has a built-in system for pressure correction due to the changes in the hydrostatic level between the heart and the finger in freely moving subjects [15]. Semi-invasive blood pressure measurements by Portapres® were compared to the invasive measurements performed by brachial artery catheter which served as a ground truth. The experiment has shown that the differences in PI, DBP and mean blood pressure were not significant, while changes in SBP could be overcome by corrections [16], thus verifying the reliability of the Portapres® system.

C. Methods

Understanding the relationship between systolic blood pressure and heart beats is crucial for cardiovascular system analysis. The major (but not the only) regulation is governed by the baroreflex, a negative feedback that increases heart rate



Figure 1. Portapres® system: (1) The waist belt-contains sections for the main unit (electronics and memory card, air pump and lithium battery - allows 60 hours of operation in transmissive mode) (2) Frontend Unit for Portapres® (double finger cuffs systems) (3) set of cuffs (large, medium and small) (4) output box (A/D converter) [10].

(and shortens the pulse intervals) if the systolic blood pressure decreases (sensed in baroreceptors that are a biological analog to pressure sensors) and vice versa, decreases the heart rate in a case of the increased SBP. It should be noted that the pulse interval (PI) is a reciprocal of the heart rate.

Numerous methods analyzing the various aspects of SBP-PI interrelationship exist. We have opted to analyze the influence of Portapres® errors in three of them – sequence method, entropy, and copula. We have included a detailed description of each of them.

Sequence method is a non-invasive method for spontaneous baroreflex (sBRR) sensitivity measurement. It is based on finding the “ramps”. The “ramps” are successive signal samples that are either monotonously increasing or decreasing. A “sequence” is increasing (or decreasing) ramp of SBP samples (an SBP ramp) that is followed by delayed increasing (or decreasing) PI “ramp” which is, as a rule, shorter, as shown in Fig 2. Delay in humans can be 0, 1 or 2 heart-beats [11]. The simultaneously increasing (or decreasing) SBP-PI pairs (usually 2, 3 or 4 pairs) form a sequence [17, 18]. For each sequence, a linear regression can be used to find the local sBRR in a form $PI = \text{sBRR} \times SBP + b$ [11].

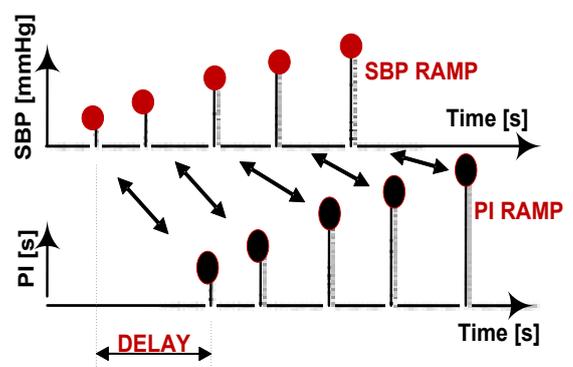


Figure 1. Ramps in SBP and PI time series that form a sequence.

Averaging the local sBRR coefficients over all sequences found in the recorded time series, the spontaneous baroreflex coefficient can be evaluated [11].

Cross-entropy estimates deeper connectivity between the observed time series, capturing their subtle relationship which lies beyond the scope of the linearity measured by the baroreflex. The most implemented types of entropy estimates used for measuring the similarity and self-similarity of biomedical data are Approximate entropy (*ApEn*) and Sample entropy (*SampEn*). Approximate entropy was introduced in [19] and well explained in [20, 21]. It initiated many variations (*FuzzyEn*, *BinEn*) [22, 23] but the *SampEn* [24] is the method that, considering its quotation rate [25], almost equals its predecessor *ApEn*. The initial entropy estimations considered the problem of self-similarity, but the potentials of cross-entropy were realized immediately [24].

The brief explanation of cross-entropy of two series recorded in parallel (e.g. **SBP** and **PI**) should be as follows: The first time series of length N , considered as “master” – e.g. **SBP**, is divided into the $N-m+1$ overlapping vectors of length m , i.e. series $\mathbf{SBP} = [SBP_i], i=1, \dots, N$ is divided into vectors $\mathbf{SBP}_i = [SBP_{i+j}], i=1, \dots, N-m+1, j=0, \dots, m-1$. Each one of $N-m+1$ vectors \mathbf{SBP}_i , in turn, becomes a “template”. The other series is “follower” – e.g. **PI** and it is also divided into $N-m+1$ vectors of length m (“followers”): $\mathbf{PI}_k = [PI_{k+j}], k=1, \dots, N-m+1, j=0, \dots, m-1$. Then each master template is compared to all the follower vectors to find the similarity rate. The criterion of similarity is a distance between the master (template) vector \mathbf{SBP}_i and the follower vector \mathbf{PI}_k that is, for *ApEn* and *SampEn*, calculated as maximal absolute difference of signal samples: $distance(\mathbf{SBP}_i, \mathbf{PI}_k) = \max |SBP_{i+j} - PI_{k+j}|, j=0, \dots, m-1$. This method of distance calculation, obviously, requires that time series should be normalized and centralized (z-normalization) [24].

The number of follower vectors that are at the distance less than the predefined threshold r is counted, thus defining a probability that the vector \mathbf{SBP}_i from the master series is similar to the observed time series **PI** [19]:

$$\hat{p}_i^{(m)} = \frac{1}{N-m+1} \sum_{k=1}^{N-m+1} I\{distance(\mathbf{SBP}_i, \mathbf{PI}_k) < r\} \quad (1)$$

Here $I\{\}$ denotes a mathematical function known as “indicator function” [26] that is equal to one if the condition it indicates (in this case: distance between the vectors \mathbf{SBP}_i and \mathbf{PI}_k is less than the threshold r) is fulfilled and zero otherwise. Finding the threshold level appropriate for the observed time series is a critical issue which has been elaborated in numerous contributions [27]-[29]. For this paper we used the method for cross-entropy proposed in [20].

The difference between *ApEn* and *SampEn* is related to the probability (1) processing: *ApEn* averages the logarithm of probabilities defined in (1) [19], while *SampEn* first averages the probabilities (1), and only then calculates the logarithm of this average [24]. This makes *SampEn* more robust but less sensitive.

The copula method gives another aspect of the mutual relationship of time series recorded in parallel: it provides a possibility to visualize their dependency structure. This visualization is obtained via “copula density” that shows the regions of dependency concentration.

A copula is a mathematical concept that decomposes a joint distribution function (of **SBP** and **PI** series in our case) into their univariate marginals and then measures the statistical dependency among the marginal components.

The crucial step in copula procedure is the probability integral transform (PIT) [30]. It transforms any random variable “ x ” with arbitrary distribution (x) into a random variable (RV) “ u ” with uniform distribution. The RV transformation is performed using an inverse of the distribution function (x) [30]. If analytical expression (x) is not known, it can be empirically estimated from the source random variable series, as it is done in case of **SBP** and **PI** signals.

The joint distribution function of the transformed time series (with uniform marginals) is then compared to the family of theoretical distribution functions known as “copulae”. The theoretical copula that is the closest to the empirically generated joint distribution function in a maximum likelihood sense is the winner and yields the level of accordance between the **SBP** and **PI** time series.

Numerous copula families exist, but pharmacological validation has shown that Frank copula is the most suitable choice for the cardiovascular signals [31]: it is unbounded and symmetric, it is equal to zero if the signals are statistically independent, it is more sensitive for SBP-PI signal changes than the other families of explicit and implicit copulas, and in SBP-PI case it models both the comonotonic and the countermonotonic dependence. Application examples of Frank copula in a context of SBP-PI relationship are shown in [32]. The Frank copula distribution is given by the following relation [33]:

$$C^{(F)}(u_1, u_2) = \frac{-1}{\theta} \log \left[1 + \frac{(e^{-\theta u_1} - 1)(e^{-\theta u_2} - 1)}{(e^{-\theta} - 1)} \right]. \quad (2)$$

In (2) “ u_1 ” and “ u_2 ” denote PIT (i.e. uniform) counterparts of **SBP** and **PI**. The first derivative of distribution function (2) yields the copula density that enables a visual presentation of the dependency structure.

The copula parameter θ shows the level of accordance between the time series. To obtain it, it is sufficient to perform the PIT over the observed time series (**SBP** and **PI**), find the empiric copula density (or distribution), and fit the density (distribution) to the densities (distribution) generated by (2). The density that is closest to the empirically estimated one yields the desired dependency level θ .

For the sake of comparison, the dependency measures assessed by the copula parameter are compared to the results of the linear Pearson’s product-moment correlation, Kendall’s rank correlation and Spearman’s rank correlations, as they are related to the copula parameter [33]. Pearson’s product-moment correlation measures linear relationship between variables. Kendall’s correlation reflects the number of concordances and discordances in time series, regardless of their degree. Spearman’s correlation measures the correlation between the ranked data [34].

III. RESULTS

A. Artifacts: source, statistics, and correction

There are three types of characteristic artifacts in the blood pressure waveforms of Portapres[®] signal. The first type is due to the tracking procedure (Fig. 3, upper panel). The second type is due to the periodical active cuff change (Fig. 3, middle panel). The third type occurs at the end of the recording (Fig. 3, bottom panel). The first and the third type are easy to manage: the erroneous start and end of the recorded signals are simply cut out. The visual inspection prior to the signal cuts is necessary since the tracking length can be variable. Some signals are tuned easily and tracking errors do not exist, while in some patients, several attempts to achieve the locking position have to be made, so the tracking lasts a couple of minutes. Sometimes the recording session must be abandoned since the tracking procedure fails to lock. The average duration of tracking and interrupts are presented in Table I.

The interrupts that are shown in the middle panel of Fig. 3 occur within the data region. From this region, the cardiac parameters for further analysis are extracted. From Table I it is clear that average duration of interrupt is equal to 3s, so it affects a couple of SBP-PI pairs.

Beatscope[®] software automatically corrects this issue, as shown in Fig. 4: it interpolates both the position and the amplitude of blood pressure waveform maximum, so that recorded stream of SBP, PI, and other cardiac parameters at the first glance seem to be without the interruption. However, it can also be seen that the last interpolated SBP is close to the subsequent maximum of the pressure waveform, i.e. the particular pulse interval between them is unusually short and might affect the results of the analysis.

Table II shows the absolute value of relative parameter change if the parameter is estimated from the raw signal (without the correction) and if the same parameter is estimated from the corrected signal shown in Fig. 4. The parameters include the classical moments (mean of SBP and PI signals) and the baroreflex sequence values (number of detected sequences and their average slope that correspond to the sBRR sensitivity).

B. Correction and its influence considering the analytical tools

The initial mean values of SBP and PI signals before correction were 97.38 ± 19.14 mmHg and 0.83 ± 0.26 s respectively. These two values remained almost the same after the correction: the absolute value of the relative change was

TABLE I. ARTIFACT DURATION

ARTIFACTS	DURATION
TRACKING DURATION [S]	42.25 ± 44.01
TRACKING DURATION [BEATS]	52.81 ± 55.12
DURATION OF INTERRUPTS/600 BEATS [S]	50.43 ± 12.77
DURATION OF INTERRUPTS/600 BEATS [BEATS]	16.26 ± 3.77
SINGLE INTERRUPT DURATION [S]	3.12 ± 0.44

Results are presented as mean \pm standard deviation

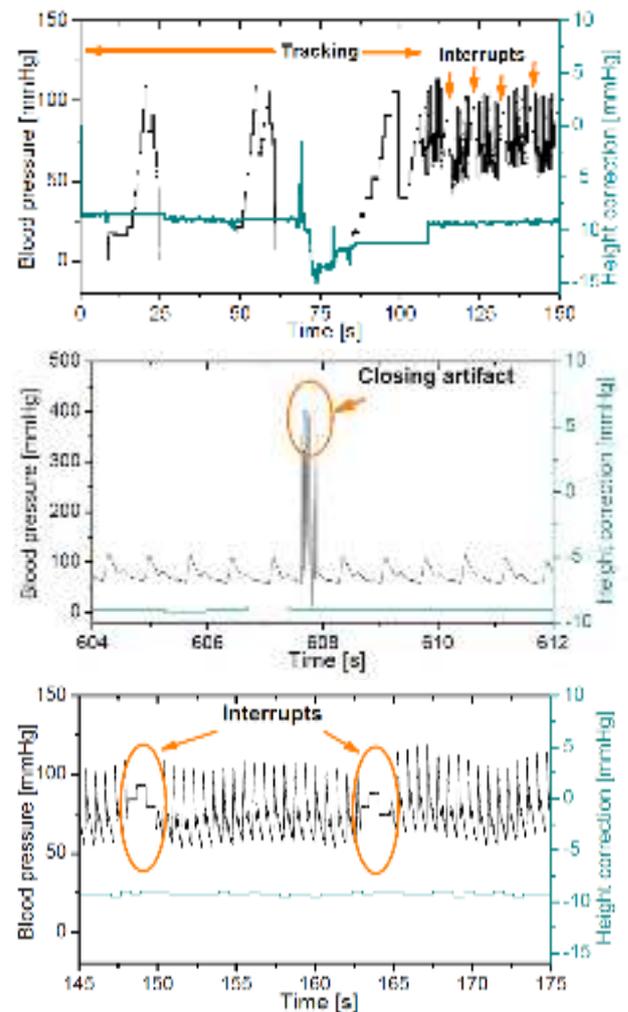


Figure 3. Blood pressure waveforms and artifacts; upper panel: tracking artifacts; middle panel: closing artifacts; lower panel: signal interrupts; note the pressure correction signal (green signal and y-axis on the right).

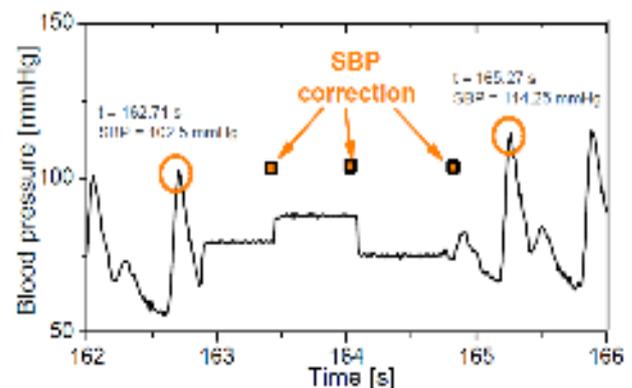


Figure 4. Interrupt correction: three SBP samples and the corresponding four pulse intervals (PI) are inserted.

TABLE II PARAMETER CHANGES IN [%] DUE TO THE INTERRUPT CORRECTION

PARAMETER	RELATIVE CHANGE [%]
SBP	0.17±0.02
PI	0.13±0.02
NUMBER OF SEQUENCES	5.27±5.29
NUMBER OF SEQUENCES, LENGTH > 1	10.63±17.89
SBRR SENSITIVITY	3.93±4.28
SBRR SENSITIVITY, LENGTH > 1	3.94±6.15

Results are presented as mean ± standard deviation; the changes are absolute, expressed in [%] in respect to the case without the correction.

less than 0.2%. It points out that the correction performed by Beatscope® software interpolates the missing SBP peaks in such a way that the mean values of the existing peaks (their amplitude and their mutual distance) remain unaltered.

Considering the more complex analysis, the change of slope of baroreflex sequences (i.e. the spontaneous sBRR sensitivity), is below than 4%; this change is almost the same both for the sequences with length > 1 and for the sequences without any length constraint. Therefore, the impact of interrupt correction is only moderate and the obtained – corrected - signals can be safely used for the baroreflex analysis.

Considering the entropy analysis, the results are not so promising. Table III shows changes of cross-entropy analysis using *ApEn* and using *SampEn*, when SBP signal is master and when PI signal is master. Since only 7 signals satisfied the constraints for reliable entropy estimation [20], Table III presents the results for all seven subjects.

From Table III it may be seen that the entropy results obtained from the corrected signal and from the source signals are not consistent. Fig. 5 presents the SBP and PI signals with marked correction for Subjects 1 and 7: the entropy estimated from the first subject exhibited the least discrepancy in entropy estimation, while the opposite holds for the subject 7. Although the amount of corrections is similar for both subjects, and the corrections are similarly scattered within the respective signals, it seems that the difference of signal variability caused the inconsistency.

Signal no. 1 has low variability, so the corresponding corrections form an embedded signal of low variability as well,

so this embedded signal has a low impact on temporal analysis such as entropy estimation. On the other hand, the corrective samples embedded within the signal no. 7 are of high variability in order to be aligned with the properties of the signal. This destroys the temporal properties inherent in a signal that affects the entropy study.

Copulas express the dependency structures of signals with uniform marginals, related to the distribution/density functions that destroy the temporal characteristics of the signal. To penetrate the relationship that exists between the SBP and PI signals, an example of dependency structures is shown in Fig. 6, for four characteristic delays of PI signal with respect to SBP, expressed in heartbeats. Panels b) and c) show empirical copulas estimated from signals without and with the correction, while the panels a) and d) show the corresponding theoretical density obtained by (2). From the middle panels (b and c) an increased diagonal density can be observed, in particular for a delay equal to one and two beats, which is characteristic for human patients.

Fig. 7 shows the dependency level evaluated using Frank’s copula, and Kendall, Pearson, and Spearman methods, while in Fig. 8 the relative difference between the original (uncorrected) and corrected signals is shown. The signal with the largest difference is chosen – the difference of the other signals is less than 10%. This confirms the assumption that changes in entropy are due to the temporal sample dependency that is, in copula study, destroyed, as well as in Kendall’s and Spearman’s rank test. On the other hand, Pearson is close to the classical correlation that slides over the signal samples and for this reason, the inconsistency of corrected and uncorrected signals is great.

IV. CONCLUSION

The Portapres® is a device with a unique option to record non-invasively blood pressure waveforms. From these waveforms important cardiovascular features, such as systolic blood pressure and pulse interval, can be extracted. The Portapres® signals, unfortunately, suffer distortions that can be automatically corrected by the Beatscope® software. The aim of this paper was to test an amount of these distortions and to analyze the reliability of parameters estimated from uncorrected signals (ground truth that requires supervised analysis and visual inspection) and from corrected signals (unsupervised, automatic analysis).

TABLE III CROSS-ENTROPY CHANGES DUE TO THE INTERRUPT CORRECTION IN SBP AND PI TIME SERIES

SUBJECTS	Cross-ApEn changes [%]		Cross-SampEn changes [%]	
	SBP vs. PI	PI vs. SBP	SBP vs. PI	PI vs. SBP
1	1.5	-7.28	-0.01	-0.02
2	6.47	37.95	36.08	36.16
3	3.66	0.97	6.6	6.64
4	20.54	2.78	14.85	14.81
5	5.08	-0.38	4.2	4.22
6	-1.09	0.16	8.79	8.75
7	39.16	56.31	50.27	50.21
ABSOLUTE MEAN	11.07	15.12	17.26	17.26
STANDARD DEVIATION	12.99	20.95	17.33	17.32

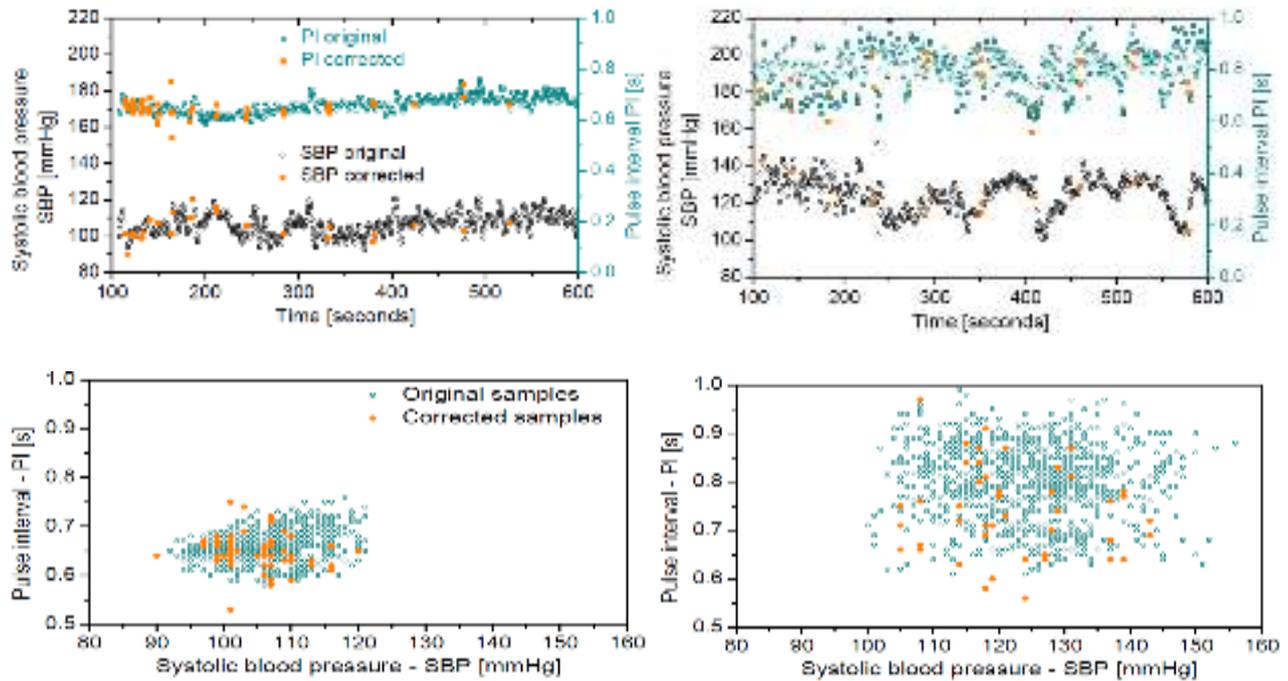


Figure 5. SBP and PI time series (top panels) and signal pairs in SBP-PI plane (bottom panels). Panels in left: signal from subject 1 that exhibited no changes in entropy after the correction is performed (yellow points added); panels in right: signal from subject 7 that exhibited a substantial change in entropy after the correction is performed.

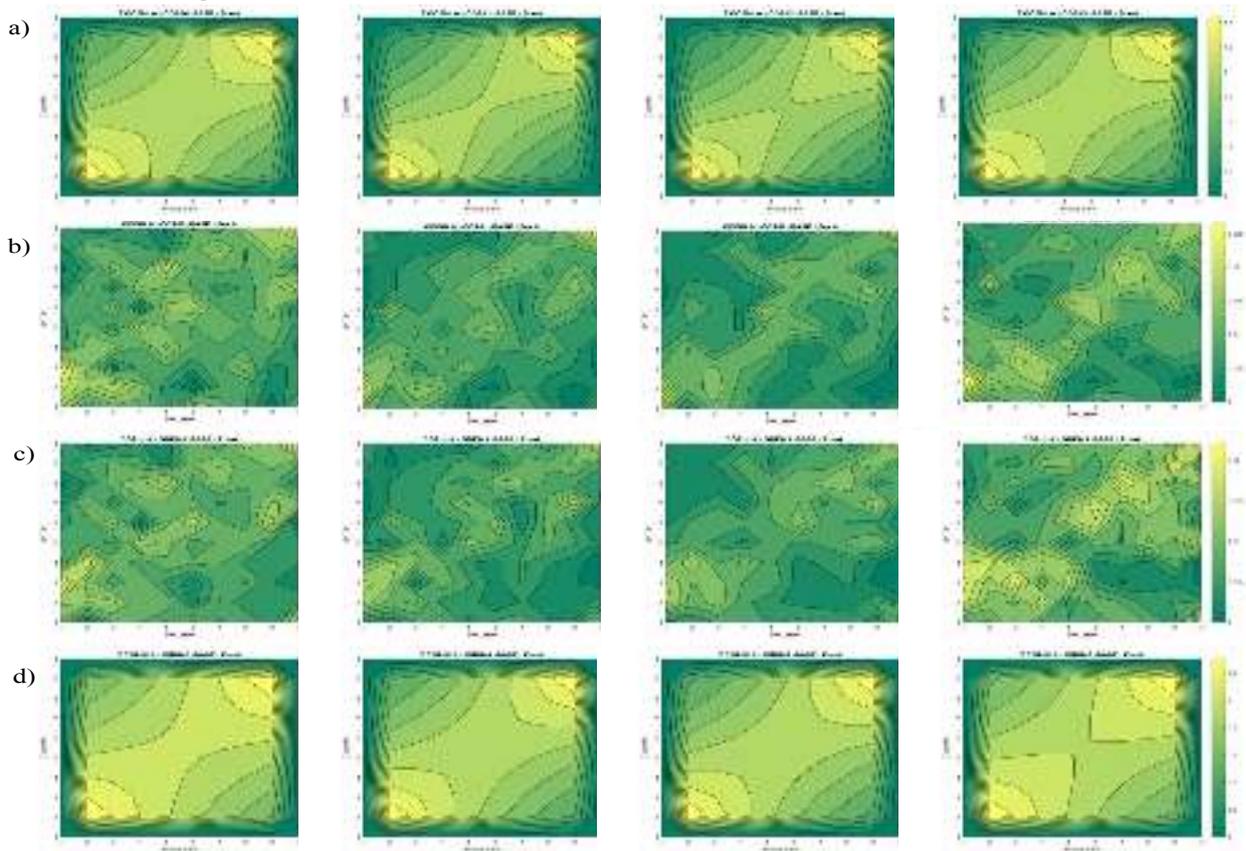


Figure 6. Copula density of Subject 4 with the greatest change of copula parameter after the interrupts have been automatically corrected; from left to right: the delay of PI in respect to SBP is 0, 1, 2 and 3 heart beats respectively; Panels b) and c): empirical dependency structures – note the diagonal dependency concentration; Panels a) and d): theoretical counterparts of the empirical structures according to the (2).

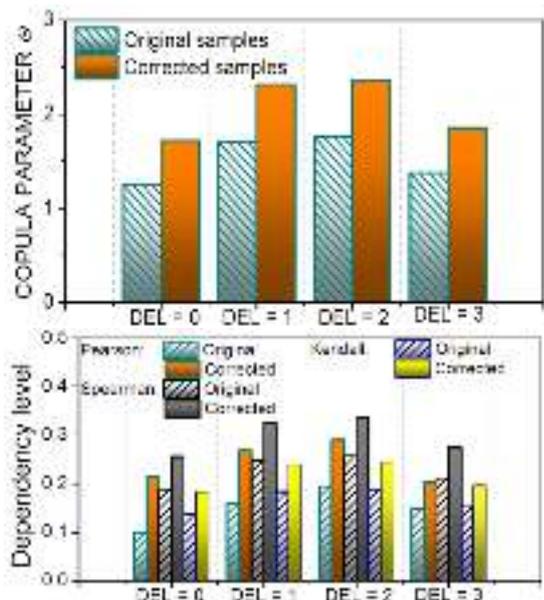


Figure 7. SBP-PI dependency level for different delays of PI signal in respect of SBP; upper panel: dependency expressed as a copula parameter θ ; lower panel: dependency expressed as Pearson's, Kendall's and Spearman's parameters; note that θ bigger than the other parameters by an order of magnitude, and that the trend of dependencies in respect to delay is the same for all the parameters.

The parameters that are investigated reveal the complex relationship between SBP and PI. These parameters are extensively estimated in research considering the cardiovascular diseases. The parameters include baroreflex sequences that measure linear SBP-PI relationship; copula parameter that measures non-linear relationship of SBP-PI sample pairs; and entropy that measures broad temporal statistics of SBP-PI vector (m adjacent samples) pairs.

Baroreflex analysis, an approved method to achieve the relationship between the systolic blood pressure and pulse interval as its linear cardiac response is shown to be a stable method as the correction procedure, aiming to preserve the trend of signal peaks, do not alter significantly the increasing or decreasing sequences required to estimate baroreflex parameters. Copula dependency structures, based on the joint histograms of the transformed SBP and PI series, are stable as well – the number of samples in a two-dimensional histogram bins is stabilized by their uniform marginal distribution; their slight changes are insufficient to induce the change in the dependency level.

Entropy methods rely on the sequential window-sliding search along the recorded data to produce master and follower vectors that capture temporal statistical dependency of m adjacent signal samples. Frequent signal interrupts distort this dependency. The results are unreliable – in some patients corrected and uncorrected results are aligned, in some patients diagnostic significance in corrected signals is inverted in respect to the uncorrected version. Although $ApEn$ and $SampEn$ are the most quoted and implemented analytical tools in cardiovascular investigations, their use in Portapres® signals should be avoided.

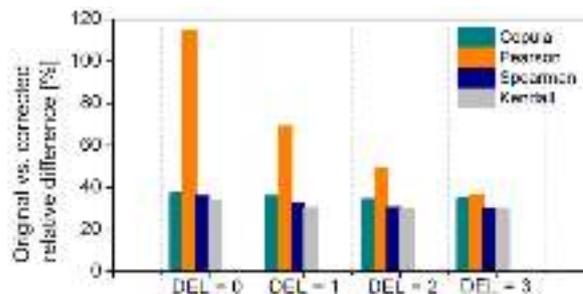


Figure 8. Relative change of dependency parameters induced by signal correction; in all other subject the changes were smaller; the changes are consistent considering the methods and delay of PI in respect to SBP, except for the Pearson's coefficient that is based on temporal sliding.

Although entropy estimates are useful in investigation of non-linear relationship, in a context of heavily distorted signal the non-linear nature of Frank copula parameter can serve as a complement to linear sBRR sensitivity and it can be a reliably entropy substitute.

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