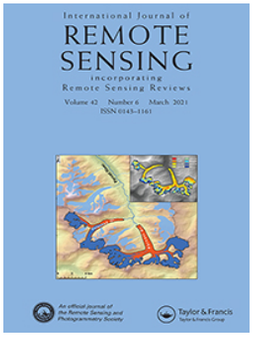

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ARTICLE

Remote sensing natural time analysis of heartbeat data by means of a portable photoplethysmography device

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ABSTRACT

Very recent work reported that patients can monitor their heartbeat at home and specify their heart conditions by means of a millimetre wave radar, but there exist serious limitations because the radar sensor is sensitive to significant body motions that cause Doppler frequency shifts. Such limitations do not exist when using a recently constructed portable photoplethysmography (PPG) electronic device, which gives results comparable with a standard electrocardiogram (ECG). Since all portable modern devices such as smart phones tablets etc support Bluetooth communication that allows easy and direct communication with our PPG device, it may give us remote sensing heart related information. Applying natural time analysis to data simultaneously collected with an ECG system and a PPG device and using two complexity measures quantifying the entropy change in natural time under time reversal, a distinction is achieved between healthy (H) individuals and congestive heart failure (CHF) patients. Employing a support vector machine classifier for CHF discrimination to a total of 99 individuals (including 67 CHF), we obtained 97.7% sensitivity. In a follow up study challenging results are obtained since during the subsequent period six individuals died, who remarkably obeyed additional complexity measures that may distinguish sudden cardiac death individuals from CHF.

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1. Introduction

Various heart rate variability (HRV) studies showed that, in healthy subjects (H), heart-rate fluctuations display 1/*f* behaviour and fractal dynamics with long-range correlation (Peng et al. 1993a, 1993b; Goldberger et al. 2002). Specifically, the correlation between HRV and 1/*f* noise is established by the $1/f^{\alpha}$ with $\alpha \approx 1$ behaviour observed in the Fourier power spectrum of the interbeat intervals and becomes even more evident if one studies the interbeat interval increments, see, e.g., Figure 2(c-d) of Ivanov et al. (1998). Later work

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(e.g., (Ivanov et al. (1999, 2001)) revealed that healthy heartbeat dynamics exhibits even higher complexity, characterized by a broad multifractal spectrum, which breaks down in illness (e.g., Kotani et al. (2005); Ivanov et al. (2004)). The decreased long ranged fluctuations are accompanied with increased mortality in congestive heart failure (CHF) patients (Ivanov et al. 1999, 2001; Amaral et al. 2001; Ivanov et al. 2004).

A simple evolution model that exhibits the $1/f^{\alpha}$ behaviour with α close to unity was suggested by Sarlis, Skordas, and Varotsos (2009) based on a new time domain, termed natural time χ, introduced in the beginning of 2000s (Varotsos, Sarlis, and Skordas 2001, 2002). The analysis in natural time conforms to the desire to reduce uncertainty and extract signal information as much as possible (Varotsos, Sarlis, and Skordas 2011a). Natural time leads to complexity measures that separate H from CHF patients as well as from sudden cardiac death (SCD) individuals as it will be further discussed below.

It is most likely that physiological time series contain both stochastic and deterministic components (Varotsos et al. 2004; Costa, Goldberger, and Peng 2002, 2005; Varotsos, Sarlis, and Skordas 2011b). In view of the fact that entropy can be applied to stochastic as well as deterministic processes, it has been used to electrocardiogram (ECG) analysis Varotsos et al. (2004). This approach differed from previous studies, because the entropy employed has been defined in the natural time domain (Varotsos, Sarlis, and Skordas 2003) being essentially different from others. Both the entropy S in natural time as well as the entropy in natural time under time reversal S_{-} have been found of usefulness in the analysis of ECGs. Complexity measures quantifying the variability of the entropy fluctuations upon changing either the length scale or shuffling the consecutive events randomly have been also introduced (Varotsos et al. 2003, Varotsos et al. 2004, 2005a). Furthermore, complexity measures Λ_l which result upon considering how the statistics of the time series $S - S_{-}$ [$\equiv \Delta S$] changes upon varying the scale l have been employed (see next Section for Λ_l definition). Such an application to the analysis of ECG reveals that we can separate H from from SCD and CHF (Varotsos et al. 2007; Sarlis, Skordas, and Varotsos 2009; Sarlis, Christopoulos, and Bemplidaki 2015). Note that SCD is a frequent cause of death and may occur even if the ECG seems to be similar to that of H. More people die from SCD than AIDS, breast cancer, lung cancer, and stroke combined (Arora, Frisch, and Kadish 2007). According to recently published research data, in men's population of the United States of America, SCD incidence exceeds other causes of death, including cancer, chronic respiratory disease, diabetes, and cerebrovascular disease. In women, SCD incidence is similar to that of lung cancer and cerebrovascular disease. It is higher than that of other causes of death, including breast cancer, colorectal cancer, and Alzheimer's disease (Kuriachan, Sumner, and Brent Mitchell 2015; Stecker et al. 2014).

The above results have been obtained by analysing ECGs taken from publicly available Databases (Goldberger et al. 2000) (e.g., www.physionet.org). In a more recent study (Baldoumas et al. 2019), the same analysis was applied to data from H and CHF volunteers in the second Department of Cardiology, Medical School of Ioannina, Greece, by comparing simultaneous recordings from an ECG system and a photoplethysmography (PPG) device. In particular, our database contained 32 H and 67 CHF patients. The results obtained by PPG showed that these complexity measures Λ_l led to 90% sensitivity for the H and 81% for the CHF. It has been also shown that statistically significant differences exist for Λ_l between the H and CHF individuals measured either by PPG or ECG. Furthermore, statistical significance emerged from Receiver Operating Characteristics

(ROC) having comparable area under the ROC curve for PPG and ECG. The classification between CHF and H was also achieved by means of non-linear radial basis function Support Vector Machines (SVM) that led to a CHF sensitivity of 97.7%. These results were obtained by using solely two complexity measures associated with the entropy change under time reversal in natural time domain, while previous works by other workers tried to identify differences between CHF and H using various pattern recognition algorithms, but the number of features used has mostly exceeded 10, resulting in poor generalization performance (Hua et al. 2019). In the present work, which is a follow up study of Baldoumas et al. (2019), we focus on six CHF patients (out of 67 identified in our previous investigation), already died. Here, we investigate whether these 6 cases obeyed complexity measures, which have been developed in the frame of natural time to distinguish CHF from SCD.

2. Natural time analysis: Complexity measures associated with the entropy change under time reversal

In a time series comprising N events (heartbeats), we define an index for the occurrence of the k-th event by $\chi_k = k/N$, which we term natural time. We then study the pairs (χ_k, Q_k) or (χ_k, p_k), where Q_k is the energy and $p_k = Q_k / \sum_{n=1}^{N} Qn$ the normalized energy for the k-th event (Varotsos, Sarlis, and Skordas 2001, 2002, 2011a). The entropy S in natural time, which is a dynamic entropy (Varotsos et al. 2005b) is given (Varotsos, Sarlis, and Skordas 2001, 2003; Varotsos et al. 2004) by

$$S = \langle \chi \ln \chi \rangle - \langle \chi \rangle \ln \langle \chi \rangle, \tag{1}$$

where the symbols $\langle \ \ldots \ \rangle$ stand for averages with respect to the distribution p_k, i.e., $f(\chi) \equiv \sum_{k=1}^{N} f(\chi_k) p_k$. Upon considering time reversal T, i.e., $Tp_k = p_{N-k+1}$, the value of S changes to a value S_-:

$$S_- = \langle \chi \ln \chi \rangle_T - \langle \chi \rangle_T \ln \langle \chi \rangle_T, \tag{2}$$

where $\langle f(\chi) \rangle_T \equiv \sum_{k=1}^{N} f(\chi_k) p_{N-k+1}$. The physical meaning of the entropy change $\Delta S \equiv S - S_-$ under time reversal has been discussed in Varotsos et al. (2007, 2008); Varotsos, Sarlis, and Skordas (2011a). The quantity ΔS has found useful applications in the study and the analysis of ECG (Varotsos et al. 2007; Sarlis, Skordas, and Varotsos 2009; Varotsos, Sarlis, and Skordas 2011a). Using a sliding window of l heartbeats, S and S_- are determined for each event (heartbeat) in the time series. When the moving window is sliding through the RR or NN interval time series (cf. NN intervals are (Task Force 1996) the beat to beat intervals resulting from consecutive pairs of normal beats, while intervals surrounding an ectopic beat are discarded), we define the complexity measures

$$\Lambda_l = \frac{\sigma(\Delta S_l)}{\sigma(\Delta S_3)} \tag{3}$$

where $\sigma(\Delta S_l)$ denotes the standard deviation of the $\Delta S_l \equiv S_l - (S_-)_l$ time series.

For randomly shuffled data, i.e., when we randomly shuffle the RR or NN time series and repeat the calculation for ΔS_l which is now labelled $\Delta S_{l,\text{shuff}}$, the standard deviation $\sigma[\Delta S_{l,\text{shuff}}]$ is proportional to the ratio of the standard deviation σ over the mean value μ of the

RR or NN intervals (Varotsos et al. 2007), thus Λ_l being a ratio of $\sigma(\Delta S_l)$'s should be independent of σ/μ (see Equation (3.78) of Varotsos, Sarlis, and Skordas (2011a)).

The complexity measure $N_3 \equiv \sigma[\Delta S_{3,\text{shuff}}]/\sigma[\Delta S_3]$ together with $\sigma[\Delta S_7]$ have been used in Varotsos et al. (2007) for the distinction of SCD from H and CHF. Subsequently, in Sarlis, Christopoulos, and Bemplidaki (2015) was found that Λ_l are complementary to the complexity measures used in Varotsos et al. (2007). In particular, it was found that by plotting also Λ_{49} versus Λ_7 and using the horizontal line corresponding to $\Lambda_{49} = 2.07$ and the vertical line corresponding to $\Lambda_7 = 1.97$ the aforementioned distinction of SCD from H and CHF is improved.

The three scales $l = 3$, 7, and 49 involved in the complexity measures Λ_3, Λ_7 and Λ_{49} are closely related to the spectral properties of heart rate variability (Task Force 1996) since the following bands in heart rate have been established (Malpas 2002): (i) A high frequency (HF) band, which lies in the range 0.15 to 0.40 Hz (Bigger et al. 1995; Prokhorov et al. 2003), (ii) a low frequency (LF) band from 0.04 to 0.15 Hz (i.e., at around 0.1 Hz), and (iii) a very low frequency band (VLF) in the region 0.003 to 0.04 Hz (Task Force 1996). Hence the scale $l = 3$ corresponds to HF, while $l = 7$ and $l = 49$ lie near to the transition from the HF to the LF band and from the LF band to the VLF band, respectively. For the physical mechanisms behind these three bands see Varotsos et al. (2007) and Sarlis, Christopoulos, and Bemplidaki (2015).

3. Data collection

Our database contains simultaneous ECG and PPG recordings from 32 H individuals (9 women and 23 men), aged 24 to 58, and 67 records from CHF patients (22 women and 45 men), aged 55 to 87 that were collected in the setting of second Department of Cardiology, University Hospital of Ioannina, Ioannina, Greece. Additional details on data collection can be found in Baldoumas et al. (2019).

The data obtained from ECG and PPG have been analysed in natural time and the complexity measures Λ_7 and Λ_{49}, as well as N_3 and $\sigma[\Delta S_7]$, for each individual, have been determined (cf. for the identification of the heartbeat intervals using either ECG or PPG see Figures 4 and 5 of Baldoumas et al. (2019), respectively).

4. Results

As explained in Baldoumas et al. (2019), we employed SVM (Cortes and Vapnik 1995; Vapnik 1999; Joachims 1999; Vapnik 2000; Cristianini and Scholkopf 2002; Lewes 2015), by using the computer code SMV$^{\text{light}}$ (Joachims 1999, 2019) with a Gaussian radial basis function $K(\boldsymbol{a},\boldsymbol{b}) = \exp(-\gamma|\boldsymbol{a} - \boldsymbol{b}|^2)$, e.g., see Equation (5.35) on page 145 of Vapnik (2000), for the construction of the decision function

$$f(x) = \text{sign}\left\{\sum_{k=1}^{m} [y_k a_k K(x_k, x)] - b\right\} \tag{4}$$

e.g., see Equation (5.25) on page 141 of Vapnik (2000). SVM optimally provide (Cortes and Vapnik 1995; Vapnik 1999, 2000) the support vectors $\{x_k\}_{k=1}^{m}$, the quantities $y_k a_k$, and the bias b.

When we employ the SVM method (Cortes and Vapnik 1995; Vapnik 1999; Joachims 1999; Vapnik 2000; Cristianini and Scholkopf 2002; Lewes 2015; Joachims 2019), we assign the value +1 to the points with coordinates $\boldsymbol{x} = (\Lambda_7, \Lambda_{49})$ corresponding to CHF, while a value −1 is assigned to H. In Figure 1(a-b), the colour contours correspond to the values of the function in the signum of Equation (4). The accuracy A, i.e., the ratio of the sum of true Positives (TP) plus True Negatives (TN) over the totality of the positive (P) and negative (N) cases examined, $A = (TP+TN)/(P + N)$, is maximized upon changing γ. We found for ECG $A = 95\%$ (one CHF mixes with H and four H mix with CHF, see Figure 1(a)), while for PPG $A = 93\%$ (one CHF mixes with H and six H mix with CHF, see Figure 1(b)) (Baldoumas et al. 2019).

In Figure 1(a), we plot the complexity measure Λ_{49} versus the complexity measure Λ_7 obtained from ECGs of all individuals. Two threshold lines have been also inserted: a vertical straight line with value $\Lambda_7 = 1.69$, labelled $[\Lambda_7]_c$, and a horizontal straight line

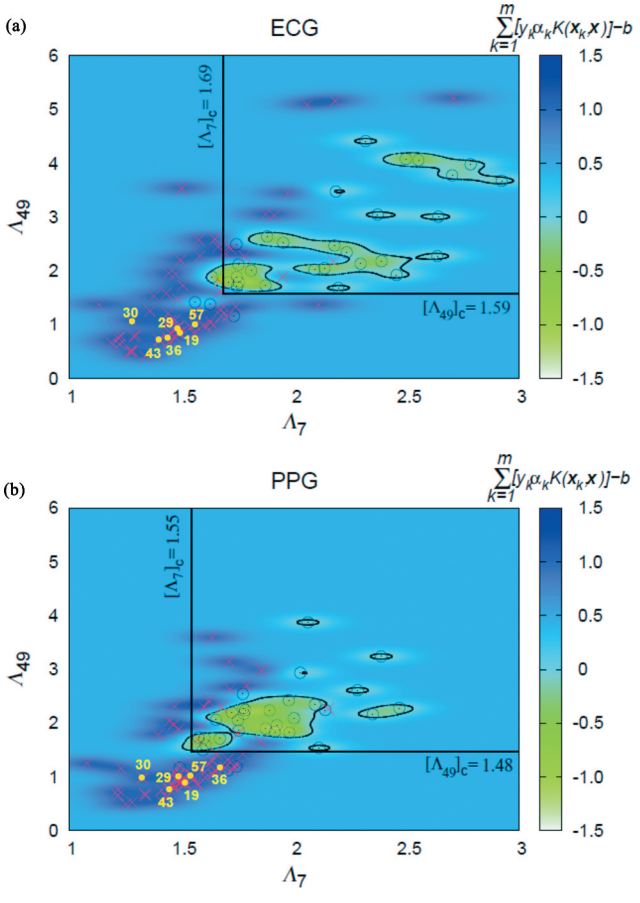

Figure 1. The results obtained from ECG (a) and PPG (b) concerning the 32 H (blue circles) individuals and 67 CHF (red crosses) patients. The colour contours denote the value of the function in the signum of Equation (4) as it resulted from SVM. The black dotted curves surround the H regions identified by SVM. The yellow dots stand for the CHF patients who died. Note that these dots are accumulated in a small region.

with value $\Lambda_{49} = 1.59$, labelled $[\Lambda_{49}]_c$. The study of this Figure reveals that the vast majority of H, 28 out of 32, lie in the right of the $[\Lambda_7]_c$ line and above the $[\Lambda_{49}]_c$ line. Especially, only four of the 32 healthy individuals are mixed with CHF and hence the sensitivity s_H (= TP/P) in this region (the H region) when the $\Lambda_7 > [\Lambda_7]_c$ and $\Lambda_{49} > [\Lambda_{49}]_c$, is $s_H = 87.5\%$. In the remaining region, the vast majority of CHF is located, i.e., 56 out of 67 (hereafter called the CHF region), thus the sensitivity for CHF is $s_{CHF} = 83.5\%$.

In Figure 1(b), we plot for all individuals the complexity measure Λ_{49} versus the complexity measure Λ_7, but for the PPG technique. We again insert two threshold lines: a vertical line with value $\Lambda_7 = 1.55$, labelled $[\Lambda_7]_c$, and a horizontal line with value $\Lambda_{49} = 1.48$, labelled $[\Lambda_{49}]_c$. We now calculate the sensitivity s in the same way as above. The vast majority of H (i.e., 29 out of 32) lies in the right of the $[\Lambda_7]_c$ line and above the $[\Lambda_{49}]_c$ line, thus in this region (H region), the sensitivity is $s_H = 90\%$. In the remaining region, the vast majority of CHF is located, i.e., 54 out of 67, thus the sensitivity for CHF is $s_{CHF} = 80.6\%$ (and only three H are mixed with CHF). This is the CHF region.

As already mentioned in the Introduction, six (out of 67) CHF died. They are marked with yellow dots in Figure 1(a-b) and correspond to the individuals numbered by 19, 29, 30, 36, 43 and 57. Since these individuals are accumulated in a small region together with other CHF patients who did not die, this dictates that the two features Λ_{49} and Λ_7 used in these figures do not enable a clear distinction between those who died from other CHF patients. Hence, we need additional measures. This raised the following very important question: From the study of Figure 3 of Varotsos et al. (2007) (in which a distinction between CHF and SCD has been achieved among others) the following two important properties emerge upon analysing the RR time series and plotting N_3 versus $\sigma[\Delta S_7]$: First, all SCD individuals exhibited N_3 and $\sigma[\Delta S_7]$ values outside the limits defined by the healthy individuals. Moreover, 11 out of the 44 CHF studied there (Varotsos et al. 2007) are mixed with H. Second, almost half of SCD exhibited $\sigma[\Delta S_7]$ values larger than the maximum value H_{max} of the $\sigma[\Delta S_7]$ values observed in H, while 17 out of the 18 SCD have $\sigma[\Delta S_7] > H_{min}$, where H_{min} stands for the minimum $\sigma[\Delta S_7]$ value of H. To visualize whether these two important properties are exhibited by the six CHF patients who died during the follow up study, we plot here N_3 versus $\sigma[\Delta S_7]$ using the values deduced either from ECG Figure 2(a) or from PPG Figure 2(b) for all CHF individuals studied together with those H who were correctly identified as such by SVM, i.e., inside the H regions of Figure 1. An inspection of Figure 2 (where the black rectangles surround the values of H) reveals that both these important properties are obeyed.

5. Discussion

The following comments are now in order:

First, the introduction of SVM greatly improves the sensitivity of our results for the distinction between CHF and H since SVM led to appreciably high sensitivity values, i.e., $s_{CHF} = 97.7\%$, upon using the two complexity measures Λ_7 and Λ_{49} either for ECG or for PPG time series. On the other hand, without employing SVM, the sensitivity values are markedly lower. In particular, in Varotsos et al. (2007) (see their Figure 3a), upon using the two complexity measures N_3 and $\sigma[\Delta S_7]$ it was found $s_{CHF} = 61.4\%$. Furthermore, in Sarlis, Christopoulos, and Bemplidaki (2015) (see their Table 1), upon using the three complexity measures Λ_7, Λ_{49} and $\sigma[\Delta S_3]$ the results showed s_{CHF}

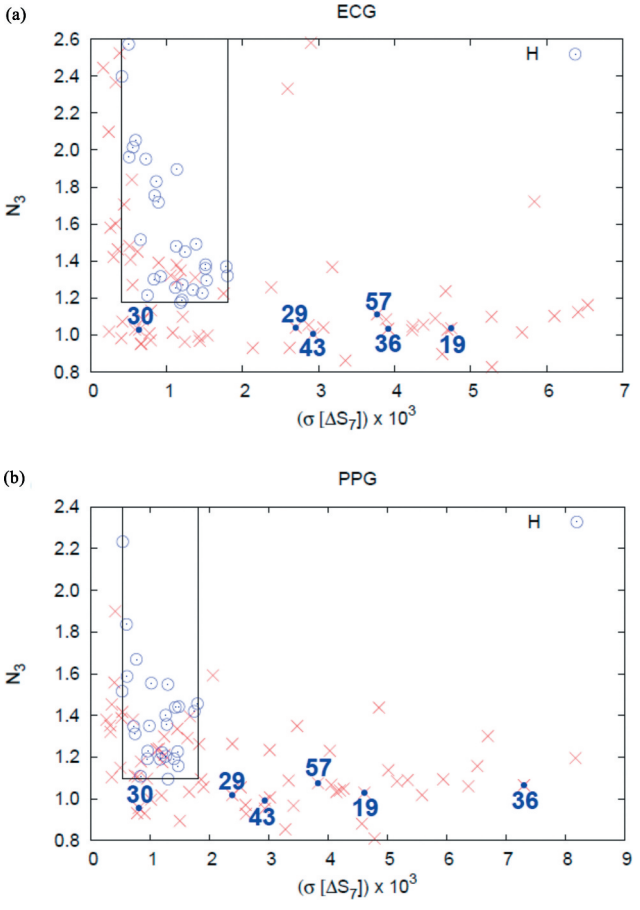

Figure 2. The complexity measure N_3 versus the complexity measure $\sigma[\Delta S_7]$ for the RR time series of (a) ECG: concerning the 28 H (blue circles) and 67 CHF (red crosses) individuals, (b) PPG: concerning the 26 H (blue circles) and 67 CHF (red crosses) individuals. The six (out of 67) CHF who died during the follow up study, are also plotted being marked with solid blue dots. In the rectangle enclosed by black lines the lower horizontal line corresponds to the minimum N_3 value computed in H. Concerning the vertical lines in this rectangle they correspond to the minimum (left) and the maximum (right) $\sigma[\Delta S_7]$ values computed in H.

= 68.2%. At this point, we should also discuss the correlation between ECG and PPG in terms of CHF diagnosis. Earlier studies (Jeyhani et al. 2015; Pinheiro et al. 2016) have shown that PPG data can be used as an alternative to ECG ones for the estimation of standard HRV time domain features (like the mean value of NN or the standard deviation of NN intervals SDNN, etc) for both H and cardiovascular patients. As concerns natural time domain complexity measures, it has been estimated (Baldoumas et al. 2018) that Λ_7 and Λ_{49} are not expected to differ significantly when PPG data are used instead of the ECG ones. The present results of Figure 1(a-b) reveal that by using natural time criteria earlier suggested (Sarlis, Christopoulos, and Bemplidaki 2015) on the basis of ECG, the PPG data may serve as good as the ECG ones for CHF diagnosis.

Second, since previous works rarely distinguish the severity levels of CHF disease, the measures N_3 and $\sigma[\Delta S_7]$ in view of the present results related to the 6 patients who died during the follow up study-may play a prominent role in a future development of a model for diagnosing the severity levels of CHF disease.

Third, as mentioned in the previous Section, all six patients who died (see Figure 2) satisfied both conditions (i.e., exhibited N_3 and $\sigma[\Delta S_7]$ values outside the limits defined by the H individuals and $\sigma[\Delta S_7] > H_{min}$) that may distinguish the majority of SCD from CHF, as found in Varotsos et al. (2007). Note that an inspection of Figure 3 of Varotsos et al. (2007) reveals that 17 out of the 18 individuals who died satisfied both these conditions.

Fourth, in recent years the millimetre wave radar system (Ren et al. 2015) has been suggested to monitor heartbeats since it is contactless, thus being suitable for some particular situations, such as burn patient monitoring. Very recent work (Zhang 2020) proposed a signal processing algorithm to extract common features of ECG recordings and radar signals to train a convolutional neural network (CNN) for radar heartbeat classification. This way the ECG dataset trained CNN can directly classify radar signals. An advantage of the mm-wave radar is that patients can monitor their heartbeat at home, and this will help the patients to track their heart conditions at any time. However, there exist serious limitations because the radar sensor is sensitive to significant body motions that cause Doppler frequency shifts (Zhang 2020). Such limitations do not exist when employing the portable PPG electronic device. Nowadays PPG technology is very common and easy to use. Furthermore, all portable modern devices such as smart phones, tablets etc support Bluetooth communication that allows easy and direct communication with our PPG device. Thus, our PPG device transfers via Bluetooth the heartbeat data to the user portable device (smartphone, tablet etc) which does the calculation of the complexity measures and shows us the result. The results can also be sent via Wi-Fi to a central recording system for continuous monitoring if needed.

6. Main conclusions

1.The portable photoplethysmography device used here enables-in view of the advantages of the PPG technology-the remote heartbeat monitoring and in addition does not suffer from the limitations in the mm-wave radar technology being sensitive to significant body motions that cause Doppler frequency shifts.

2.Upon taking advantage of the natural time analysis here we assured that we can achieve, sensitivity in CHF distinction 97.7% by using only two complexity measures quantifying the entropy change under time reversal by employing either the ECG or the PPG technique. On the other hand, previous studies by other authors (not employing natural time) have attempted the distinction between CHF and H individuals by means of pattern recognition, but the number of features used has mostly exceeded 10, leading to poor generalization performance.

3.In a follow up study of our database comprising 67 CHF and 32 H, six CHF patients died. The investigation of these six cases revealed that they exhibited two important properties of additional complexity measures of the entropy change under time reversal at the two scales 3 and 7 heartbeats related to the two frequency bands (HF and VF) of heart rate variability that may distinguish SCD from CHF (Varotsos et al. 2007).

Data availability statement

The data that support the findings of this study are available from the corresponding author, N.V.S., upon reasonable request.

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