Classification of cardiac arrhythmias based on alphabet entropy of heart rate variability time series

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Abstract

Background: Symbolic dynamics' methods provide a description of time series variability that allows inference of new predictive markers. Classification of disorders using symbolic dynamics is accomplished through the use of nonlinear entropies, measured upon encoded series.

Method: This work applies a recently developed symbolic dynamics method, alphabet entropy (AlphEn) to heart rate variability (HRV) analysis in order to improve automatic classification of cardiac arrhythmias. Experiments are conducted on PhysioNet MIT-BIH Arrhythmia Database. The approach is experimentally compared with other HRV linear and nonlinear feature combinations established in literature. AlphEn is experimentally compared with other common nonlinear entropies: Shannon's entropy, approximate entropy, sample entropy, etc. Feature selection using symmetrical uncertainty is used for discovering relevant AlphEn features and random forest algorithm is used for arrhythmia classification.

Results: The best classification result obtained for six heart rhythms on 20 s segments is achieved for AlphEn no-change threshold $\theta = 100$ ms. AlphEn features improved mean sensitivity of other feature combinations by 2% on average, with the best results achieved: SENS: 91.2%, SPEC: 97.1%, AUC: 99.0%. AlphEn may be used efficiently by adding top 10 ranking features, obtained with symmetrical uncertainty, to other established combinations. AlphEn provides the best incremental result to linear feature combination with respect to the inspected entropies.

Conclusions: AlphEn improves the results of established HRV feature combinations on the problem of automatic cardiac arrhythmia classification. The method enables the extraction of a number of potentially significant, domain-oriented features. It can be used as an accurate first-hand screening for arrhythmia problems.

Keywords: nonlinear dynamics; entropy; classification; feature selection; cardiac arrhythmia

1. Introduction

One of the most studied, and not yet fully understood, biomedical signals is the heart rhythm. The analysis of the fluctuations of the heart inter-beat intervals (RR-intervals) is known as heart rate variability (HRV) analysis. It is an important prognostic marker of cardiac health [1]. Research shows that heart rhythm of healthy subjects displays interesting short- and long-scale complex fluctuations. HRV decreases with the occurrence of cardiac disorders and aging [2,3]. Through the analysis of HRV, the researchers, among other objectives, aim at classifying heart rhythm patterns [3,4], obtaining accurate cardiac disorder models [5,6], and predicting the onset of cardiac disorders [7].

Disorder modeling using HRV usually includes feature extraction. Biomedical time series variability features in general can be classified into: statistical, geometric, informational, energetic, and invariant [8]. Additionally, several transformations of the heart rate series are possible, with the most common ones being frequency domain transformations: discrete Fourier transform [9], bispectrum calculation [10], higher-order spectrum calculation [11], discrete cosine transform [12], and Hilbert-Huang transform [13]. Other transformations are also possible, such as wavelet transform [14] and symbolic dynamics [15]. The purpose of these transformations is to adapt the time series into a more suitable form that will enable the calculation of some highly accurate domain-oriented modeling features.

In this work, the focus is on symbolic dynamics transformation methods. These methods were first introduced into heart rhythm analysis by Voss et al. [16]. There are several known approaches to symbolic dynamics analysis of HRV [17,18]. Two phases can be perceived in the approaches. In the first phase, the original signal is transformed into a new series by discretizing the numerical values into a set of categories, with the potential to obtain more relevant information. This phase is termed symbolization and leads to an overall loss of signal information [19]. It can be achieved by: 1) calculating first derivatives of the series values and retaining only binary information (heart beat shortening or prolongation) [20], 2) taking several categories between minimum and maximum value of the signal (coarse-graining) [17], or 3) taking several categories based on the distance from the series' mean value [19,21]. The second phase includes analyzing the newly encoded sequence using complexity measures such as approximate entropy [20,22], Lempel-Ziv complexity [23], Rényi's

entropy [21], or permutation entropy [24], with the aim of quantifying the characteristics of the observed signal.

This work presents the application of a recently developed symbolic dynamics method, appropriately named alphabet entropy [25], to the analysis of HRV. Alphabet entropy preserves both qualitative and quantitative information about the biomedical time series' dynamics on short time scales. It starts by transforming the original signal into a sequence of alphabet letters. The method proposes 27 possible letters of the alphabet, which are encoded by observing four-by-four consecutive measurements and by analyzing their possible changes (prolongation, shortening, or no-change). The method then proceeds to calculate the expanded version of properly adapted Carnap's one-dimensional entropy for each quadruple of measurements. Our previous research showed that the method is highly sensitive to significant changes in the signals, but due to a threshold parameter for no-change, it is mostly insensitive to noise [25]. Also, previous results indicated that common nonlinear measures improve the results of automatic classification of cardiac disorders in comparison with standard linear time and frequency measures [26,27], which supports the use of nonlinear entropy measures in feature combinations.

In order to test the capabilities of the method, the aim of this work is to apply it to automatic classification of cardiac arrhythmias. While classification of arrhythmias based on the whole ECG can provide us with highly accurate results [28,29], classification based on HRV is more challenging. When using HRV alone, accuracy of the constructed models is high only in the cases where the arrhythmias are markedly different, as shown by Asl et al. [3] and Yaghouby et al. [30].

However, the classification of significantly different arrhythmias has limited applicability in practice, because there are several types of cardiac arrhythmias that are not noticeably different if HRV information is used alone (e.g. atrial vs. ventricular arrhythmias), but are quite common in patients [27]. The arrhythmias ought to be classified as accurately as possible in order to enable early detection of potentially significant cardiac disorders.

Therefore, this work focuses on the application of alphabet entropy to classification of several, not easily discernible cardiac arrhythmias. The problems are analyzed on a set of records taken from MIT-BIH Arrhythmia Database from PhysioNet web portal [31].

The major goal of this paper is to discover whether alphabet entropy can increase the accuracy of models of linear and nonlinear HRV feature combinations on the problem. This could be clinically relevant, because more accurate models would enable more reliable detection of arrhythmias, which would lead to earlier treatment for patients. The secondary goal is to compare alphabet entropy with other commonly used entropy features in order to establish its relevance.

The paper is structured into the following sections. In section 2, a brief overview of symbolic dynamics methods is given in order to provide a rationale for exploring and utilizing an additional symbolic dynamics method. Section 3 describes the alphabet entropy method and its resulting features. Considerations of applying alphabet entropy to HRV series is given in section 4. Evaluation methodology is presented in section 5 and results are shown in section 6. The results are discussed and conclusions are drawn in sections 7 and 8, respectively.

2. Symbolic dynamics methods overview

Symbolic dynamics methods have been used extensively in biomedical time series analysis: HRV [18,20,32,33], ECG [23,34], EEG [35,36], and joint time series analysis [15]. Most researchers perform binary encoding of the original series [18,32,34], although ternary encoding (with adjustable threshold) can also be applied, particularly for those signals where the lack of significant change is relevant for classification [33]. Coding to a richer alphabet has occasionally been explored [19].

Several complexity features of such encoded sequences are usually analyzed, such as:

1. Entropy and information-based features calculated from short-term encoded sequences' distributions [18,33,34].
2. Other complexity features, e.g. Lempel-Ziv complexity [35] and detrended fluctuation analysis (DFA) [15].
3. Similarity measures between encoded sequences [32].

The commonly used topological entropy measures include: Shannon's entropy (ShEn) [37], correlation entropy (CorrEn) [38], and Rényi's entropy (RenEn) [21,39]. These methods quantify the information in a topological setting where there is no reference to movement of the system's trajectory over time.

The entropy methods that do consider the movement of the system trajectory over time are based on approximations of Kolmogorov's entropy for a smaller number of measurements [40]. These include: approximate entropy (ApEn) [22], sample entropy (SampEn) [41], corrected conditional Shannon entropy (CCShEn) [37], and more recently, fuzzy approximate entropy (FuzzyApEn) [42]. These entropy methods proved to be successful for the majority of biomedical time series [35,43], although theoretically, they still require the analysis of several hundred measurements, at least [44].

A different topological approach to measuring system entropy was proposed by Carnap in 1977, as presented in the work of Pudmetzky [45]. The idea was that, instead of dividing a *d*-dimensional phase space R^d into a number of cells (bins) with a fixed volume v^d, one should divide the space into cells that are attributed to each measurement point. The division of the phase space into such environments is called Voronoi tessellation [46]. The entropy measure that Carnap defined on the Voronoi diagram of an arbitrary finite dimension *d* is known as Carnap's entropy (CarnEn).

The issues with some of the existing symbolic dynamics' methods, including CarnEn, can be summarized as:

1. Separation of the encoding process method (qualitative) and the complexity evaluation method (quantitative) [18,19,32].
2. Lack of assurance that the complexity evaluation method will provide different results for two sets of different sequences, because of different binning options. This limits the precision of such methods [24,45].
3. Effective application of common entropy methods depends on a large number of available measurements [22,44].

The methodology that we use, based on alphabet entropy, is derived from CarnEn and explained in section 3. Our approach is novel and timely, because it solves all the three aforementioned issues related to efficient and accurate quantification of time series changes.

3. Alphabet entropy

Alphabet entropy has already been presented in a recent work that describes its successful application in the analysis of industrial signals for quality control [25]. In this work, the method is adapted for HRV modeling. For the sake of completion, the necessary segments of the method's theory are repeated in subsection 3.1. Reader is referred to Jovic, F. et al. [25] for additional details.

3.1 Deriving alphabet entropy

Alphabet entropy is derived from two theories: Carnap's one-dimensional entropy [45] and the matrix of differences for discrete measurements [47]. CarnEn in one dimension was originally proposed as:

$$CarnEn_{1D} = \sum_{i=1}^{N} \log_2 \frac{|d_i|}{x_N} \quad (1),$$

where $|d_i|$ is the size of the environment of the point x_i, and N is the number of points in the series. The measure is adapted in order to scale for the absolute values of the measurements and to handle the borderline measurements:

$$CarnEnAd_{1D} = -\left(\frac{x_1+x_2}{2x_N}\log_2\frac{x_1+x_2}{2x_N} + \right.$$

$$\left. + \sum_{i=2}^{N-1} \frac{x_{i+1}-x_{i-1}}{2x_N}\log_2\frac{x_{i+1}-x_{i-1}}{2x_N} + \frac{x_N-x_{N-1}}{2x_N}\log_2\frac{x_N-x_{N-1}}{2x_N}\right) \text{ (bits/sequence span)} \quad (2).$$

Here, x_i is a point placed on a line (one-dimension). This adaptation does not consider the evolution of the system, because the points on the line do not necessary appear in the same order as in the original signal.

From theoretical perspective, the changes between the measurements can be expressed qualitatively as a positive unit change (Δ), a negative unit change (-Δ), or no change (0):

$$s_i = \begin{cases} 0, & \text{if } |x_{i+1} - x_i| \leq \theta \\ \Delta, & \text{if } x_{i+1} - x_i > \theta \\ -\Delta, & \text{if } x_{i+1} - x_i < \theta \end{cases} \quad (3),$$

where θ is the threshold for no-change, dependent on the nature of the signal. The letters L of the alphabet are formed as possible combinations of $s_i,\ i = 1..3$. There is a total of 27 possible combinations, labeled as $L = \{A, B, \dots, Z, AA\}$. It can be shown that the information content based on

CarnEnAd (2) for the letters of the alphabet is not unique for each alphabet letter, i.e. some letters have equal unit changes information content, e.g. letters B, H, and Q [25].

Alphabet entropy (AlphEn) is the extension of CarnEnAd that takes four-by-four discrete measurements in the signal and proceeds to describe their entire informational content. This includes the absolute values of the measurements as well as differences between each of the measurements. The evolution of the changes is recorded in order to keep the information about the system trajectory.

Let $X = (x_1,\ x_2,\ x_3,\ x_4),\ x_i \in \mathbb{R}$ be a quadruple of sequential quantitative measurements of the signal. An expansion of the alphabet information content is considered that accommodates changes between measurements in order to quantify the dynamics of the system. The matrix of differences for this quadruple can be presented as:

$$\begin{bmatrix} d_{1,2} & d_{2,3} & d_{3,4} \\ \times & d_{1,3} & d_{2,4} \\ \times & \times & d_{1,4} \end{bmatrix} \quad (4),$$

where $d_{i,j}$ is a change between measurements x_i and x_j, and × stands for an irrelevant element of the matrix. The expansion vector $(d_{1,2}\ \ d_{2,3}\ \ d_{3,4}\ \ d_{1,3}\ \ d_{2,4}\ \ d_{1,4})$ encodes all possible changes between four consecutive measurements and adds the information on second- and third-order differences. The alphabet is shown in Table 1.

In order to keep the information about absolute values of the measurements, another sextuple is defined as:

$Y = (y_1,\ y_2,\ y_3,\ y_4,\ y_5,\ y_6)$, where: $y_1 = x_1 + d_{1,2} = x_2,\quad y_2 = x_2 + d_{2,3} = x_3,\quad y_3 = x_3 + d_{3,4} = x_4,\quad y_4 = y_3 + d_{1,3},\quad y_5 = y_4 + d_{2,4},\quad y_6 = y_5 + d_{1,4}$.

Since there is no guarantee that the values in Y are given in an ascending order, which is necessary for calculation (2), the values are sorted prior to the entropy's calculation.

Let $Z = (z_1,\ z_2,\ z_3,\ z_4,\ z_5,\ z_6)$ be the sextuple of the sorted values of Y. Alphabet entropy can be calculated for any four consecutive measurements as:

$$AlphEn = -\left(\frac{z_1 + z_2}{2z_6}\log_2\frac{z_1 + z_2}{2z_6} + \right.$$

$$\left. + \sum_{i=2}^{5}\frac{z_{i+1} - z_{i-1}}{2z_6}\log_2\frac{z_{i+1} - z_{i-1}}{2z_6} + \frac{z_6 - z_5}{2z_6}\log_2\frac{z_6 - z_5}{2z_6}\right) \text{ (bits/sequence span)} \quad (5).$$

Table 1. Alphabet letters and the encoded symbolic dynamics changes

Letter	Changes encoded by the letter	Qualitative representation of the expansion vector
A	0 0 0	0 0 0 0 0 0
B	0 0 +	0 0 + 0 + +
C	0 0 -	0 0 - 0 - -
D	0 + 0	0 + 0 + + +
E	0 - 0	0 - 0 - - -
F	0 + +	0 + + + + +
G	0 - -	0 - - - - -
H	0 + -	0 + - + 0 0
I	0 - +	0 - + - 0 0
J	+ 0 0	+ 0 0 + 0 +
K	- 0 0	- 0 0 - 0 -
L	+ 0 +	+ 0 + + + +
M	+ 0 -	+ 0 - + - 0
N	- 0 -	- 0 - - - -
O	- 0 +	- 0 + - + 0
P	+ + 0	+ + 0 + + +
Q	+ - 0	+ - 0 0 - 0
R	- - 0	- - 0 - - -
S	- + 0	- + 0 0 + 0
T	+ + +	+ + + + + +
U	+ + -	+ + - + 0 +
V	+ - +	+ - + 0 0 +
W	+ - -	+ - - 0 - -
X	- - -	- - - - - -
Y	- - +	- - + - 0 -
Z	- + -	- + - 0 0 -
AA	- + +	- + + 0 + +

The information content is unique in this case for each alphabet letter [25]. Note that if there are some equal measurements within the sextuple, then the logarithms in (5) cannot be calculated. In such a case, some logarithms are taken into consideration multiple times, while those that contain equal measurements are omitted.

3.2 Alphabet entropy features

It is evident from the expression (5) that AlphEn quantifies very short-term variability of the original time series. The shortest time frame that can be analyzed with this method is therefore dependent on the sampling, but always includes only four measurements. The largest time frame is, however, not limited to only four measurements, as the entropy can be calculated sequentially for each four-by-four measurements.

Formally, any signal segment $\{x_i\}$ can be encoded into its corresponding letter series $\{L_i\}$ using (3), such that the length of the letter series equals $|L| = len(\{L_i\}) = len(\{x_i\}) - 3$.

AlphEn can be calculated for each letter L_i in $\{L_i\}$. This yields a series of alphabet entropies $\{AlphEn_i\}$ corresponding to letters $\{L_i\}$, calculated using (5). From letters series $\{L_i\}$ and alphabet entropies series $\{AlphEn_i\}$, numerous statistical features can be extracted. Some of these may include:

1. Average alphabet entropy in segment:

$$AverAlphEn = \frac{\sum_{i=1}^{|L|} AlphEn_i}{|L|} \quad (6);$$

2. Alphabet entropy variance in segment:

$$AlphEnVar = \sqrt{\frac{\sum_{i=1}^{|L|}(AlphEn_i - AverAlphEn)^2}{|L|-1}} \quad (7);$$

3. Maximum alphabet entropy in segment:

$$MaxAlphEn = \max_i AlphEn_i \quad (8);$$

4. Average alphabet entropy for each letter in segment:

$$AverAlphEn(L_i) = \frac{\sum_{j=1}^{|L_i|} AlphEn_j}{|L_i|}, i = 1..27 \quad (9);$$

5. Alphabet entropy variance for each letter in segment:

$$AlphEnVar(L_i) = \sqrt{\frac{\sum_{j=1}^{|L_i|}\left(AlphEn_j - AverAlphEn(L_i)\right)^2}{|L_i|}}, i = 1..27 \quad (10);$$

6. Maximum alphabet entropy for each letter in segment:

$$MaxAlphEn(L_i) = \max_j AlphEn_j,\ L_i \sim AlphEn_j, j = 1..|L_i|, i = 1..27 \quad (11);$$

7. Letter existence in segment:

$$Exists(L_j), \text{ if } L_j \in \{L_i\}, j = 1..27 \quad (12);$$

8. Letter occurrence rate in segment:

$$Rate(L_j) = freq(L_j)/|L|, L_j \in \{L_i\},\ j = 1..27 \quad (13).$$

All of these features are not computationally demanding and can be obtained quickly from segments of various lengths.

4. Considerations of alphabet entropy application to heart rate variability analysis

The heart rate series may display discrepancies from normal behavior in the case of some cardiac arrhythmias or other cardiac disorders. A restriction to theoretical consideration about the nature of these disorders will be applied here, as biodiversity and specific disease states may sometimes show somewhat different types of abnormal patterns. In Fig. 1, an example of premature ventricular contraction (PVC) arrhythmia is given and the alphabet entropy letters that are typical for this disorder are marked. For example, letter C (0 0 -) indicates that there were no significant changes between the second and the first, and between the third and the second RR-interval, respectively, but that there was a shortening between the fourth and the third RR-interval because of the PVC. It should be noted that the letters C (0 0 -) and K (- 0 0) could have resulted from normal behavior (significant heart rate deceleration). However, the letters I (0 - +), Z (- + -), and Q (+ - 0) are much more specific for PVC identification. Similar representations can be given for other heart rhythm patterns.

In Table 2, the theoretical alphabet encodings for normal sinus rhythm (NSR) and abnormal patterns: premature atrial contraction (PAC), PVC, atrial fibrillation (AFIB), ventricular bigeminy (VBI), and ventricular trigeminy (VTR) are presented. The information about the arrhythmias in Table 2 is based on Garcia & Holtz [48] and on consultations with medical experts. It is clear that some of the letters

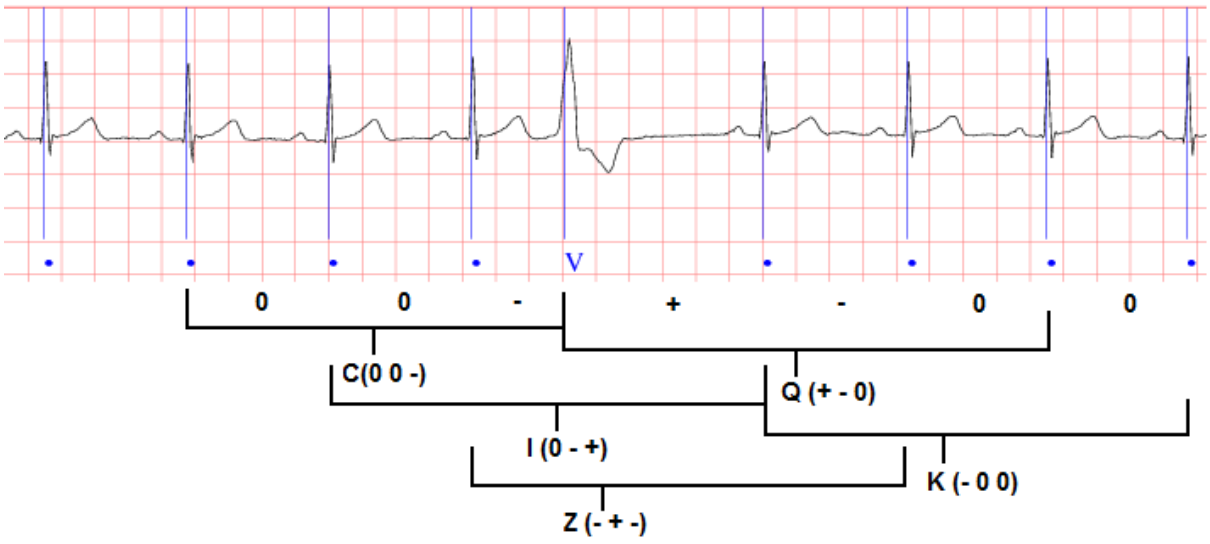

Fig. 1. An example of premature ventricular contraction (PVC) arrhythmia and its corresponding alphabet entropy letters

Table 2. The theoretical alphabet encoding for normal sinus rhythm and other rhythm patterns

Rhythm pattern	Example of RR-interval changes	Alphabet letters	Expected frequency
NSR	0000000	A	Common
	000+000	A,B,D,J	Occasional
	000-000	A,C,E,K	Occasional
	000+-00	A,B,H,Q,K	Rare
	000++00	A,B,F,P,J	Rare
	000--00	A,C,G,R,K	Rare
PAC	000-+00	A,C,I,S,J	Common
	000-+-00	A,C,I,Z,Q,K	Common
PVC	000-+-00	A,C,I,Z,Q,K	Common
	000-+00	A,C,I,S,J	Occasional
	000-++00	C,I,J,P,AA	Rare
AFIB	Irregular	All letters	Common
VBI	+-+-+-+	V,Z	Common
	000-+-+-	A,C,I,V,Z	Common
	-+-+-000	A,K,Q,V,Z	Common
	000-+-+-00	A,C,I,K,Q,V,Z	Common
VTR	-+--+--+	W,Y,Z	Common
	000-+--+--+-00	A,C,I,K,Q,W,Y,Z	Common
	+--+-0-+--+-	I,N,Q,W,Y,Z	Occasional

and letter sequences are specific for certain disorders. For example, letters W, Y, and Z are common for VTR, while practically any combination is possible in the case of an irregular rhythm such as AFIB. Ventricular arrhythmias are different from atrial arrhythmias in that the compensation after the premature ventricular beat is usually more pronounced. This results in a significant shortening after the compensation, i.e. the letter Z (- + -) occurs in PVC instead of J (- + 0).

In practice, some of the beat disorders can be masked by other disorders so that it is not easy to distinguish the exact beat types based on heart rhythm alone. For example, a PVC followed by a normal beat and then a couplet of two PVCs may lead to a non-detection of either the PVC or the couplet, or both, because the letter sequence is not the same as the theoretically expected one anymore. There are also other concerns. For example, VBI is not present in the segment if there is only a single letter Q (+ - 0), because alternation of at least three normal-abnormal beats should be present [48]. To resolve these issues, a statistical approach using features (6)-(13) is applied, and disorders are detected based on the analysis of the whole segment. If two or more rhythm disorders are present within a segment, the one that is clinically the most significant is considered. It should be noted that the disorders that usually span more than four RR intervals (e.g. sustained supraventricular tachycardia) cannot be detected by AlphEn and are therefore not considered here.

5. Evaluation method details

5.1 Dataset description

For the analysis of cardiac arrhythmias, the MIT-BIH Arrhythmia Database, with 44 non-pacemaker records (pacemaker records 102, 104, 107, 217 excluded), first half-hour, is used [31]. The signals in the database were band-pass filtered at 0.1–100 Hz and digitized at 360 Hz. The database contains the information on many types of anomalous beats. The records are used as-is, without additional preprocessing of beats, because the aim was to discover potential arrhythmic patterns using HRV features. The rhythm was considered normal (NSR) in a segment if there were no anomalous beats marked in the beat annotations.

The records were divided into segments of 20 s, which was already shown to be near-optimal for automatic classification of arrhythmias based on short-term HRV analysis [27]. The analyzed rhythm patterns included: NSR (1520 segments), PAC (197 segments), PVC (437 segments), AFIB (364 segments), VBI (210 segments), and VTR (106 segments). The total number of valid segments (feature vectors) was 2834. All of the segments that contained other types of disorders (e.g. atrial bigeminy, atrial trigeminy, bundle branch blocks, 2nd degree block, ventricular tachycardia, paced rhythm) were disregarded because of either of the following two reasons: too few different patient records contained the disorder, or the rhythm itself is not considered to be distinguishable from normal rhythm using features of HRV alone [48]. A small number of segments that contained multiple disorders (e.g. PACs and PVCs), or couplets (atrial, ventricular, or mixed) were also disregarded.

5.2 Methods Description

Four different analyses were performed for distinguishing between several types of arrhythmic patterns. The first analysis aims to: 1) discover the optimal threshold θ (3) for AlphEn, which is to be used in the other arrhythmia analyses, and 2) discover the minimal set of AlphEn features that completely describes arrhythmia classification problem. The search for the optimal threshold included examining the classification results of the combination of all AlphEn features (combination #0, Table 3) on the dataset for threshold values of $\theta = \{5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 150, 200\}$ ms. When the optimal threshold was found, filter-based feature selection using symmetrical

uncertainty [49] measure was performed on the feature set with the optimal threshold. Symmetrical uncertainty of a feature is given by the expression:

$$SymmU(C,F) = 2\frac{H(C)-H(C \mid F)}{H(C)} + H(F) \quad (14),$$

where C is the goal (class) variable, F is the evaluated feature, $H(C)$ is the Shannon's entropy of the class variable, $H(F)$ is the Shannon's entropy of the evaluated feature, and $H(C \mid F)$ is the conditional Shannon's entropy of the class variable C given the feature F.

Feature selection was deemed necessary as it is unexpected that all of the AlphEn features are useful for the specific set of analyzed arrhythmias. The minimum number of features that do not reduce accuracy of the full set of features is retained. This feature combination is named combination #1 in Table 3.

The second analysis included an evaluation of different feature combinations for cardiac arrhythmia classification. The goal was to discover whether the addition of AlphEn features can improve the classification potential of the most promising feature combinations according to literature [1,3,27,54,55]. For comparison purposes, we used four different combinations of features, with details outlined in Table 3. The combination #2 is based only on standard linear time-domain and frequency domain features recommended by HRV analysis guidelines [50]. The combination #3 is a balanced combination that includes both linear and nonlinear features. Here, the linear features are the same as in #2, and the nonlinear ones were taken from a recent review paper on HRV [1], with details on recurrence plot features taken from [51], considering only those features from the review that can be reasonably estimated from short-term segments. The combination #4 is also a balanced and well-known combination of linear and nonlinear HRV features proposed for automatic arrhythmia detection [3]. The combination #5 was more recently shown to be near-optimal for arrhythmia classification on short-term HRV series [27]. The combinations #2 - #5 were considered alone and with the addition of relevant AlphEn features (comb #1). For all estimations of spectral parameters, Lomb-Scargle periodogram method was used, because recent work found it more appropriate than traditional Fourier and Autoregressive spectrum estimates for HRV data [52].

The third analysis included direct comparison of AlphEn with other nonlinear entropy features. In

Table 3. Feature combinations considered for cardiac arrhythmia classification and CHF detection

#	Feature combination	Number of features
0	Mean, AverAlphEn, AlphEnVar, MaxAlphEn, AverAlphEn(A) - AverAlphEn(AA), AlphEnVar(A) - AlphEnVar(AA), MaxAlphEn(A) - MaxAlphEn(AA), Exists(A) - Exists(AA), Rate(A) - Rate(AA)	138
1	MaxAlphEn, Exists(Z), Rate(Z), AverAlphEn(Z), MaxAlphEn(Z), AverAlphEn, Rate(A), Rate(V), AlphEnVar, Exists(V), Exists(I), MaxAlphEn(I), MaxAlphEn(V), AverAlphEn(I), AverAlphEn(V), Rate(I), Exists(Q), Rate(Q), AverAlphEn(C), MaxAlphEn(C)... (for the whole list see Table 7)	70
2	Mean, SDNN, RMSSD, SDSD, pNN50, HRV Triangular Index, TINN, (LF, HF, LF/HF)* [50]	10
3	Mean, SDNN, RMSSD, SDSD, pNN50, HRV Triangular Index, TINN, (LF, HF, LF/HF)*, SD1/SD2, ApEn3 0.2, LLE, SampEn3 0.2σ, DFA alpha short, Recurrence plot features: REC, Lmean, DET, LAM [1,51]	19
4	Mean, SDSD, RMSSD, pNN5, pNN10, pNN50, SD1/SD2, LLE, (SpectEn, LF/HF)*, STA1, STA2, ApEn3 0.2σ, DFA alpha short [3]	14
5	Mean, SDNN, RMSSD, SDSD, pNN5, pNN10, pNN20, pNN50, HRV Triangular Index, TINN, (LF, HF, LF/HF, total PSD)*, SD1/SD2, Fano factor, Allan factor [27]	17

* spectral features were obtained using Lomb-Scargle periodogram method [52]

order to perform a proper evaluation, the linear combination #2 was taken. Then, a single nonlinear entropy feature was appended to this combination of linear features and the classification results of the complete combinations were compared. The nonlinear features included: ApEn [22], SampEn [41], ShEn [37], CCShEn [37], CorrEn [38], CarnEn (using (1)), FuzzyApEn [42], and AlphEn (using (5)). Rényi's entropy (RenEn) [44] was not considered in this work because of too short segments for a reliable estimate. All of the entropies were considered in a way that their respective parameters were varied and the single most accurate feature was reported. Details about the entropies' parameters are provided in Table 4. The goal of the analysis was to discover which of the nonlinear entropy measures possesses the highest incremental contribution in classification accuracy to standard linear features.

In the fourth analysis, a detailed examination of the behavior of AlphEn, when it is applied to real-life heart rhythm patterns, was pursued. Herein, we first report on the statistical properties of the relevant AlphEn features from comb #1. Second, for each heart rhythm pattern, we perform a thorough search for the frequently reoccurring letter combinations in 20 s segments (considering all possible AlphEn letters). The search is set to determine in what manner do the individual heart rhythms differ qualitatively, with respect to the used alphabet.

5.3 Analysis tools and evaluation

Cardiac records preprocessing and feature extraction was performed using HRVFrame framework [53], v2.1. The framework is available from the website [54]. AlphEn was implemented as an

Table 4. Entropies and their parameters used in the comparison analysis

Entropy	Parameters	Total no. of examined features
ApEn	m = {1,2,3}, r = {0.1, 0.15, 0.2, 0.25, ApEnMax*} σ	15
SampEn	m = {1,2,3}, r = {0.1, 0.15, 0.2, 0.25, SampEnMax*} σ	15
FuzzyApEn	m = {1,2,3}, r = {0.1, 0.15, 0.2, 0.25, FuzzyApEnMax*} σ	15
ShEn	dim = {2,3}, no. of bins = {5, 10, 15}	6
CCShEn	dim = {2,3}, no. of bins = {5, 10, 15}	6
CorrEn	dim = {2,3}, no. of bins = {5, 10, 15}	6
CarnEn	non-parametric	1
AlphEn	AlphEn features from Table 3, comb. #1	70

* radius *r* for which the maximum value of the corresponding entropy is obtained

additional method in the framework, while other nonlinear entropy methods had already been implemented in earlier versions. The framework is freely available under GPL 2.0 license.

Feature selection and classification was performed in the Weka platform for knowledge discovery and data mining [55]. 10x10-fold stratified cross-validation evaluation method was employed on the segments obtained from all patients for all analyses. The dataset is considered to be sufficiently large for all of the heart rhythm patterns so that there was no need to consider subject-specific modeling. Total classification accuracy = mean sensitivity (SENS), mean specificity (SPEC), and mean Area Under Curve (AUC) are reported. Details on these measures can be found in Hastie et al. [56]. Symmetrical uncertainty (SymmetricalUncertAttributeEval in Weka) was used for feature selection. Information gain and OneRule filter based feature selection methods [55,57] were also tried, but symmetrical uncertainty obtained the most favorable results regarding the accuracy of the models and the number of included features. For classifier construction on the multi-class (heart rhythm patterns) problem, random forest (RF) [58] classifier was employed. AdaBoost.M1+C4.5 and rotation forest ensembles were also tried, as our earlier papers indicated it [27,59], but the overall results were not better and the training times were longer compared to RF. The size of the forest was set to 300 trees and no limit to tree size for all analyses. Visualization of the results was performed in Matlab R2013a.

6. Results

The results for optimal threshold using all AlphEn features (#0, Table 3) and mean RR interval is shown in Fig. 2. It can be seen that the maximum values of total classification accuracy, which equals mean sensitivity for all rhythms, are achieved for threshold values of θ = <70–110 ms> with a peak at θ = 100 ms. This threshold range shows that ectopic beats (PAC, PVC) can be detected most reliably from cardiac rhythm if there is a shortening or prolongation larger than 70 ms and smaller than 110 ms. Setting the threshold to 120 ms or more obscures some of the ectopic beats, while setting it to 60 ms or less takes some of the normal beats as ectopic ones. Small variations of changes in accuracy for threshold range <70–110> ms can be attributed to the given sample. Other datasets with the same arrhythmia types may exhibit similar, but not exactly the same behavior in the range <70–110> ms, especially when the numbers of feature vectors per arrhythmia class differ significantly from the current ones.

The results of symmetrical uncertainty feature selection is shown in Fig. 3. It can be seen that the accuracy at θ = 100 ms is achieved most efficiently when top 70 AlphEn features are included (out of 138). These features form comb #, which is reported in Table 3 and used in further analyses. In Table

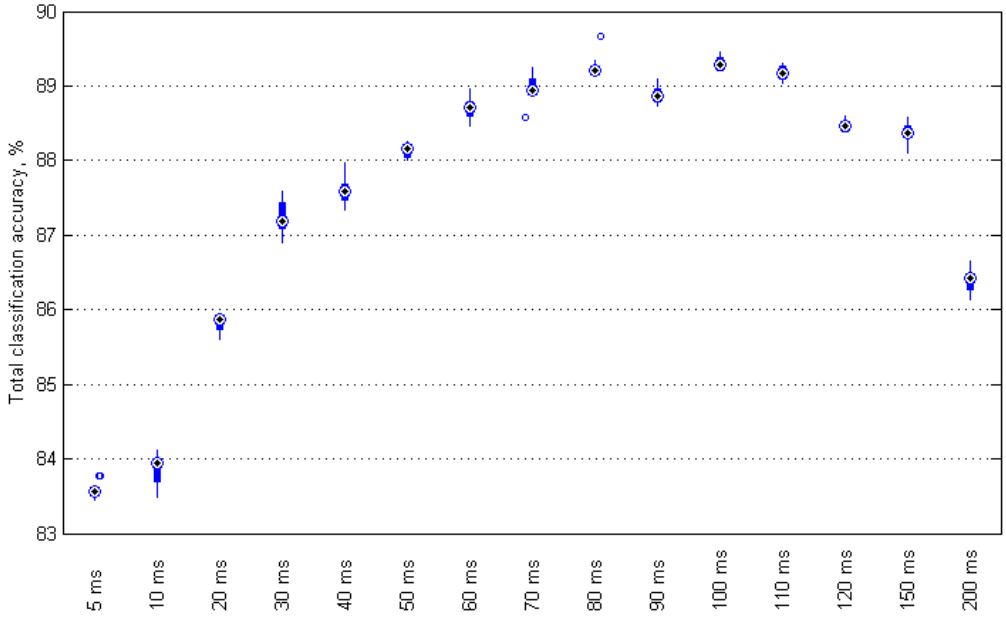

Fig. 2. Analysis of AlphEn's optimal threshold for arrhythmia classification

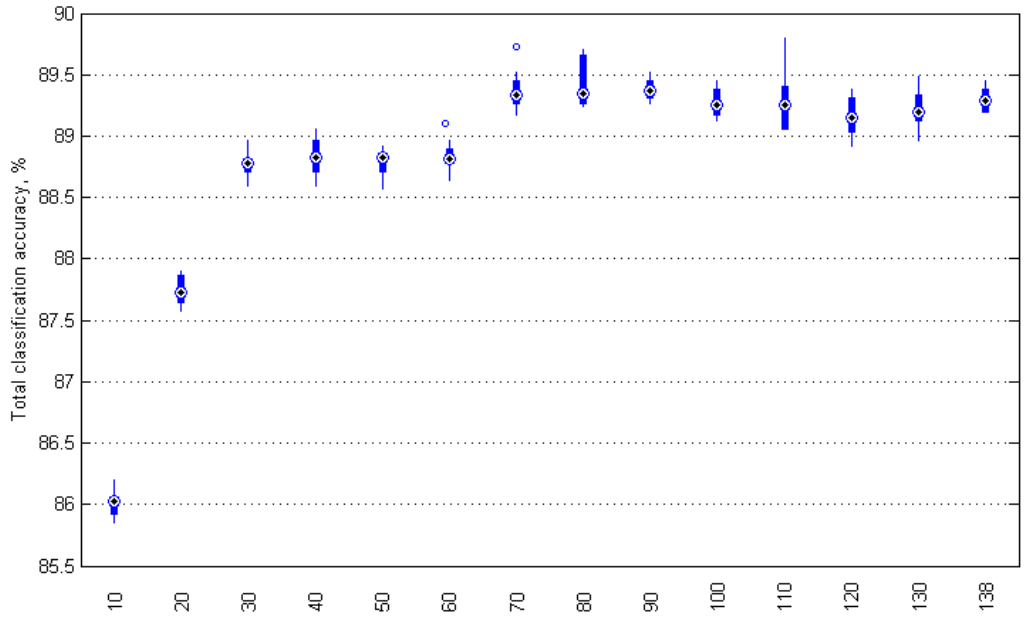

Fig. 3. Classification with AlphEn features: the *x*-axis depicts the number of included features, ranked with the symmetrical uncertainty measure

3, we report only the first 20 ranked features, while the complete combination is given later in the paper with statistical details in Table 7.

In Fig. 4, the box-and-whisker plot of mean sensitivity and mean specificity for the feature combinations #1 - #5 listed in Table 3 is shown, with and without the addition of AlphEn features. It can be seen that relevant AlphEn features (comb #1) alone are comparable to other HRV-based cardiac arrhythmia feature combinations used in literature. The addition of relevant AlphEn features to the known combinations improves sensitivity of other combinations by 2%, on average. Specificity does not show any major changes with the addition of AlphEn to all combinations. AlphEn combination has the lowest mean specificity (roughly 0.6%) and the highest mean sensitivity (roughly 0.3%) among the examined combinations. Linear combination (comb #2) appears to have somewhat better specificity

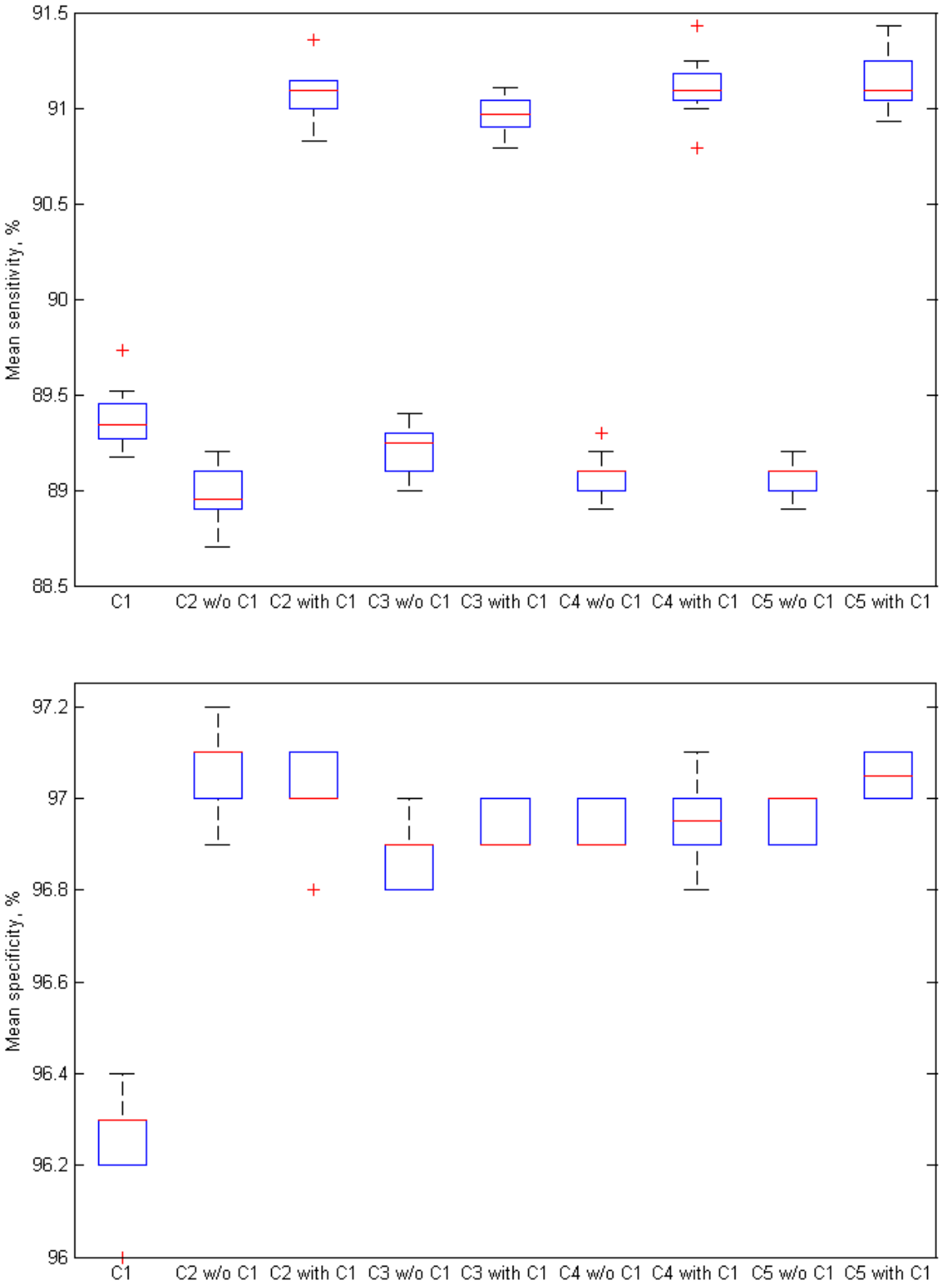

Fig. 4. Mean sensitivity and mean specificity box-and-whisker plot for arrhythmia classification for five feature combinations from Table 3, with and without the addition of AlphEn (comb #1 = C1)

than more complicated combinations, but all the differences are within 0.3%. Overall, the best combinations with respect to mean sensitivity and mean specificity appear to be #2 and #5, with the addition of AlphEn features (C2 with C1: mean SENS: 91.10%, mean SPEC: 97.01%, mean AUC: 98.99%; C5 with C1: mean SENS: 91.15%, mean SPEC: 97.05%, mean AUC: 99.00%).

Table 5 shows the influence of adding only a number of relevant AlphEn features to the combinations #2 - #5. The addition of the first ranked AlphEn feature slightly increases mean sensitivity for all combinations, while the addition of 5 highest ranking features increases mean sensitivity by 1%, on average, for all combinations. Although adding all 70 relevant features increases mean sensitivity by roughly 2%, the gain in mean sensitivity is only 0.5% with respect to adding only the first 10 highest ranking features. This means that the majority of relevant information necessary to boost the efficiency of established feature combinations is hidden in the first 10 highest ranking AlphEn features. It is interesting to note that mean specificity tends to increase up to the number of 10 highest ranking AlphEn features, while a decline is observed afterwards, which may be explained with insignificance of the majority (but not all) of the remaining AlphEn features. In Table 6, we provide details on the

Table 5. The analysis of influence of adding a number of highest ranking AlphEn features from combination #1 (C #1) to feature combinations #2 - #5

***X*=**		**C #*X* w/o C #1**	**C #*X* with 1 AlphEn**	**C #*X* with 3 AlphEn**	**C #*X* with 5 AlphEn**	**C #*X* with 10 AlphEn**	**C #*X* with 20 AlphEn**	**C #X with all C #1**
2	SENS, %	88.97	89.12	89.90	90.14	90.50	90.44	91.10
	SPEC, %	97.07	97.00	97.08	97.18	97.28	97.06	97.01
3	SENS, %	89.21	89.60	90.06	89.98	90.26	90.56	90.97
	SPEC, %	96.87	97.04	97.08	96.98	97.00	96.90	96.94
4	SENS, %	89.08	89.70	89.99	90.02	90.66	90.94	91.09
	SPEC, %	96.94	97.20	97.30	97.28	97.30	97.14	96.95
5	SENS, %	89.06	89.40	89.88	90.00	90.48	90.70	91.15
	SPEC, %	96.96	97.08	97.14	97.20	97.34	97.22	97.05

Table 6. Detailed classification results for all rhythm types for combination #5 + 10 highest ranking (C #6) and for combination #5 + all relevant AlphEn features (C #7), mean of 10x10-fold cross-validation

Rhythm	**Sensitivity, %**		**Specificity, %**		**AUC, %**	
	C #6	**C #7**	**C #6**	**C #7**	**C #6**	**C #7**
NSR	98.96	99.16	97.13	96.34	99.66	99.62
PAC	71.90	72.29	98.73	99.17	97.36	97.62
PVC	83.74	83.09	95.77	96.96	97.32	97.46
AFIB	93.85	96.14	97.70	97.10	99.40	99.30
VBI	77.85	79.50	98.98	98.96	98.70	98.82
VTR	44.42	50.80	99.54	99.66	96.77	97.88

classification results for each rhythm type for the best combination #5, with 10 AlphEn features (C #6) and with all relevant AlphEn features (C #7) added. It can be seen that the addition of all relevant features improves sensitivity compared to C #6 for almost all rhyhtms (except PVC). However, specificity is somewhat lower for NSR and AFIB (and higher for other rhythms), which leads to an overall drop in specificity when all relevant features are included (see Table 5), because NSR and AFIB have a high number of individual feature vectors that contribute to the overall mean specificity. AUC is also decreased for NSR and AFIB in C #7 (and increased for other rhythms), however, the decrease is very small.

Fig. 5 shows the results' comparison of several nonlinear entropy measures (added to the basic linear combination) with AlphEn. The best results with respect to the sum of mean sensitivity and mean specificity for all rhythms were obtained for parameters: (ApEn: m = 2, r = ApEnMax; SampEn: m = 1, r = 0.25σ; FuzzyApEn: m = 2, r = 0.2σ, ShEn: d = 3, bins = 5; CCShEn: d = 2, bins = 5; CorrEn: d = 2, bins = 15; AlphEn: Rate(V)).

From Fig. 5, it can observed that ApEn, SampEn, ShEn, FuzzyApEn and AlphEn all improve mean sensitivity and mean specificity of linear combination, while CarnEn increases mean specificity but

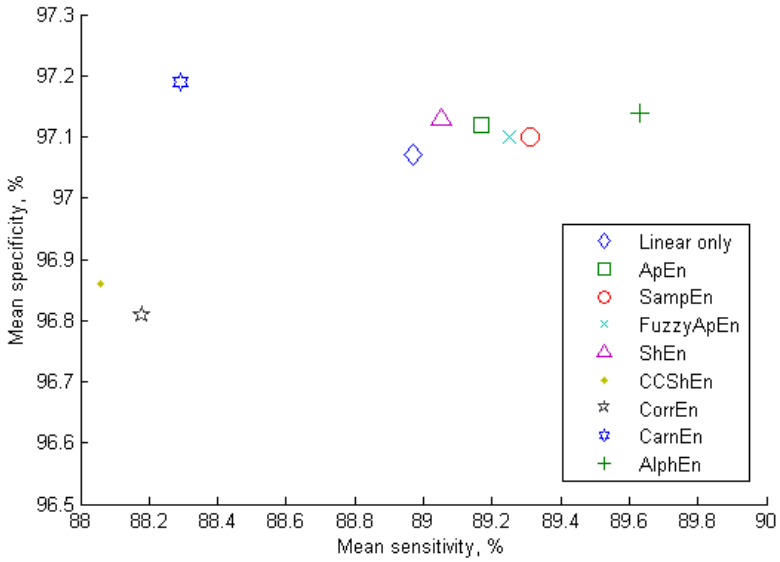

Fig. 5. Best arrhythmia classification results achieved for several different entropies appended to the basic linear feature combination (comb #2, Table 3)

decreases mean sensitivity. CCShEn and CorrEn decrease both measures. AlphEn entropy stands out the most with significant improvement in mean sensitivity.

In Table 7, statistical data on the relevant AlphEn features (comb #1) is presented. We report on the mean value, standard deviation, minimum value, maximum value, and symmetrical uncertainty score with respect to the goal class for numerical features, and on the category counts and symmetrical uncertainty score for categorical (Exists(*X*)) AlphEn features.

There are several interesting statistical properties of AlphEn features that can be inferred from Table 6. For example, the maximum AlphEn in segment for all letters (MaxAlphEn) has a maximum score of 4.48 bits/sequence span. This was achieved by AlphEn for letter Y (-,-,+), as can be seen for feature MaxAlphEn(Y). The letter Y is mostly related with VTR arrythmia, as seen in Table 2. Next, the rate of letter A (Rate(A)), which shows the rate of four-by-four beats with no significant changes in segments, is ranked quite high and also has a high mean value: the segments thus have, on average, 63% of four-by-four beats with no changes (at 100 ms threshold). Also, the letters Z (-,+,-) and V (+,-,+) seem to be very relevant for distinguishing arrhythmia types, as 6 out of 10 highest ranking

Table 7. Statistical properties of the relevant AlphEn features, ranked in descending order of symmetrical uncertainty (SymmU) measure

Rank	Feature name	Mean/StDev/Min /Max/SymmU or category count/SymmU	Rank	Feature name	Mean/StDev/Min /Max/SymmUnc or category count/SymmU	Rank	Feature name	Mean/StDev/Min /Max/SymmUnc
1.	MaxAlphEn	2.55/1.36/1.00/4.48/0.403	25.	Rate(Y)	0.01/0.03/0.00/0.31/0.204	49.	AverAlphEn(O)	0.35/1.01/0.00/4.11/0.139
2.	Exists(Z)	yes=1041/no=1793/0.390	26.	MaxAlphEn(W)	0.54/1.29/0.00/4.34/0.194	50.	Exists(K)	yes=1135/no=1699/0.134
3.	Rate(Z)	0.06/0.10/0.00/0.54/0.387	27.	AlphEnVar(V)	0.01/0.05/0.00/1.11/0.193	51.	Exists(O)	yes=411 / no=2423/0.132
4.	AverAlphEn(Z)	1.13/1.58/0.00/4.20/0.380	28.	AverAlphEn(W)	0.54/1.27/0.00/4.34/0.192	52.	Rate(J)	0.02/0.03/0.00/0.20/0.128
5.	MaxAlphEn(Z)	1.17/1.63/0.00/4.24/0.370	29.	AverAlphEn(K)	1.03/1.62/0.00/4.18/0.190	53.	Exists(A)	yes=2530 / no=304/0.127
6.	AverAlphEn	1.63/0.79/0.81/3.88/0.367	30.	Rate(S)	0.01/0.03/0.00/0.25/0.189	54.	AlphEnVar(I)	0.01/0.08/0.00/1.43/0.125
7.	Rate(A)	0.63/0.38/0.00/1.00/0.366	31.	MaxAlphEn(K)	1.05/1.64/0.00/4.18/0.187	55.	Rate(N)	0.01/0.03/0.00/0.28/0.124
8.	Rate(V)	0.03/0.09/0.00/0.53/0.322	32	MaxAlphEn(Y)	0.42/1.11/0.00/4.48/0.187	56.	Rate(E)	0.01/0.03/0.00/0.25/0.123
9.	AlphEnVar	0.58/0.68/0.00/4.19/0.318	33.	Exists(W)	yes=431 / no=2403/0.187	57.	MaxAlphEn(N)	0.41/1.19/0.00/4.16/0.122
10.	Exists(V)	yes=613 / no=2221/0.290	34.	MaxAlphEn(S)	0.52/1.17/0.00/4.08/0.186	58.	AverAlphEn(N)	0.41/1.18/0.00/4.11/0.122
11.	Exists(I)	yes=1088/no=1746/0.286	35.	AverAlphEn(Y)	0.41/1.08/0.00/4.48/0.185	59.	MaxAlphEn(M)	0.36/1.04/0.00/4.07/0.119
12.	MaxAlphEn(I)	0.97/1.47/0.00/4.31/0.282	36.	Exists(Y)	yes=376 / no=2458/0.184	60.	Rate(B)	0.03/0.04/0.00/0.21/0.119
13.	MaxAlphEn(V)	0.69/1.36/0.00/4.14/0.279	37.	Rate(C)	0.03/0.03/0.00/0.25/0.182	61.	Exists(N)	yes=300 / no=2534/0.116
14.	AverAlphEn(I)	0.94/1.44/0.00/4.31/0.276	38.	AverAlphEn(S)	0.51/1.15/0.00/4.07/0.180	62.	AlphEnVar(Q)	0.01/0.09/0.00/1.62/0.115
15.	AverAlphEn(V)	0.66/1.31/0.00/4.05/0.272	39.	Rate(H)	0.01/0.03/0.00/0.25/0.174	63.	AverAlphEn(M)	0.36/1.03/0.00/4.05/0.115
16.	Rate(I)	0.03/0.05/0.00/0.28/0.255	40.	Exists(S)	yes=605 / no=2229/0.173	64.	AverAlphEn(E)	0.44/1.07/0.00/3.84/0.111
17.	Exists(Q)	yes=1052/no=1782/0.249	41.	Exists(C)	yes=1141/no=1693/0.164	65.	Exists(M)	yes=438 / no=2396/0.105
18.	Rate(Q)	0.03/0.05/0.00/0.27/0.242	42.	Rate(O)	0.01/0.03/0.00/0.25/0.163	66.	Rate(U)	0.00/0.01/0.00/0.16/0.105
19.	AverAlphEn(C)	1.14/1.66/0.00/4.06/0.228	43.	Rate(K)	0.03/0.04/0.00/0.25/0.161	67.	MaxAlphEn(E)	0.44/1.08/0.00/3.84/0.103
20.	MaxAlphEn(C)	1.15/1.68/0.00/4.07/0.228	44.	Exists(H)	yes=575 / no=2259/0.146	68.	AverAlphEn(U)	0.19/0.75/0.00/3.95/0.101
21.	MaxAlphEn(Q)	0.98/1.51/0.00/4.18/0.224	45.	MaxAlphEn(H)	0.55/1.24/0.00/4.17/0.146	69.	AlphEnVar(W)	0.01/0.09/0.00/2.57/0.100
22.	AverAlphEn(Q)	0.96/1.47/0.00/4.17/0.215	46.	Rate(M)	0.01/0.03/0.00/0.33/0.145	70.	Rate(D)	0.02/0.03/0.00/0.24/0.098
23	Rate(W)	0.01/0.04/0.00/0.36/0.210	47.	AverAlphEn(H)	0.54/1.22/0.00/4.13/0.143			
24.	AlphEnVar(Z)	0.02/0.07/0.00/1.14/0.208	48.	MaxAlphEn(O)	0.36/1.03/0.00/4.17/0.140			

features are related to them, including quantitative entropy measures for the letter Z.

Additionally, in Fig. 6, we present a comparison of the results when adding a single AlphEn feature to the linear combination (comb #2) for the top 10 features from comb #1. It is important to notice that using the highest ranking feature, MaxAlphEn, does not lead to the best results when used with the linear combination. Rate(V) should be used instead, which leads to significant improvement in both mean sensitivity and mean specificity. When compared with the results from Table 5 (for comb #2), it becomes apparent that some of the top 10 features contribute more significantly than others to the overall success of the combination. Nevertheless, including all 10 highest ranking AlphEn features has the highest contribution to the success of all combinations.

Table 7 presents the most common letter combinations in the analyzed segments. It should be noted that all the alphabet letters were found in the arrhythmia records, probably because AFIB irregular

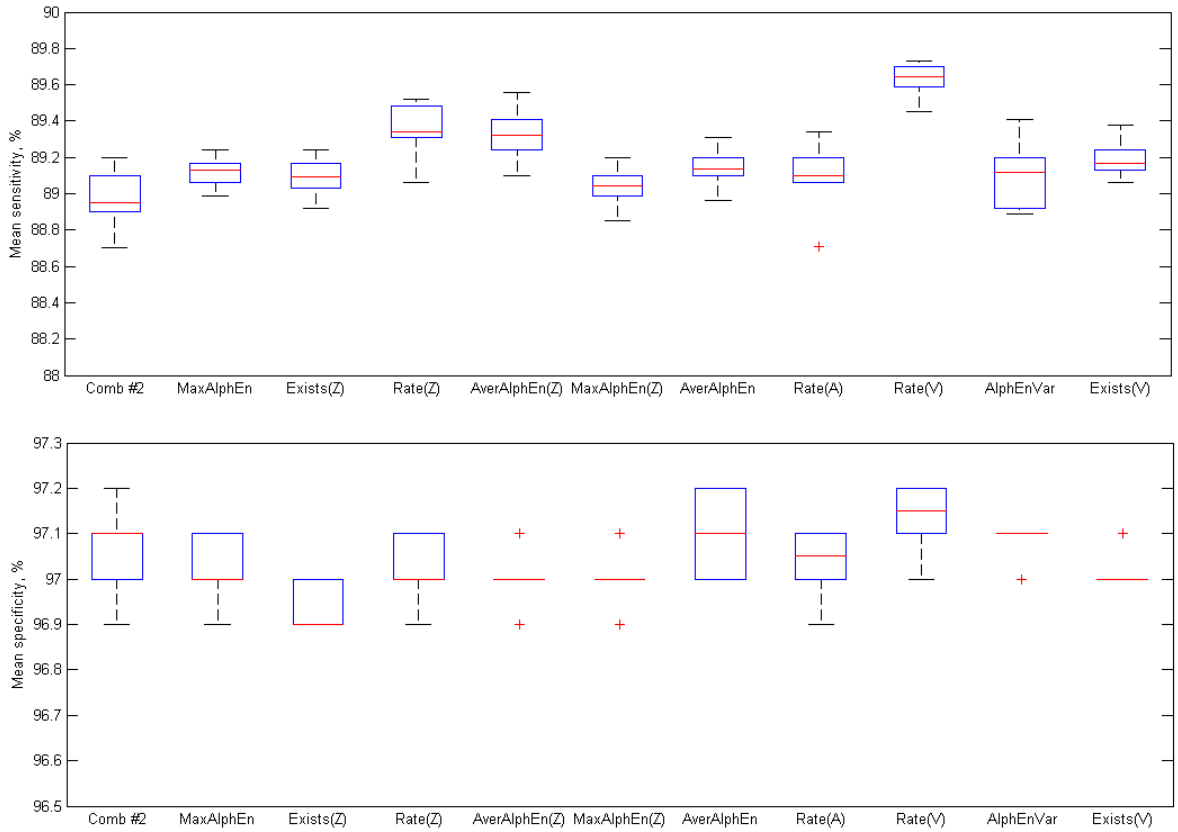

Fig. 6. Improvements in classification results when adding a single AlphEn feature from the top 10 relevant features to the linear combination #2

Table 7. The most common AlphEn letter combinations in 20 s segments for arrhythmia classification, threshold θ = 80 ms

Heart rhythm	Letter combination	Segments with the combination	Example of RR-interval changes
NSR, 1520 segments	A only	965	00000
	B,D,J	81	00+00
	C,E,K	53	00-00
	B,C,D,E,J,K	21	00-000+00
	B,H,K,Q	13	00+-00
	B,D,H,J,K,Q	7	00+00+-00
PAC, 197 segments	C,I,K,Q,Z	46	00-+-00
	C,I,J,S	32	00-+00
	C,I,J,K,Q,S,Z	17	00-+00-+-00
PVC, 437 segments	C,I,K,Q,Z	136	00-+-00
	C,I,K,N,Q,Z	13	00-+-0-+-00
	B,D,J	13	00+00
	I,N,Q,Z	11	-0-+-0
	C,I,K,Q,V,Z	9	00-+-+-00
	C,I,K,Q,W,Y,Z	8	00-+--+-00
VBI, 210 segments	V,Z	43	-+-+-+-
	V,W,Y,Z	11	+-+--+-+-
	C,I,K,Q,V,Z	9	00-+-+-+-00
	C,I,K,N,Q,V,Z	7	00-+-+-0-+-00
	C,I,N,Q,V,W,Z	7	00-+-+-+-0-+--
AFIB, 364 segments	Mostly 9 - 18 different letters in segment	N/A	N/A
VTR, 312 segments	C,I,K,Q,W,Y,Z	23	00-+--+--+-00
	I,M,S,W,Y,Z	6	-+--+0-+--+

episodes were considered. Letters that represent ectopic beats such as I (0 - +), Q (+ - 0), and Z (- + -) are common. PAC and PVC had the same most common pattern, with letters C, I, K, Q, Z: 00-+-00, which is theoretically unusual, because PAC should not have large compensations after the anomalous beat [53]. Aside from typical combination C, I, J, S that is present in PAC and absent in PVC, a possibility to distinguish these two beat types is presented through quantification of the compensation with AlphEn (5).

7. Discussion

Comparing studies related to classification of cardiac arrhythmias from HRV time series is challenging because there are rarely any two studies that use the same dataset with the same preprocessing methods and with classification of the same arrhythmias. Nevertheless, for the sake of completeness, a summary of related relevant studies is provided in Table 9. It should be noted that in

the cases of multiple arrhythmias classification, only mean sensitivity and mean specificity are reported in Table 8. Details on sensitivity or specificity for a particular arrhythmia may be available in the original literature.

One may argue that the number of extracted AlphEn features (138) may hinder the application of our method. However, as we have shown, a rather simple filter feature selection method such as symmetrical uncertainty may be used prior to construction of the final feature combination in order to identify only relevant AlphEn features. In addition, as shown in the second analysis, one can add only top 10 AlphEn features ranked by symmetrical uncertainty to an established combination and still achieve high results. Moreover, the features themselves are very fast to calculate, as they rely only on basic algebra for sets of four-by-four measurements. Still, discovering the optimal set of AlphEn features that should be added to established combinations is troublesome, as the exhaustive search procedure is computationally unfeasible due to the high number of features.

It should be noted that the number of relevant AlphEn features certainly depends on the number and quality of the analyzed arrhythmias. Hence, the resulting set of relevant AlphEn features presented in

Table 8. Relevant studies dealing with classification of cardiac arrhythmias from HRV series

Author	Dataset	Features	Classifier	Arrhythmias	ACC | SENS | SPEC, %
Tsipouras & Fotiadis [60]	MIT-BIH Arrhythmia Database	Linear time and time-frequency sets of features	Neural network	Normal / arrhythmia	N/A | 90.0 | 92.9
Asl et al. [3]	MIT-BIH Arrhythmia Database	Linear (7) and nonlinear (7) (comb #3)	SVM (binary classification) +GDA feature reduction	Normal, premature ventricular contraction, atrial fibrillation, ventricular fibrilation, sick sinus syndrome, second degree block	99.2 | 95.8 | 99.4
Yaghouby et al. [30]	MIT-BIH Arrhythmia Database	Linear (5) and nonlinear (4)	Neural network + GDA feature reduction	Left bundle branch block, first degree heart block, supraventricular tachyarrhythmia and ventricular trigeminy	100.0 | 100.0 | 100.0
Mohebbi & Ghassemian [61]	Atrial Fibrillation Prediction Database (AFPDB)	Spectral (2), bispectral (6), nonlinear (4)	SVM	Normal / Paroxysmal atrial fibrillation	N/A | 96.3 | 93.1
Jovic, A. & Bogunovic [27]	MIT-BIH Arrhythmia Database	Linear (14), nonlinear (3) (comb #5)	AdaBoosted C4.5	Normal, paced, premature atrial contraction, premature ventricular contraction, atrial fibrillation, ventricular tachycardia, ventricular bigeminy, ventricular trigeminy, second degree block	87.5 | 87.5 | 95.6 |
This study	MIT-BIH Arrhythmia Database	Comb #2 (10) + comb #1 (70) or comb #5 (17) + comb #1 (70)	Random forest	Normal, premature atrial contraction, premature ventricular contraction, atrial fibrillation, ventricular bigeminy, ventricular trigeminy	91.2 | 91.2 | 97.1

this work should only be used with the analyzed six rhythm types. For other rhythm types, the procedure applied in this work should be repeated in order to find feature combinations of high quality.

Results presented in Fig. 4 and Table 5 strongly support the addition of AlphEn features to known expert combinations. However, the idea of replacing established feature combinations entirely with AlphEn features remains controversial. Although mean sensitivity is somewhat higher for comb #1 than for the established combinations, the mean specificity is lower. Thus, using only AlphEn features for a classification problem may be possible in situations where sensitivity is more important than specificity or in the case of classification of disorders that do not have established feature combinations available.

8. Conclusion

The aim of the current study was to establish the relevance of AlphEn in HRV analysis. It has been shown that AlphEn may be considered as a traditional short-term complexity measure of a signal, comparable to ApEn, FuzzyApEn, and others. It has also been shown that the strength of AlphEn lies in domain-oriented feature extraction and classification of arrhythmia from HRV series, where it can be used in addition to other established feature combinations to boost the performance. The qualitative aspect of AlphEn, as reflected in features determined by (12) and (13) may be used to explain the cause of variability in a segment, as well as to achieve classification accuracy improvement. The quantitative aspect of AlphEn, as calculated with features (6)-(11) should mostly be used in discerning between disorder types that do not differ significantly in its qualitative aspect (e.g. PAC and PVC). As a result of these findings, it can be recommended that the main application areas of AlphEn would be automatic classification systems, especially for first-hand screening for arrhythmia problems, as well as in decision support systems in medicine.

Future work will focus mostly on applying AlphEn to other common disorders such as congestive heart failure and to other cases of biomedical time series variability, e.g. in ECG and EEG series, as well as in examining the entropy's potential for online analysis of patient records.

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Conflict of interest statement

None declared.