A Hybrid Two-Stage Approach for Paroxysmal Atrial Fibrillation Prognosis Problem

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Abstract

We develop a hybrid two-stage approach for paroxysmal atrial fibrillation (PAF) prognosis based on features extracted from short-term heart rate variability (HRV) sequences. At the first stage, a data-mining-based approach is used to identify crucial medical-oriented features that can distinguish PAF HRV sequences from non-PAF HRV ones. However, PAF patients can experience PAF without exhibiting the medical-oriented features. To detect this type of patients, at the second stage, we employ a machine-learning-based approach to select certain nonlinear features that can classify HRV sequences into classes of PAF or non-PAF.

The developed approach was trained on the PAF Prediction Challenge Database and was tested on the dataset consisting of 30-minute HRV episodes extracted from MIT-BIH Atrial Fibrillation Database and the MIT-BIH Normal Sinus Rhythm Database. It was obtained from the numerical evaluation that the developed approach achieved about 85% of accuracy in short-term prognosis of PAF by using the first stage approach alone and around 90% of accuracy with the combination of both stages. Furthermore, the developed medical-oriented features can be clinically valuable to the cardiologists for providing insights to the initiation of PAF.

1. Introduction

Proceeding from our previous research [1] in the Computer in Cardiology Challenge 2001 [2], in this paper, we aim to develop a systematic approach to solve the PAF prognosis problem which can be described as: "Given a short-term (say 30-minute) human HRV sequence containing no significant arrhythmias, determine whether the corresponding subject will experience PAF in the near future (say 30-minute)."

Inspired by the clinical observation that premature atrial beats (PABs) are frequently observed before the onset of PAF but not all PAF patients experience PABs before the onset of PAF, a hybrid two-stage approach is developed to solve the PAF prognosis problem. In section 2, the developed approach will be described in detail. The performance of the developed approach will then be presented in section 3. And finally, the possible medical interpretations of the computed results will be discussed in section 4.

2. Materials and methods

The developed approach was trained on the PAF Prediction Challenge Database (106 PAF records and 94 non-PAF HRV records, including the training and test parts of the database) and was tested on the dataset consisting of 54 30-min pre-AF episodes extracted from MIT-BIH Atrial Fibrillation Database and 54 30-min non-PAF episodes extracted from the MIT-BIH Normal Sinus Rhythm Database [3]. The employed datasets are summarized in Table 1.

Table 1. Summary of the training and test dataset

	Training Set	Test Set
PAF HRV sequences	106 (PAF Prediction Challenge Database)	54 (MIT-BIH Atrial Fibrillation Database)
Non-PAF HRV sequences	94 (PAF Prediction Challenge Database)	54 (MIT-BIH Normal Sinus Rhythm Database)

The two stages of prognosis in the proposed approach are performed heuristically. The first stage aims to determine medical-oriented features in the HRV sequence representing certain subclass of abnormal beats that are related to the onset of PAF so that if certain amount of such subclass of the abnormal beats are detected in an subject's short-term HRV sequence, one can prognose the subject to have PAF. However, PAF patients can experience PAF without showing such subclass of the abnormal beats before the onset of PAF. To detect this type of PAF patients, we proposed to separate their HRV sequences from those of the non-PAF subjects by nonlinear features at the second stage.

2.1. The first stage

In our work, the medical-oriented features are the PAF-pairs each of which represents two consecutive points in the HRV sequence that are related to the onset of PAF. The problem to be solved at this stage is to identify the PAF-pairs from all pairs of points in HRV

sequences. The 2-D Poincaré plot is used to extract all pairs in an HRV sequence. By using the 2-D Poincaré plot, the problem becomes to determine the critical regions (the PAF-related regions) in the plot so that once a short-term HRV sequence whose 2-D Poincaré plot has more than certain amount of points lying in such regions, it can be prognosed to have PAF.

To identify the PAF-related regions in the 2-D Poincaré plot, we first confine the range of 2-D Poincaré plot to possible heartbeat range, say $[B_L, B_U]\times[B_L, B_U]$ where B_L and B_U are lower and upper bounds of possible beating range. The confined range is then divided into, say $R\times R$, regions. A feature selection algorithm is then developed to identify the PAF-related regions from the total R^2 regions. In our work, a best-neighbor based algorithm aided with a feature-exploring list is developed to select the PAF-related regions from the R^2 regions. The feature-exploring list is an ordered list of the R^2 regions based on the difference between their appearances in the 2-D Poincaré plots of PAF HRV sequences and those of non-PAF ones. The feature-exploring list helps the search algorithm in two senses: (1) it provides an initial guess; (2) it provides guidance to the search algorithm on reaching a plateau area.

To generate the feature-exploring list, we need to first compute two matrices: the PAF appearance matrix and the non-PAF appearance matrix. The PAF appearance matrix, M_p, is a R-by-R matrix whose (i, j)-th component, $1 \le i, j \le R$, is the number of PAF HRV sequences (in the training dataset) whose Poincaré plot exhibits points in the corresponding region of the confined 2-D Poincaré plot range while for the non-PAF appearance matrix, M_n, its (i, j)-th component is the number of non-PAF HRV sequences (in the training dataset) whose Poincaré plot exhibits points in the corresponding region of the confined 2-D Poincaré plot range. An R-by-R matrix Q is then computed via $Q = M_p - M_n$. The matrix Q provides the information of how frequently the 2-D Poincaré plots generated from PAF HRV sequences in the training dataset exhibit points in the R^2 regions more than those generated from non-PAF ones. The R-by-R matrix Q is then rearranged into an R^2-by-1 vector in a column-wise fashion, and the feature-exploring list is the R^2 sorted indices (in descending order) of the resultant column vector based on the magnitudes of the vector elements.

To select the PAF-related regions from the R^2 regions, a best-neighbor based algorithm is developed. The algorithm is detailed below.

Step 1: **select** the first d elements in the feature-exploring list as initial guess and let the set of the d elements be **S**, the set of the remaining $R^2 - d$ elements be **T**;

Step 2: **let** $F_p(\mathbf{S})$ denote the function that computes the number of PAF HRV sequences whose 2-D Poincaré plot exhibits no less than θ points in the regions specified by **S** and $F_n(\mathbf{S})$ be the function that computes the number of non-PAF HRV sequences whose 2-D Poincaré plot shows less than θ points in the regions specified by **S**.
compute the number of HRV sequences in training dataset that are correctly prognosed: $d_0 = F_p(\mathbf{S}) + F_n(\mathbf{S})$;

Step 3: **set** the threshold value θ = 0;

Step 4: **set** the loop-control valuable $v = 0$;

Step 5: **perform** the following iterative process:

while $v = 0$ **do**

begin

determine the element s in **S** such that

$$d_1 = \max_s [F_p(\mathbf{S} - s) + F_n(\mathbf{S} - s)];$$

if more than one elements in **S** reach the same d_1, choose the one that is nearest to the end of **S**;

determine the element t in **T** such that

$$d_2 = \max_t [F_p(\mathbf{T} - t) + F_n(\mathbf{T} - t)];$$

if more than one elements in **T** reach the same d_2, choose the one that is closest to the top of **T**;

if $\max(d_1, d_2) > d_0$

if $d_1 \ge d_2$

set $d_0 = d_1$, $\mathbf{S} = \mathbf{S} - s$, and $\mathbf{T} = \mathbf{T} + s$ (remove s from **S** and add it to the end of **T**);

else

set $d_0 = d_2$, $\mathbf{S} = \mathbf{S} + t$, and $\mathbf{T} = \mathbf{T} - t$ (remove t from **T** and add it to the end of **S**);

endif;

else

set $v = 1$;

endif;

end;

Step 6: **Repeat** the above process with θ = θ + 1, until the maximum d_0 is found.

2.2. The second stage

Many nonlinear features such as detrended fluctuation analysis (DFA), slope of the $1/f$ spectrum, and approximate entropy have been used to perform medical signal analysis and classification. However, since the HRV sequences are highly complex, none of conventional nonlinear feature alone has been reported to achieve satisfactory result on PAF prognosis.

In addition, due to the non-autonomous and noisy nature of the HRV sequences, nonlinear features that compute the power-law relationship between measurements at different measuring resolutions cannot accurately represent the nonlinear properties as they are designed to. To resolve this problem, we propose to use the vector composing of measurements at different measuring resolutions instead of the index that evaluates the power-law relationship between such measurements.

Six nonlinear features are selected from conventional nonlinear features due to their superior performances to the PAF prognosis problem. The six nonlinear features are detrended fluctuation analysis (DFA) [4], $1/f$

spectrum slope, divider dimension [5], correlation dimension [6], histogram, and approximate entropy [7]. The rescaled fluctuation analysis (RFA), which is a modification of the DFA, is also used as primary features. The RFA is similar to DFA except that (1) the sequence is not integrated; (2) the sum of maximum fluctuation instead of sum of detrended fluctuation is computed at different measuring resolutions.

A two-level neural network structure is developed to perform the prognosis task at this stage, as shown in Figure 1. Each of the seven first-level networks acts as an expert and each of the seven nonlinear features is the expertise of the corresponding expert. Upon presenting an HRV sequence, each of the experts makes prognosis (PAF or non-PAF) based on his expertise. These prognosis results are then fed to the second-level network, which acts as a manager who makes the final decision based on the liabilities (weights of the second-level network computed from training dataset) of the experts.

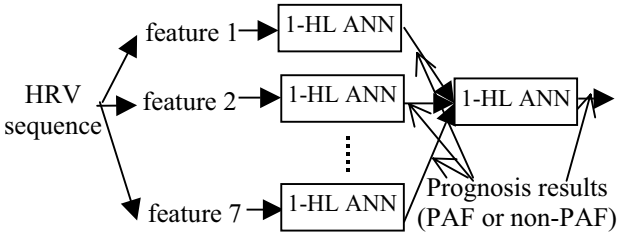

Figure 1. The developed two-level neural network structure (1-HL ANN: one hidden-layer artificial neural network)

A network-pruning algorithm – the modified optimal brain surgeon (OBS) is applied to the second-level network to select crucial nonlinear features at the training phase to reduce the redundancies among the seven primary features. The original OBS [8] iteratively removes the least significant connection (connection with smallest saliency) from the network without significantly degrading the network performance. The modified OBS, however, iteratively removes the least significant input node (input node whose connections has smallest sum of saliencies) from the network until the performance of the network drop significantly.

The feature selection algorithm developed for solving the second-stage PAF prognosis problem is presented below.

Step 1: **compute** the features from an HRV sequence;
Step 2: **train** the first-level neural networks using their corresponding nonlinear features;
Step3: **train** the second-level neural network using the outputs of the first-level networks and compute the performance of the network, p;
Step4: **perform** the following iterative process:
while $p \geq \theta$ (a predetermined threshold value) **do**
begin
find out the input node of the second-level network with the smallest sum of saliences and remove the node;
re-train the second-level network and compute its performance, p;
end;

3. Results

3.1. The first stage

Since the proposed approach aims to prognose PAF for subjects with no serious heart disease, the heartbeat range [B_L, B_U] is set to [40 140]. The range of the 2-D Poincaré plot confined to the [40 140]×[40 140] area is further divided into 20-by-20 regions. With such settings, the regions in the 2-D Poincaré plot representing the PAF-pairs that are selected by the developed best-neighbor based algorithm are shown in Figure 2.

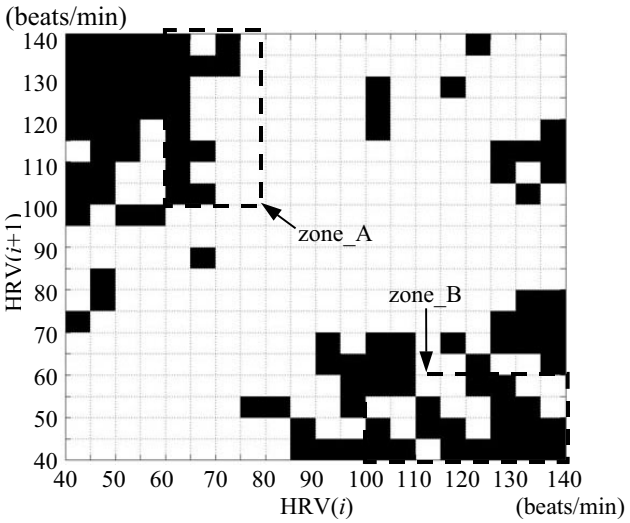

Figure 2. The PAF-related regions in 2-D Poincaré plot

Based on Figure 2, if the 2-D Poincaré plot of a 30-min HRV sequence exhibits more than one point (also determined by the developed feature-selection algorithm) in the black regions, the HRV sequence is prognosis as PAF, or otherwise non-PAF. Using such criterion, the prognosis accuracy of the first stage approach is shown in Table 2.

Table 2. Summary of the prognosis result (stage 1)

	Sensitivity	Specificity	Accuracy
Training dataset	83.19% (94/113)	86.21% (75/87)	84.50% (169/200)
Test dataset	81.67% (49/60)	89.58% (43/48)	85.19% (92/108)

3.2. The second stage

To reduce the false-negative cases misclassified by the

first-stage approach, all HRV sequences with less than 4 PAF-pairs are sent to the second stage for further examination.

By using the modified OBS, the final two-level neural structure and the corresponding nonlinear features are shown in Figure 3. The performance of the stage-2 approach is shown in Table 3.

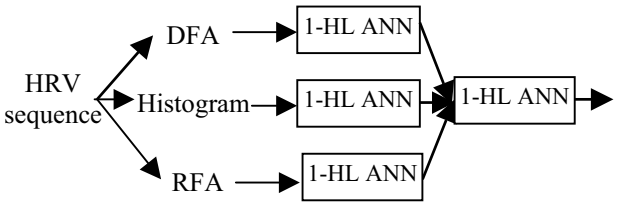

Figure 3. The final two-level neural structure and the corresponding nonlinear features

Table 3. Summary of the prognosis result (stage 2)

	Sensitivity	Specificity	Accuracy
Training set	100%	97.40%	96.77%
Test set	100%	98.18%	98.41%

3.3. The overall system

The flowchart of the developed PAF prognosis system is shown in Figure 4. The prognosis accuracy at each stage is indicated in the figure and the details are provided in Table 4.

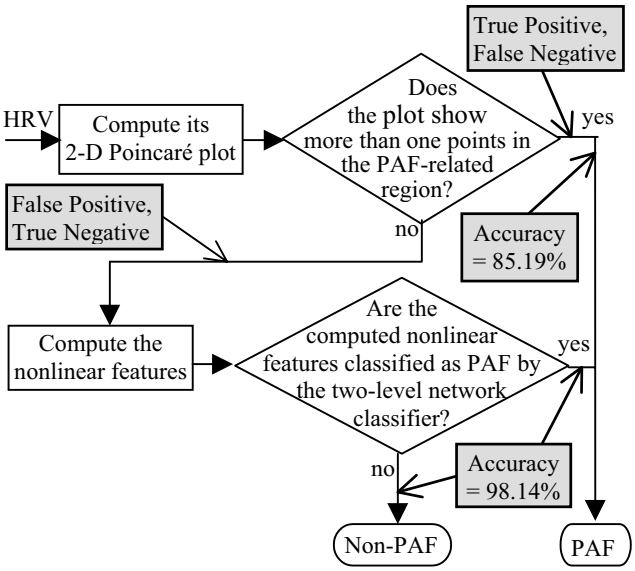

Figure 4. The flowchart of the overall system

Table 4. Summary of the prognosis result

	Sensitivity	Specificity	Accuracy
Training dataset	84.30% (102/121)	94.94% (75/79)	88.5% (177/200)
Test dataset	88.83% (53/60)	97.92% (47/48)	92.59% (100/108)

4. Discussions

Zone_A in Figure 2 represents the pairs in HRV sequence consisting of a normal beat followed by a premature beat. As shown in zone_A, not all the premature beats are related to the onset of PAF. It can be seen that according to the training data, the premature beats following a slower normal beat are more likely to lead to the PAF than those following a faster normal beat. Zone_B in Figure 2 represents the pairs in HRV sequence consisting of a premature beat followed by a lengthened beat. According to zone_B, it also suggests that the premature beats followed by a longer lengthened beat is more likely to result in PAF than those followed by a shorter lengthened beat. Other black regions in Figure 2 may also imply some other medical insights to the cardiologists about the initiations of PAF.

From Figure 4, it can be seen that the false-negative cases are the major problem of the stage-1 approach. By examining these cases, we find that most of the false-negative cases are caused by lack of information in distinguishing premature atrial beats from premature ventricular beats due to the usage of HRV sequences. This problem can be resolved by checking the original ECG signal once a premature beat is detected.

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