AN OPTIMIZATION METHOD BASED ON GENETIC ALGORITHM FOR HEART RATE VARIABILITY ANALYSIS IN THE PREDICTION OF THE ONSET OF CARDIAC ARRHYTHMIA

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Dedicated to my beloved family.

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ABSTRACT

Heart rate variability (HRV) is one of the common biological markers for developing a diagnostic system of cardiovascular disease. HRV analysis is used to extract statistical, geometrical, spectral and non-linear features in such diagnostic system. The diagnostic accuracy can be maximized by applying a feature selection step that selects an optimal feature subset from the extracted features. However, there are shortcomings in using only the feature selection for optimizing a diagnostic system that is based on HRV analysis. One of the main limitations is that the parameters of HRV feature extraction algorithms are not optimized for maximal performance. In addition, the feature selection process does not consider the feature cost and misclassification error of the selected optimal feature subset. Therefore, this thesis proposes a multi-objective optimization method that is based on the non-dominated sorting genetic algorithm to overcome these shortcomings in a cardiac arrhythmia prediction system. It optimizes the HRV feature extraction parameters, selects the best feature subset, and tunes the classifier parameters simultaneously for maximum prediction performance. The proposed optimization algorithm is applied in two cardiac arrhythmia cases, namely the prediction of the onsets of paroxysmal atrial fibrillation (PAF) and ventricular tachyarrhythmia (VTA). In the proposed approach, trade-off between multiple optimization objectives that contradict to each other are also analyzed. The optimization objectives include the feature count, measurement cost, prediction sensitivity, specificity and accuracy rate. The following results prove the effectiveness of the proposed optimization algorithm in the two arrhythmia cases. Firstly, the PAF onset prediction achieves an accuracy rate of 89.6%, which significantly outperforms most of the previous works. This accuracy rate is achieved even with the HRV signal length being reduced from the typical 30 minutes to just 5 minutes (a reduction of 83%). In the case of VTA onset prediction, the accuracy rate of 78.15% is achieved with 5-minute signal length. This result outperforms previous works. Another significant result is the sensitivity rate improvement with the trade-off of lower specificity and accuracy rate for both PAF and VTA onset predictions. For instance, the sensitivity rate of the VTA onset prediction system improved from 81.48% to 92.59% while the accuracy rate reduced from 78.15% to 72.59%.

ABSTRAK

Kebolehubahan kadar jantung (HRV) adalah salah satu penanda biologi yang popular untuk membangunkan sistem diagnostik penyakit kardiovaskular. Analisis HRV digunakan untuk mengekstrakkan ciri-ciri statistik, geometri, spektrum dan tidak-linear dalam sistem diagnostik. Ketepatan diagnostik boleh dimaksimumkan dengan menggunakan kaedah pemilihan ciri yang menentukan subset ciri-ciri optimum daripada ciri-ciri yang telah diekstrak. Walau bagaimanapun, terdapat beberapa kelemahan jika hanya menggunakan pemilihan ciri untuk mengoptimumkan sistem diagnostik yang berasaskan analisis HRV. Salah satu kelemahan utama ialah parameter-parameter dalam algoritma pengekstrakan ciri-ciri HRV tidak dioptimumkan untuk mencapai prestasi yang maksimum. Selain itu, proses pemilihan ciri tidak mengambil kira kos ciri dan ralat salah pengelasan dalam subset ciri optimum yang dipilih. Oleh yang demikian, tesis ini mencadangkan kaedah pengoptimuman pelbagai objektif berasaskan algoritma genetik isihan bukan dominan untuk mengatasi kekurangan tersebut dalam sistem ramalan aritmia jantung. Ia mengoptimumkan parameter pengekstrakan ciri HRV, memilih subset ciri yang terbaik dan menala parameter pengelas dengan serentak untuk prestasi ramalan yang maksima. Algoritma pengoptimuman yang dicadangkan digunakan dalam dua kes jantung aritmia, iaitu ramalan permulaan fibrilasi atrial paroksismal (PAF) dan takiaritmia ventrikel (VTA). Dalam pendekatan yang dicadangkan, tukar-ganti antara pelbagai objektif pengoptimuman yang bercanggah antara satu sama lain juga dianalisis. Objektif pengoptimuman merangkumi bilangan ciri, kos pengukuran, kadar ramalan sensitiviti, spesifisiti, dan ketepatan. Hasil berikut membuktikan keberkesanan algoritma pengoptimuman yang dicadangkan dalam dua kes aritmia. Pertama, ramalan permulaan PAF mencapai kadar ketepatan 89.6%, dan kadar ini lebih tinggi daripada kebanyakan kerja sedia ada. Kadar ketepatan ini dicapai walaupun panjang isyarat HRV dikurangkan dari tempoh tipikal 30 minit kepada hanya 5 minit (pengurangan sebanyak 83%). Dalam kes ramalan permulaan VTA, kadar ketepatan sebanyak 78.15% telah dicapai dengan isyarat HRV sepanjang 5 minit. Keputusan ini adalah lebih baik daripada kerja sedia ada. Satu lagi hasil yang penting ialah peningkatan kadar sensitiviti dengan pengurangan kadar spesifisiti dan ketepatan untuk kedua-dua ramalan permulaan PAF dan VTA. Contohnya, kadar sensitiviti dalam ramalan VTA dipertingkatkan dari 81.48% kepada 92.59% sementara kadar ketepatan berkurang dari 81.48% kepada 72.59%.

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LIST OF ABBREVIATIONS

2D	-	2 Dimensional
3D	-	3 Dimensional
ACC	-	Accuracy
AF	-	Atrial Fibrillation
AFPDB	-	Atrial Fibrillation Prediction Database
ANN	-	Artificial Neural Network
ANOVA	-	Analysis Of Variance
ANS	-	Autonomic Nervous System
API	-	Application Programming Interface
AR	-	Autoregressive
CBIR	-	Content-based Image Retrieval
CHF	-	Congestive Heart Failure
CPU	-	Central Processing Unit
DFT	-	Discrete Fourier Transform
DIT	-	Decimation-in-time
ECG	-	Electrocardiogram
FE	-	Feature Extraction
FFT	-	Fast Fourier Transform
FN	-	False Negative
FP	-	False Positive
GA	-	Genetic Algorithm
GSA	-	Gravitational Search Algorithm
HF	-	High Frequency
HOS	-	Higher Order Spectral
HR	-	Heart Rate
HRV	-	Heart Rate Variability
ICD	-	Implantable Cardioverter Defibrillator

IEEE	-	Institute of Electrical and Electronics Engineers
LF	-	Low Frequency
LSO	-	Local Search Operation
MATLAB	-	Matrix Laboratory
MI	-	Mutual Information
MOP	-	multi-objective problem
mRMR	-	Min-Redundancy and Max-Relevance
NF	-	Number of Feature
NORMAL	-	Normal Random Number Generators
NSGA-III	-	Non-dominated Sorting Genetic Algorithm III
OS	-	Operating System
PACs	-	Premature Atrial Contractions
PAF	-	Paroxysmal Atrial Fibrillation
PC	-	Personal Computer
PNS	-	Parasympathetic Nervous System
POSIX	-	Portable Operating System Interface
PSD	-	Power Spectrum Density
PVCs	-	Premature Ventricular Contractions
SA	-	Sinus Atrial
SCD	-	Sudden Cardiac Death
SD	-	Standard Deviation
SEN	-	Sensitivity
SNS	-	Sympathetic Nervous System
SPA	-	Smoothing Prior Approach
SPE	-	Specificity
SVM	-	Support Vector Machine
SVTAB	-	Spontaneous Ventricular Tachyarrhythmia Database
UNIX	-	Uniplexed Information Computing System
VF	-	ventricular Fibrillation
VT	-	Ventricular Tachycardia
VTA	-	Ventricular Tachyarrhythmia
WFDB	-	Waveform Database

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CHAPTER 1

INTRODUCTION

Over the last few decades, there has been a widespread interest in the study of variations in the beat-to-beat timing of the heart, known as heart rate variability (HRV). The analysis of HRV has been used to develop the automated classification algorithm that is able to diagnose various types of cardiovascular diseases. This chapter introduces the overview of HRV analysis, defines research problems, objectives as well as research contribution and novelty of the work.

1.1 Heart Rate Variability Analysis - Overview

Heart rate (HR) represents the number of contractions per minute that occurs in the heart. The heart rate variation (HRV) occurs because of the rising and falling of heart rate that are affected by various factors such as human activity or cardiovascular related diseases. The irregularity of time interval in human heartbeats was first noted in the early 1600s. However, its physiological importance was only appreciated in 1965 when Hon and Lee [1] found that the changes in pattern of HR pattern preceded the fetal distress before changes in the baseline heart rate (average heart rate over 60 seconds). In late 1980, clinical importance of HRV became apparent when it was confirmed that the HRV was a strong and independent predictor of mortality following an acute myocardial infarction [2].

Today, there are active research interests in using the HRV as a biological marker to diagnosis various cardiovascular related diseases such as arrhythmia, diabetes and heart failure. Such interests arise because researchers have proved that the HRV is one of the most promising marker to assess the autonomic nervous system (ANS) activity [3], which can be correlated to the cardiovascular disease.

ANS is peripheral nervous system of the human body that is able to influence the activity of the internal organs below the level of consciousness. It affects digestion, heart rate, respiratory rate, salivation, perspiration pupillary dilation sexual arousal, urination and etc. There are two subsystems in ANS: parasympathetic nervous system (PNS) and sympathetic nervous system (SNS). Both subsystems operate independently in some responses and work co-operatively in others [4]. Researchers have found that the increased SNS activity or decreased PNS activity is associated with heart rate acceleration and vice versa. The relationship between ANS and HRV has encouraged the development of HRV markers.

The HRV markers can be obtained through HRV analysis [3]. The HRV analysis involves the use of different techniques or algorithms to evaluate the variation of the heart rate mathematically. These techniques can be divided into three categories: time domain, frequency domain, and non-linear analysis. Based on these techniques, various features are extracted and studied for the application in various medical research problems. The main objective is to use the HRV features to diagnose the patient, to detect occurrence of the disease event in real-time and even predict such event before it happens.

1.2 Cardiac Arrhythmia

Among the HRV based research problems, the interest of this thesis is focus on improving the algorithm that uses the HRV analysis to predict the onset of the cardiac arrhythmia [3, 5]. Cardiac arrhythmia is a condition in which the electrical impulses that regulate dilation and contraction of heart do not function properly. This will cause the abnormal heart rhythm in which the heart beat too fast, too slow or irregularly (erratically). When this happens, the heart may not pump enough blood to the body and consequently damage the brain, heart and other organs.

Arrhythmia needs to be treated by specialist physician. There are many types of arrhythmia and can be classified according to the heart rate and mechanism. Arrhythmia is called tachycardia when heart beats too fast (over 100 beats per minute) and called bradycardia when heart beats that is too slow (less than 60 beats per minute). Other examples of arrhythmia include premature atrial contractions (PACs), Atrial Fibrillation (AF), ventricular fibrillation (VF), premature ventricular contractions (PVCs), heart block (First, Second and Third Degree) and more.

Arrhythmia can also be divided into life threatening and non-life-threatening arrhythmia. Occurrence of life-threatening arrhythmia such as ventricular tachyarrhythmia (VTA) can cause immediate death to a patient. Non-life threatening arrhythmia has no immediate threat to health and life of patient. However, it has long term negative impact on the health of patient. One of the more common non-life threatening arrhythmia is Atrial Fibrillation (AF). The AF increases the risk in mortality rate, stroke, heart failure and also leads to impaired cognitive function [6]. They are three types of AF, namely paroxysmal AF (PAF), persistent AF, and chronic AF. Patients often start with PAF and slowly evolving to persistent AF and chronic AF.

One of the popular equipment that can treat the arrhythmia is Implantable cardioverter defibrillator (ICD) [7]. It has small form factor (2cm-3cm) and is battery-powered device. It is implanted in the human body through clinical surgery. Its primary function is to detect the arrhythmia and restore it back to normal rhythm by using an electrical pulse to shock the heart muscle. It is used to treat prevalence arrhythmia such as atrial fibrillation and ventricular tachyarrhythmia.

1.3 Problem Statement

Two major research problems are considered in this thesis. The first issue is about the optimization of the HRV based prediction methods, and the second is about overcoming weaknesses of existing arrhythmia prediction methods.

The block diagram in Figure 1.1 shows the overview of the classification system that uses the HRV analysis for diagnosis. It shows stages of data acquisition, pre-processing, HRV feature extraction, and a supervised classifier. Initially, electrocardiogram (ECG) signal is acquired and fed to the pre-processing stage. During the pre-processing, QRS complexes of the ECG signal are detected for HRV quantification. The quantified HRV are also corrected and HRV sequences are resampled to certain frequency. Then, different HRV features are extracted in feature extraction stage. Optionally, the feature selection process is applied to select the best HRV features that can lead to high prediction performance. Finally, the supervised classification model is trained with extracted HRV features for disease diagnosis.

There are several research gaps regarding the feature selection algorithms, which have been used to optimize the performance of the HRV based classification

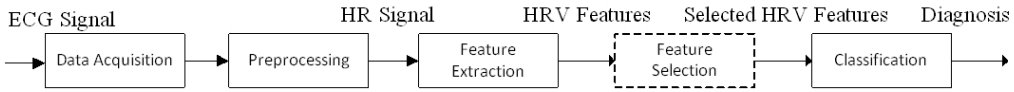

Figure 1.1: Simplified block diagram of HRV based classification system.

system.

The first outstanding issue in the optimization process is the parameter values and settings in both HRV pre-processing and feature extraction stages are not optimized (tuned) for maximum classification performance. Most previous works based on HRV analysis simply adopt the pre-defined parameter values and settings from other works. To maximize the discrimination capability of the extracted features, parameters of feature extraction algorithm should be tuned for different application and database [8]. This issue arises mainly because of the lack of automatic methods to simultaneously tune different algorithms except either by grid search or trial and error. For example, it is difficult to optimize both pre-processing and feature extraction stages at the same time. Therefore, an optimization algorithm that is able to simultaneously tune the parameters and settings in both stages for maximum classification performance is required.

Another research issue is that feature cost is not minimized explicitly during feature selection process. In previous works [9, 10], the main objective of the feature selection is to optimize (select) a HRV feature subset with respect to a single objective only. Therefore, the feature cost may be reduced but not minimized. Feature cost can be divided into two types: feature count (number of features in the selected subset) and measurement cost (time taken to extract all features in the selected subset). Both costs are important factors that affect the complexity and implementation of the classification algorithm, especially when it operates in real-time. Minimization of the measurement cost can reduce the feature extraction time in HRV feature extraction stage while minimizing the feature count can reduce complexity of the trained supervised classifier.

The existing HRV based works typically does not take into account the misclassification cost. The misclassification cost can affect both classification sensitivity and specificity rate. In medical applications, sensitivity rate is more important than specificity rate and accuracy rate because it is the success rate in recognizing the patient with disease. The failure to diagnose a patient has larger negative consequences than a failure to diagnose healthy person. Therefore, it is desired that the HRV based classification algorithms have higher sensitivity rate while

maintaining the good accuracy rate.

Genetic algorithm (GA) is usually adopted to solve multi-objective optimization problem. However, the simple GA, which is employed in previous related works, is not suitable for this work because multiple-objective optimization is required. One of the reason is that the multiple fitness functions need to be linearly combined with different weights in simple GA. Trial and error is required to tune the weights values in order to obtain a solution with desired performance. It is further complicated by the need to combine different fitness functions with difference units. Moreover, trade-off analysis between multiple fitness functions is required during the solution selection in multiple objective optimization.

In previous works based on HRV analysis, there is a shortcoming in the feature selection model of the GA: the possibility to select a feature that is affected by noisy data. This issue is well known in feature selection methods based on heuristic search such as GA. In non-HRV research works, hybrid simple GAs have been proposed to reduce this possibility. Under this model, the statistical significance test or mutual information (a types of correlation measures) of the feature is examined before it is selected to form the final feature subset. This hybrid feature selection model is integrated into the proposed optimization algorithm.

In the case of PAF onset prediction, most of the existing HRV based methods require a 30 minutes signal duration for feature extraction in order to achieve acceptable prediction accuracy levels (80% and above). Although there have been some research [11, 12, 13] that investigated the use of shorter HRV signal duration for PAF onset prediction, their prediction accuracy rates were significantly lower than 80%, as achieved by other previous works that employed 30 minutes signal [14, 5, 15, 16]. Long time duration of signal for feature extraction process is not suitable when the prediction system is implemented in implantable cardioverter defibrillator (ICD). Using the ICD to restore the PAF back to normal rhythm [17] through electrical pulse is one of the main treatments for PAF patient. A PAF onset predictor enable ICD to continuously predict the PAF onset, and possibly allowing it to be terminated early.

In recent years, much research [7, 18, 19] have shown interest in addressing the power consumption issue of the battery powered device such as ICD or similar devices, which use the HRV analysis for real time disease diagnosis. In the case of PAF onset prediction methods, the main concern is that long duration of signal and

compute-intensive HRV analysis may burden the ICD battery life, and consequently shortening its operation time. It can lead to more frequent surgery processes for battery replacement, which can affect the health of the patient [7]. (Generally, the ICD device is expected to operate for more than 5 years after it is implanted in the human body). Therefore, one of the research problem in this thesis is to reduce the required HRV signal length from 30 minutes to 5 minutes, while achieving acceptable prediction accuracy rate. The idea of the signal length reduction is also inspired by Chesnokov et al [20], who have suggested one of their future work is to examine the use of 5-15 minutes HRV signal for PAF onset prediction. Furthermore, HRV signal length of 5 minutes is the minimum length that can produce reliable HRV spectral features [4, 21].

1.4 Objective

The goal of this research is to propose a multi-objective GA based optimization algorithm for application in cardiac arrhythmia prediction system that requires shorter signal length for HRV analysis. In detail, the objectives are:

1. To propose an optimization method, based on the non-dominated sorting genetic algorithm III (NSGA-III), that can simultaneously optimize the parameters and settings in stages of HRV feature extraction, feature selection, and classifier of a cardiac arrhythmia prediction system.
2. To analyze and demonstrate the effectiveness of the proposed optimization algorithm by applying it in the prediction of the onset of cardiac arrhythmia in two cases: (a) paroxysmal atrial fibrillation (PAF) using HRV signal duration shorter than the typical 30 minutes, and (b) ventricular tachyarrhythmia (VTA).

1.5 Scope of Work

- HRV is the main signal in this work. It is converted from ECG signal or any other type of source.
- This work is limited to two cardiac arrhythmia prediction problems: PAF and VTA onset prediction.
- HRV feature extraction stage applies time domain, frequency domain, and non-linear analyses. The classifier is based on the support vector machine (SVM)

model. In this work, with some modification, the SVM is implemented by using the open source library called LIBSVM.

- No new test datasets are created for the experimental work in this thesis. Instead, standard databases are used for fair benchmarking and analysis. They are Atrial Fibrillation Prediction Database (AFPDB) and Spontaneous Ventricular Tachyarrhythmia Database (SVTAB).
- All algorithms are implemented in C/C++, and MATLAB is used for the analysis of experimental works.
- During the optimization, the trade-off between multiple optimization objectives that contradict to each other are also analyzed. The optimization objectives include the feature count, measurement cost, prediction sensitivity, specificity and accuracy rate.
- This research is confined to solving the HRV based arrhythmia prediction problem, although the proposed optimization method can be used in any HRV based research problem that uses the diagnostic system that is based on the model shown in Figure 1.2.

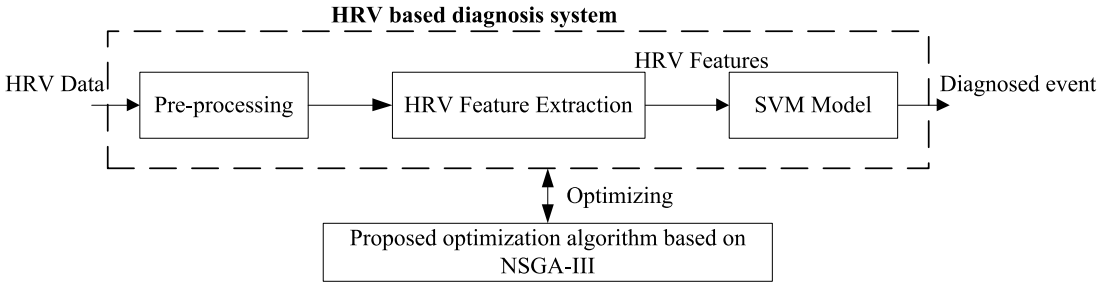

Figure 1.2: Diagnostic system model in the HRV based research.

1.6 Contributions

The contributions of the thesis are

- A multi-objective optimization algorithm is proposed to improve the performance of the HRV based prediction system. It is based on non-dominated sort genetic algorithm III (NSGA-III), which is a state-of-the-art optimization algorithm that employs the Pareto optimal concept. To our knowledge, it is the first attempt to use NSGA-III in the optimization of the HRV based prediction

system. Various modifications are proposed for the NSGA-III in order to tackle the various optimization goals.

- By applying the proposed optimization algorithm, the shortcomings in two arrhythmia prediction problems are overcome:
  - In the **PAF** onset prediction, the required length of HRV signal for the prediction is reduced by 83% from 30 minutes to 5 minutes, while improving the accuracy rate to 89.62%. Even with stricter performance evaluation approach, this accuracy rate is still higher than the previous works, which cannot achieve the accuracy above 70% when using less than 10 minutes HRV signal for prediction.
  - In the **VTA** onset prediction, the prediction system achieves prediction accuracy of 78.15%. It outperforms all previous works even with the application of stricter performance evaluation.
- The improvements of the proposed optimization algorithm over existing methods are:
  - The optimization process is extended from feature selection only to whole HRV based prediction system simultaneously, which include HRV pre-processing, feature extraction and SVM classifier.
  - The **hybrid feature selection model** is used to examine the quality of the features before they are used to form the feature subset. It increases the confidence level of the selected feature subset by reducing the possibility to select the features that are affected by noisy data.
  - A novel **duplication handling algorithm** that suits the hybrid selection model is proposed to handle the duplicate chromosome issue when adapting the NSGA-III. The end result is that the computation cost of the optimization process is reduced by partially avoiding the redundant evaluation of the duplicates, while the accuracy of the selected feature subset is improved.
  - The **feature costs**, which are represented by feature count and measurement cost, are minimized during the feature selection.
  - The optimization of the **misclassification cost** is taken into account. The experimental results prove that the sensitivity rate of the prediction system can be improved but at the expense of reduced specificity and accuracy rate. It should be noted that the reduced accuracy rate is still acceptable when compared to previous works.
  - The optimization concept in the NSGA-III allows the HRV based

system designer to analyze the trade-off between multiple optimization objectives that contradict to each other. Furthermore, trial and error is not required to tune the weight coefficients because different objectives are not linearly combined into single composite objective.

1.7 Thesis Organization

The rest of the thesis is organized as follows. Chapter 2 summarizes the literature reviews and comparisons of related previous works to clarify the research rationale. Chapter 3 provides the fundamental background knowledge regarding the research. Chapter 4 presents research methodology. Chapter 5 presents the detail description of the HRV based arrhythmia prediction system and the proposed optimization algorithm. Chapter 6 presents the analysis and discussion about the verification and benchmarking of the algorithm. In the last chapter, the contribution of the research work is summarized and the potential future works are stated.

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