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Technical Note

Matlab-based tool for ECG and HRV analysis

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ABSTRACT

Delivery of electroporation pulses in electroporation-based treatments could potentially induce heart-related effects. The objective of our work was to develop a software tool for electrocardiogram (ECG) analysis to facilitate detection of such effects in pre-selected ECG- or heart rate variability (HRV) parameters.

Our software tool consists of five distinct modules for: (i) preprocessing; (ii) learning; (iii) detection and classification; (iv) selection and verification; and (v) ECG and HRV analysis. Its key features are: automated selection of ECG segments from ECG signal according to specific user-defined requirements (e.g., selection of relatively noise-free ECG segments); automated detection of prominent heartbeat features, such as Q, R and T wave peak; automated classification of individual heartbeat as normal or abnormal; displaying of heartbeat annotations; quick manual screening of analyzed ECG signal; and manual correction of annotation and classification errors.

The performance of the detection and classification module was evaluated on 19 two-hour-long ECG records from Long-Term ST database. On average, the QRS detection algorithm had high sensitivity (99.78%), high positive predictivity (99.98%) and low detection error rate (0.35%). The classification algorithm correctly classified 99.45% of all normal QRS complexes. For normal heartbeats, the positive predictivity of 99.99% and classification error rate of 0.01% were achieved.

The software tool provides for reliable and effective detection and classification of heartbeats and for calculation of ECG and HRV parameters. It will be used to clarify the issues concerning patient safety during the electroporation-based treatments used in clinical practice. Preventing the electroporation pulses from interfering with the heart is becoming increasingly important because new applications of electroporation-based treatments are being developed which are using endoscopic, percutaneous or surgical means to access internal tumors or tissues and in which the target tissue can be located in immediate vicinity to the heart.

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1. Introduction

Electroporation is a phenomenon resulting in transient increase in the cell membrane permeability due to exposure to an electric field during delivery of short, high-voltage electric pulses, i.e., electroporation pulses [1–4]. Increased membrane permeability allows molecules with intracellular targets, which under physiological conditions cannot cross the cell membrane, to enter the cell and exert their cytotoxicity [5]. Electroporation can be either reversible or irreversible, depending on electrical conditions and tissue characteristics, and both have been used in biomedical applications [6–11]. These applications include electrochemotherapy [12–18], electrotransfer for gene therapy and DNA vaccination [19–24], transdermal drug delivery [25–29], cell electrofusion [30–34], and tissue ablation [35–39]. Electroporation is also used in biotechnology and other areas [11,40].

Some of electroporation-based treatments, like electrochemotherapy, gene electrotransfer for gene therapy and DNA vaccination and non-thermal irreversible electroporation, are being successfully introduced into clinical practice. But when electroporation pulses are applied to visceral or other internal tumors and tissues there is an increased risk of inducing heart-related effects, especially when the treatment area is in vicinity of the heart [15,38,41–48]. These heart-related effects can be detected by analyzing electrocardiogram (ECG) signals recorded before, during and after the therapy.

A software tool for reliable and effective analysis of potential side-effects of electroporation pulses on ECG or heart rate

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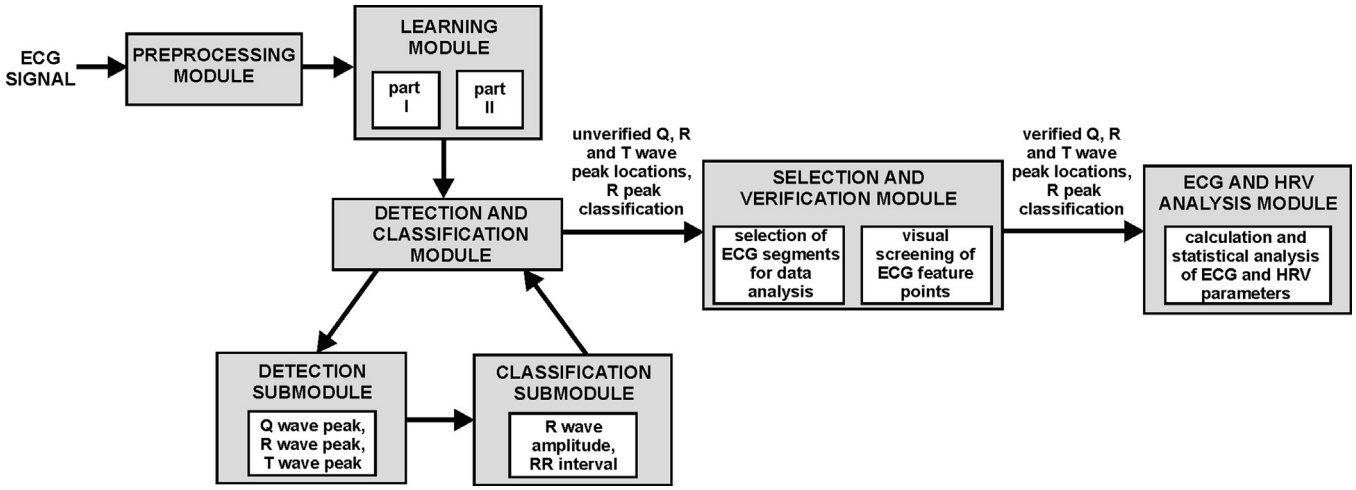

Fig. 1. The structure of the software tool with five main modules for: (i) preprocessing; (ii) learning; (iii) detection and classification; (iv) selection and verification; and (v) ECG and HRV analysis.

variability (HRV) parameters is therefore needed. A software tool should provide selection of ECG segments from ECG signal according to a user-defined selection criteria; detection of prominent heartbeat features, such as Q, R and T wave peaks, and classification of individual heartbeat either as normal or abnormal; and displaying, screening and possible correction of detected and classified heartbeats from analyzed ECG signal. Several software tools for HRV analysis that include calculation of various HRV parameters exist (such as Kubios, SyneScope, Biopac, Nevrokard HRV system) but none of them provides all required functionalities listed above. The objective of our study was therefore to develop a software tool that does.

2. Methods

2.1. Outline and description of the tool

Our software tool consists of five distinct modules for: (i) preprocessing; (ii) learning; (iii) detection and classification; (iv) selection and verification; and (v) ECG and HRV analysis (Fig. 1). The software tool was developed for analysis of Holter ECG signals sampled at 200 Hz. Appropriate adjustment of the implemented digital filters in the detection module would therefore be needed for signals sampled at a different frequency. Currently, the software tool accepts input ECG signals only in plain text format because we are planning to analyze the ECG signals from different origins, such as various Holter devices, Biopac system and different ECG databases. Therefore, ECG signals in other formats have to be transformed to plain text first.

2.1.1. Preprocessing module

The raw ECG signal is first preprocessed in sequence by band-pass filtering, differentiation, squaring, and moving-window integration, thus following the well-known Pan-Tompkins algorithm [49]. Three different signals are used for ECG analysis and serve as inputs to the learning and the detection and classification modules: the original raw ECG signal (Y_{ECG}), the output of the band-pass filter (Y_{BPF}) and the output of the moving-window integration with 30-sample window size (150 ms) (Y_{MWI}).

2.1.2. Learning module

The learning module consists of two parts. Part I is used to initialize the main threshold parameter, i.e., the threshold for QRS detection (d_{th}). Its value is extracted from the initial section of the preprocessed ECG signal Y_{MWI} (defined in Section 2.1.1), which is derived from 16 s of noise- and arrhythmias-free ECG signal and which is divided into 1-second subintervals. Within each 1-second subinterval, the maximum value of Y_{MWI} is sought for. Four largest and four smallest maximum values of Y_{MWI} are discarded and the remaining eight values are averaged. This averaged value is used to initialize the d_{th}. In further processing of the ECG signal in detection and classification module, d_{th} is updated by running averaging after each new heartbeat detected as described in Section 2.1.3.

Part II of the learning module is used to initialize values of parameters for the classification in detection and classification module; i.e., the running averages of R wave amplitude (R_{th}) and RR interval (RR_{th}). This part requires detection of 17 consecutive QRS complexes and determination of location and amplitude of 17 R wave peaks. 16 RR intervals between consecutive R wave peaks are calculated. For the details of QRS and R wave peak detection see Section 2.1.3.1. For calculation of R_{th} the eight most recent values of R wave amplitude (among the 17 available) are used. Two largest and two smallest values of R wave amplitude are discarded and the remaining four values are averaged and used as the initial value of R_{th}. In calculation of the average RR intervals, all 16 RR interval values are considered; four largest and four smallest values are discarded and the remaining eight values are averaged and used to initialize RR_{th}. After the learning phase, R_{th} and RR_{th} are updated with every new detected heartbeat.

2.1.3. Detection and classification module

This module consists of the detection submodule and the classification submodule (Fig. 1). The algorithm for detection and classification of heartbeats is used to determine Q, R and T wave peak locations of individual heartbeats and to classify heartbeats as either normal or abnormal. The algorithm is based on analysis of Y_{ECG}, Y_{BPF} and Y_{MWI} signals and operates on individual signal samples in time-domain.

2.1.3.1. The detection submodule. The detection of QRS complex is based on a well-known Pan-Tompkins QRS detector [49] and supplemented with additionally extracted parameters (such as Q, R and T wave peak location, R wave amplitude, RR interval) to achieve reliable QRS detection and classification performance.

Initial detection of QRS complex is determined using adaptive threshold (d_{QRSth}) on Y_{MWI} signal. The initial value of d_{QRSth} is taken from the part I of the learning module ($d_{QRSth} = 0.125 \cdot d_{th}$). The scale factor of 0.125 was determined empirically. When the current value

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