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Chaotic Phase Space Differential Algorithm for Real-Time Detection of Ventricular arrhythmias: Application in Animal Model

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Abstract—**Life-threatening ventricular arrhythmias remain the main cause of death among patients with cardiovascular diseases. Efforts have been spent on early detection of such fatal cardiac signs. We have previously reported a novel chaotic phase space differential (CPSD) algorithm in discriminating VPC, VT, and VF from normal sinus rhythm with both good sensitivity and specificity. In this article, we apply this algorithm on the rat model of calcium induced ventricular tachycardia. Peaked CPSD values can be observed along with the occurrence of ventricular tachycardia. In addition, minor ECG changes such as new onset S wave or sinus arrhythmia can also be noted on CPSD tracing. We believe that the CPSD algorithm not only is capable of detecting lethal ventricular arrhythmias, but also is potentially a good tool for long-term monitoring the change of ECG signals.**

I. Introduction

Although the prevention and medical management of cardiac disease is fast evolving, sudden cardiac death (SCD) remains the most common cause of death in the United States[1-3]. The mechanism of the onset of SCD is believed to be ventricular tachycardia that rapidly progresses to ventricular fibrillation and circulatory collapse. In addition, sustained ventricular arrhythmias also complicate 2% to 20% acute myocardial infarctions and are associated with increased in-hospital mortality[4].

To decrease the mortality from such life-threatening events, efforts must be addressed on timely recognition of ventricular arrhythmias and access to the emergency medical care as early as possible. The recognition of potentially lethal ventricular arrhythmias is of great importance because delayed or missed diagnosis can cause disastrous outcome. In previous literatures, we have developed the Chaotic Phase Space Differential (CPSD) algorithm, based on the time-delay phase space reconstruction method, to detect critical cardiac arrhythmias. The algorithm, as Amann et al. proposed, detects VF only by evaluating the proportion of the visited boxes to all boxes of the phase space [9], and the variation among subjects is not addressed. The CPSD algorithm emphases the difference between the phase space in interest and the reference phase space. Inter-individual variability is eliminated and even minor difference from the reference signals may be enhanced[5, 10]. When tested by the BIH-MIT arrhythmia database and CU database, the CPSD algorithm exhibits both high sensitivity and specificity of 98.7% and 96.2%, respectively, on detecting ventricular premature complexes (VPCs), ventricular tachycardia (VT), and ventricular fibrillation (VF)[5].

Despite the good performance of the CPSD algorithm on differentiating VT/VF from sinus rhythm, we also interest in what will happen when applying this algorithm on live arrhythmia models, especially during the evolving and remission of ventricular arrhythmias. Because under some clinical situations (e.g., digoxin intoxication, hypo- or hyperkalemia), distinct ECG change may occur before VT/VF happens.

Calcium chloride ($CaCl_2$) has long been used in inducing ventricular arrhythmias in the rat[7, 8]. Short or profound runs of ventricular arrhythmias can be observed after injection of "standard dose" of $CaCl_2$. In this paper, we introduce a rat model of reproducible ventricular arrhythmias and aim to test the influence of different heart rhythms on the CPSD algorithm.

II. Materials and Methods

A. The CPSD algorithm

The Chaotic Phase Space Differential (CPSD) algorithm is developed based on the time-delayed phase space reconstruction method[10], designed for detecting of ventricular arrhythmias (i.e., VPC, VT and VF.) The details of this algorithm were described in our previously published literatures[5, 6]. Briefly, to apply CPSD algorithm to the ECG signals, there several steps to be involved:

1. Determine the window of length W (in seconds) of the ECG, where every single plot of the ECG data is used for constructing the phase vectors.

2. Construct the phase vector: phase vector is defined as [s(t), s(t+d)], where s(t) is any given plot of the windowed ECG, and d denotes a time-delay constant.

3. Quantize the phase and construct the phase space matrix: distribute the phase vectors into an M by M matrix by appropriate calculation. The resultant phase space matrix of the first W seconds of ECG is defined as the reference phase space matrix ($PSM_{reference}$). Phase space matrix is updated every second. The latest PSM constructed is defined as the current phase space matrix ($PSM_{current}$.)

4. Compute the differential phase space matrix, which is defined as the number of differences between $PSM_{current}$ and

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$PSM_{reference}$. The differential phase space matrix can be viewed as an index of variation of the ECG signal.

In this study, we set the window of length W to be 7 seconds, and the time-delay constant to be 0.2 seconds.

B. Experimental setup

Six male Sprague-Dawley rats, weighted between 242 315 g, are anesthetized with 2%~3% isoflurane and O2 mixture. After the desired depth of anesthesia is achieved, a 24-gauge intravenous catheter is inserted into the tail vein for administration of calcium chloride and IV fluid.

Surface ECG signals are obtained through four needle electrodes, inserted into four limbs. A biomedical measurement system with built-in amplifier and band-pass filter (KL-700, K&H MFG, Taiwan) is connected to the electrodes for pre-amplifying and filtering of the bio-signals, with a bandwidth of 1-100Hz. After been pre-processed, the ECG signal are then transmitted to the laptop through USB-6009 DAQ (National Instrument, USA) with a sampling rate of 1000Hz (Fig. 1). The algorithm is programmed by LabVIEW 8.6 (National Instrument, USA.). The raw ECG is recorded, and the CPSD value is calculated second-by-second by the LabVEIW-based platform.

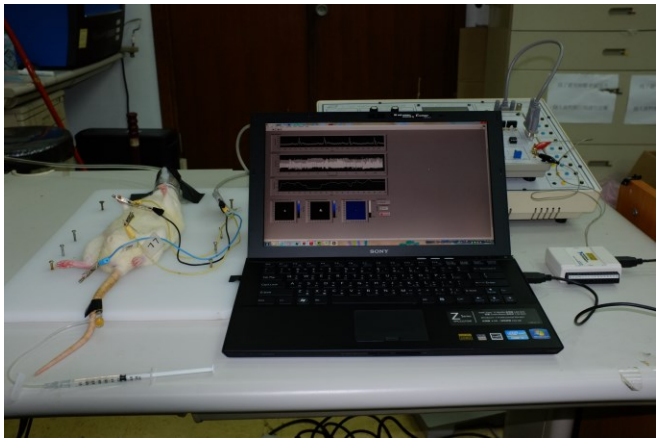

Figure 1. Experimental setup for acquisition and processing of ECG signals. The biomedical measurement system lies behind the laptop. The USB-6009 DAQ(on the right side of the laptop) digitizes and transmits the ECG signals to the laptop. The rat is anesthetised by isoglurane, and tail vein is cannulated for administration of calcium chloride.

Calcium chloride is chosen for induction of ventricular arrhythmia. Baseline ECG and CPSD values are observed for 120 seconds. Afterwards, 20 mg, 2% CaCl2 is administered via the intravenous catheter every minute. Any change of ECG rhythm and corresponding CPSD value are recorded.

III. RESULT AND DISCUSSION

Throughout the study, an average dose of 35.3 mg per 100 g body weight $CaCl_2$ is administered to induce VT and subsequent asystole. S waves on the QRS complexes are observed in all six rats, immediately after the initial bolus of $CaCl_2$.Ventricular tachycardia developed in all six rats, after 2~3 boluses of CaCl2, followed by asystole. Along with the occurrence of VT, the corresponding upstroke of CPSD value could be readily observed. Increasing amplitude and rate resulted in even higher CPSD values (Figure 2).

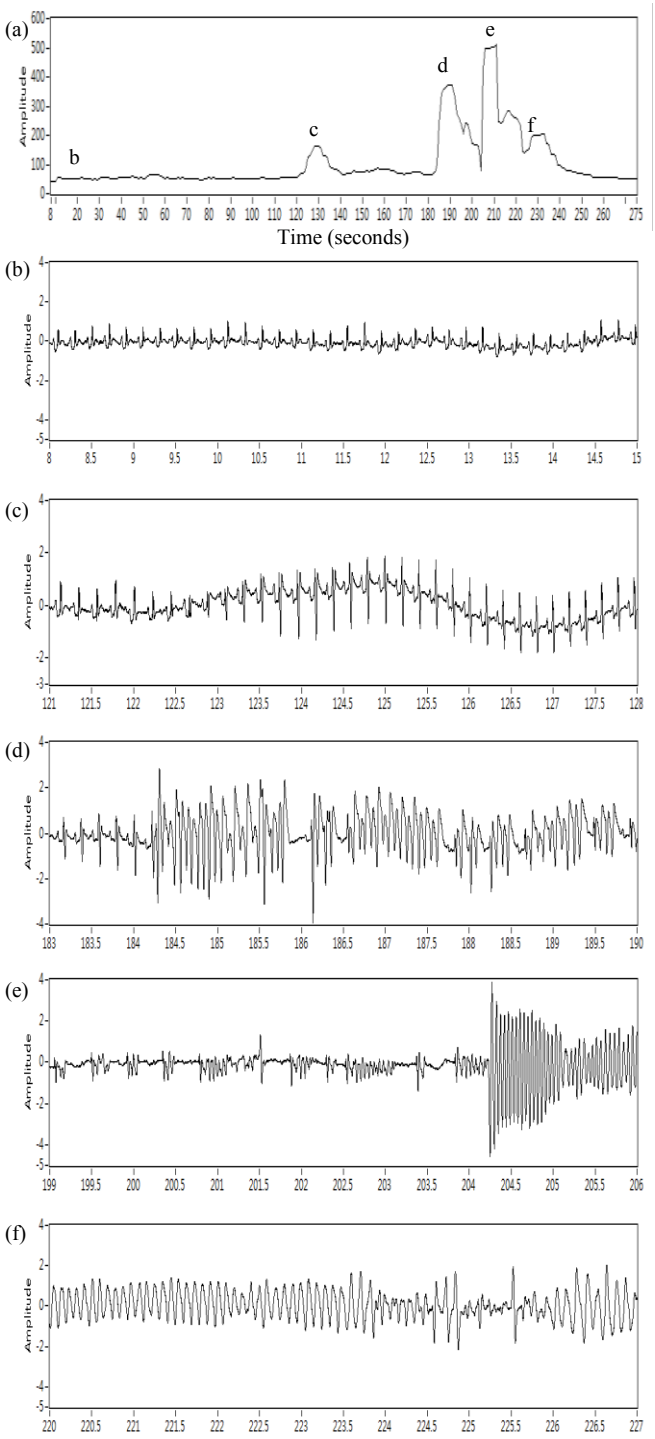

Figure 2. (a) The CPCD tracing of one rat, (b) baseline sinus rhythm, and the corresponding ECG change. After the initial dose of $CaCl_2$, there is a transient increase in the amplitud and new onset of S-waves (c), which cause the first peak on the CPSD tracing. Even higher values are observed along with the occurrence of ventricular tachycardia (d)~(f). Note that higher amplitude and rate of the ECG cause exaggerated response. The CPSD tracings of all the six rats are similar.

In addition to VT, increased amplitude of the QRS complexes (S waves) occurred after the initial administration of CaCl2. Small, but obvious peaks on the CPSD tracings could also be seen (Figure 3b, 3c). Sinus arrhythmias were observed in some subjects, which caused slight, yet not peaked, increase in CPCD (Figure 3d, 3e).

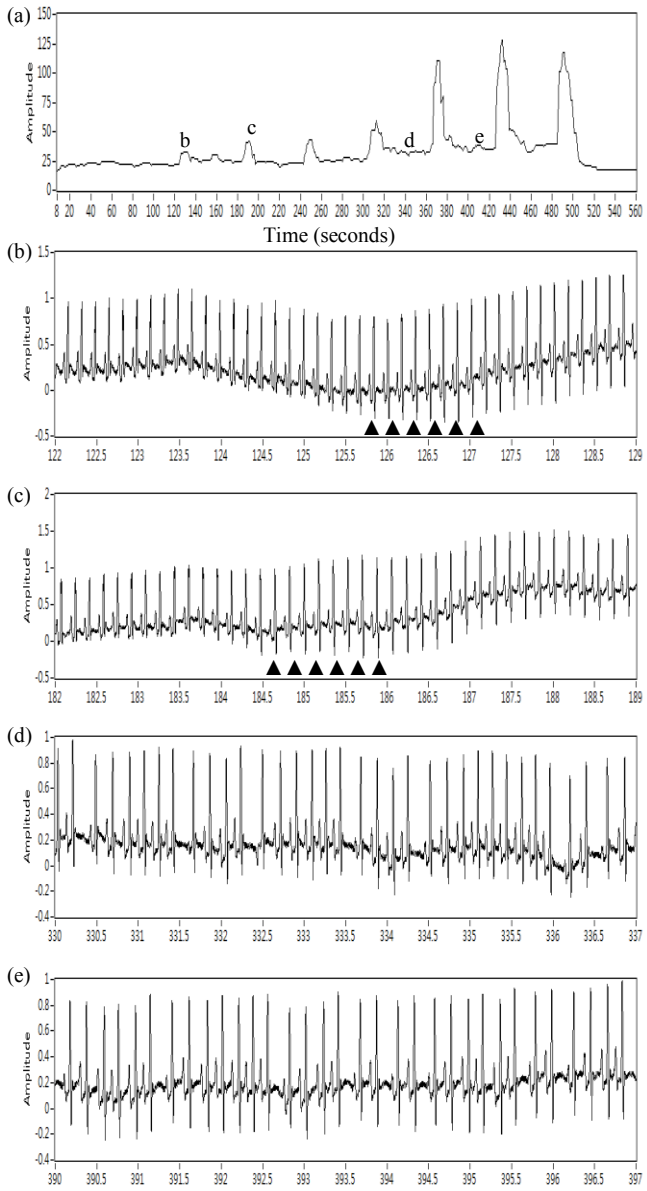

Figure 3. On another rat, the newly-onset S waves (b) and (c) cause small peaks on the CPSD tracing, as the triangles indicate. Two episodes of sinus arrhythmia, (d) and (e), result in elevated baseline on the CPSD tracing, as annotated on (a).

Previous literatures show that when using human ECG database as candidate, the CPSD algorithm can distinguish ventricular arrhythmias (e.g., VPC, VT, VF) from normal sinus rhythm at high sensitivity and specificity. The results from our animal study support this conclusion since high CPSD values are only observed with the occurrence of ventricular arrhythmia, as induced by intravenous administration of calcium chloride.

The CPSD algorithm, based on the time-delayed phase space reconstruction method, converts digitized ECG signals from each time segment into a two-dimensional phase space matrix. The resultant CPSD value is then computed by compare the changes in spatial distribution between reference and candidate phase space matrix. Theoretically, the pattern of the reconstructed phase space varies with the amplitude, time, and periodicity of the acquired signals[10]. Therefore, the rhythm, amplitude, and morphology of the QRS complex all have the contribution to the variance of PSM and CPSD.

In this study, we're not only intended to test the performance of the CPSD algorithm on an animal model of reproducible ventricular arrhythmia, but to observe the serial change of the CPSD value on the evolution of ventricular arrhythmia. In addition to ventricular tachycardia, S waves with increased voltage and sinus arrhythmia can also be observed, which result in small but distinguishable change in CPSD value. We think it of clinical relevance since before lethal ventricular arrhythmias develop; some electrocardiological changes, such as inverted T waves, tented T waves, or prolonged QTc interval, may be detected early once a proper algorithm is addressed[11]. By carefully looking into the different PSM patterns, especially in the low visited area, we have recently reported a modified algorithm to differentiate sinus rhythm, atrial fibrillation, and ventricular fibrillation[10].

Some limitations still exist. The window of length (W), time-delay constant (t), matrix size (M), and the sampling frequency determine the volume of data to be processed. Those parameters, based on our previous data, may not be optimized for this animal study. Although an inspiring result is presented, the parameters must be chosen appropriately in further studies. Higher sampling frequency also generates larger data size, and this can be reduced to 250~360Hz, as most medical devices do.

Besides, interferences from respiration, motion, and the AC power are not easily eliminated, which make the resulting $PSM_{reference}$ and baseline CPSD tracing more "chaotic". A proper filter may help enhance the difference in CPSD value between normal sinus rhythm and ventricular arrhythmia, as shown in figure 4.

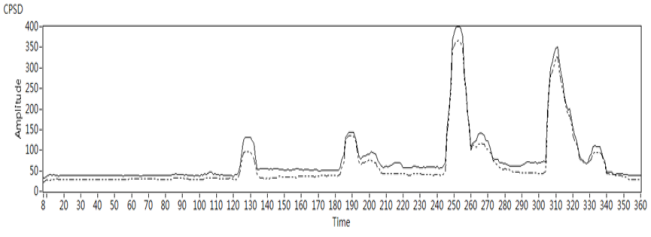

Figure 4. The CPSD tracings before (solid line) and after (dashed line) applying a 0.5~40 Hz, band-pass filter on the raw ECG. The data is processed off-line by LabVIEW 8.6. Note that the baseline CPSD tracing becomes more stable, while the peaks are still prominent.

In our previous works, the CPSD algorithm exhibits both high sensitivity and specificity on detecting ventricular premature complexes, ventricular tachycardia, ventricular fibrillation[5], and even atrial fibrillation[10] while been tested by the arrhythmia database. In this study, however,

sensitivity and specificity are not calculated because all the parameters may not be optimized in the animal model. Since the corresponding upstroke of CPSD value can be readily observed along with severe ventricular arrhythmias, we believe this algorithm is of good performance in 'real life'. It merits further investigation.

By far, the phase space reconstruction method reports the best performance to real-time discriminate VF from normal sinus rhythm. The computational task can be minimized so that it can be incorporated into a miniaturized, wearable device. We believe that, not only in detecting life-threatening ventricular arrhythmias, the CPSD algorithm can also serve as a valuable index for long-term compression, storage, or transmission of ECG signals. For example, once the CPSD value exceeds a pre-determined threshold, a strand of ECG can be stored in memory, transmitted to the physician at remote location, or the caregivers can be warned for abnormal condition. The design of the device that fulfills the above requirement has been discussed in [6].

IV. Conclusion

In this study, we introduce an animal model of reproducible ventricular tachycardia. The CPSD algorithm, which is applied to this animal model, has good performance in differentiating ventricular tachycardia from normal sinus rhythm. In addition, subtle but distinguishable changes of the CPSD value can be observed along with the occurrence of newly developed S waves or sinus arrhythmia. This implies that the CPSD algorithm not only is capable of detecting lethal ventricular arrhythmias, but also has the potential for long-term monitoring and storage of ECG signals.

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