A NOVEL SYSTEM AND STATISTICAL ANALYSIS FOR PREDICTING DEFIBRILLATION TIMING DURING VENTRICULAR FIBRILLATION

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ABSTRACT

This work proposes a new algorithm and analytical methods for predicting the successful rate of a defibrillation during ventricular fibrillation. Accurate predictions help in improving outcomes of cardiopulmonary resuscitation. This also helps in finding a good defibrillation timing to avoid ineffective defibrillation, which leads to myocardial damages and thus a poor prognosis after the resuscitation. Simulation results show that the proposed algorithm outperforms conventional methods in terms of several commonly used performance indices; meanwhile, the proposed analysis also well matches the practical experimental results.

Index Terms—amplitude spectrum area (AMSA), ventricular fibrillation (VF), defibrillation timing, frequency variation (FV).

1. INTRODUCTION

Sudden cardiac arrest is a major health problem and ventricular fibrillation (VF) accounts for 40% of initial rhythms in sudden cardiac arrest [1]. Electric defibrillation has been proved to be the only effective therapy for fatal arrhythmias. However, defibrillation also causes myocardial injury. The more the number of shocks, the more severe the myocardial injury is. Learning how to defibrillate effectively and reduce the ineffective electric shock, improve the success rate of electric shock, and accurately predict the outcome of electric shock and reduce post-shock myocardial damage, is one of the focus of current cardiopulmonary resuscitation research.

Finding the optimal timing of shock has been investigated for long time. The well-known method amplitude spectrum area (AMSA) was first proposed in [2]. AMSA evaluates the area of amplitude spectrum of the ECG signals and has been used for evaluating the effort of cardiopulmonary, predicting the success of defibrillation and suggesting optimal defibrillation timing (see *e.g.,* [3]-[6]).

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Other approaches for finding the optimal timing of shock have been presented in literature. For instance, in [7], the authors applied detrended fluctuation analysis (DFA) for finding a good timing. Whether one method would be better in predicting the result of defibrillation than another remains controversial. Besides, some of these proposed methods were also investigated as an indicator of the performance of chest compression during cardiac arrest. To better predict the result of defibrillation, new methods and their analytical models are of desired for this area.

After the amazing performance of AlphaGo, Google has announced plans to detect and treat diseases via artificial intelligence, where signal processing and statistical methods shall play a critical role. In this work, we propose a new signal processing algorithm to predict the result (success or failure) of defibrillation in treating fatal arrhythmia by using an animal model of VF cardiac arrest. High defibrillation rate was observed when the variation of VF rhythm is small. Thus, we predict the result of defibrillation according to the variation of VF by analyzing frequency domain. Simulation results show that the proposed algorithm outperforms the conventional AMSA and DFA methods.

In addition, we propose to approximate the variation of VF rhythm as a Gaussian random variable for better modeling the proposed scheme. This approximation provides a satisfactory accuracy compared to the realistic experimental results, and helps in gaining more insights and providing systematical theoretical results of the proposed system. The theoretical results obtained by the proposed approximation well match the simulation results. Consequently we conclude that the proposed algorithm helps in predicting the success of defibrillation during cardiopulmonary resuscitation. Meanwhile, the corresponding analysis also helps in building necessary theoretical basis if more sophisticated signal processing methods would like be extended based on the proposed method.

2. SYSTEM MODEL AND PROPOSED ALGORITHM

A PC-based data-acquisition system is used for recording the physiological conditions from rats. The physiological condi-

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tions are read by computer. Each recorded electrocardiography (ECG) signal $\mathbf{x}$ has a duration of three seconds before the first shock of defibrillation in ventricular fibrillation. The sampling rate F_s of $\mathbf{x}$ is 1000 Hz. Thus the length of each ECG signal is $N = 3000$.

The proposed algorithm predicts the defibrillation success by observing the variation of the dominant frequencies. First, the baseline wander was removed from the original ECG signal using a low pass filter with a cut-off frequency of 1 Hz. Let the signal after the baseline wander removal be $y[n]$. The signal $y[n]$ is normalized using the following equation:

$$y_{norm}[n] = \frac{y[n]}{\sqrt{\sum_{n=0}^{N-1} y^2[n]}}, \tag{1}$$

and its frequency domain version can be obtained by using the $L-$point discrete Fourier transform (DFT) given by

$$Y_{norm}[k] = \sum_{q=0}^{L-1} \hat{y}_{norm}[q] e^{-j\frac{2\pi}{L}kq}. \tag{2}$$

In our experiments, L is set to be 16384. However it is worth emphasizing that the value of L can be set arbitrarily once it can cover the length of ECG signals. Then the practical frequency can be obtained by

$$f = \frac{F_s \cdot k}{L}, \quad \text{for } 0 \le k \le \frac{L}{2} - 1. \tag{3}$$

Dominant frequency of a complete ECG signal. Next we introduce how to obtain the dominant frequency of a complete ECG signal. Since generally the principal components of the VF signals are within the frequency ranged from $f = 10$ to 30 Hz, which corresponding to $k = 164$ to 492, the index corresponding to the dominant frequency can be calculated by

$$l_{dominant} = \arg \max_{164 \le k \le 492} |Y_{norm}[k]|. \tag{4}$$

On the other hand, the dominant frequency $F_{dominant}$ can be obtained by substituting $l_{dominant}$ to (3). The dominant period is the reciprocal of the dominant frequency, and it reflects a vibration period of VF signals, given in microseconds by

$$T_{dominant} = round\left(10^3 \cdot \frac{1}{F_{dominant}}\right) \quad \mu\text{sec}. \tag{5}$$

Segment ECG Signal Variation. In order to observe the variation of the dominant frequencies in an ECG signal $y_{norm}[n]$, we separate the signal into several segments and calculate the dominant frequency of these segments. More specifically, we define a moving window with length being a times of the dominant period $T_{dominant}$ to cover a whole period of a VF pulse, and each time shift this moving window an interval of the dominant period. In our experiments, setting $a \ge 3$ is generally enough for covering a VF pulse in various situations. Thus, we set $a = 3$ hereafter. Let the number of window shifting be M, and m be the mth segment in $y_{norm}[n]$ for $m = 0, \ldots, M-1$. The signal in each segment is given by

$$y_m[p] = y_{norm}[p + m \cdot T_{dominant}], \tag{6}$$

where $p = 0, \ldots, aT_{dominant} - 1$.

Repeating the procedure from (2) to (3), one can obtain the dominant frequency of each segment, denoted by F_m, where m represents the mth segment.

We calculate the difference between the consecutive dominant frequencies to observe the variation of the VF. The difference between the dominant frequencies D_u for $u = 0, \ldots, U-1$ is calculated as

$$D_u = F_{u+1} - F_u, \quad \text{for} \quad u = 0, \ldots, U-1, \tag{7}$$

where $U = M - 1$. From D_u, one can determine whether or not the ECG signal has large rate variation of VF, which is our proposed conjecture to predict success or failure according to the ECG signal before the defibrillation. In an ECG signal, there are several segments and each segment has a value of D_u. If one treats the values of D_u as several measurements, the problem to predict success or failure now becomes a classic Neyman-Pearson Hypothesis problem. More specifically, we would like to find a suitable threshold, denoted it by $\mathfrak{D}_{Th}$. If the number of D_u, which exceeds the threshold, is large than a predefined value, the prediction is detected as a failure; otherwise it is detected as a success. This is to evaluate the following ratio:

$$R = \frac{Cardinality\{D_u : 0 < |D_u| < \mathfrak{D}_{Th}\}}{U}, \tag{8}$$

where $Cardinality\{\}$ is the number of elements in a set that satisfies the conditions in $\{\}$. If R is larger than a predetermined value $\mathfrak{R}_{Th}$, we regard the variation is moderate, and the result is predicted to be success. Therefore, the values of $\mathfrak{D}_{Th}$ and $\mathfrak{R}_{Th}$ shall be predetermined based on the existing ECG data for optimizing the performance. Also, different values of the thresholds lead to different detection probability (also called sensitivity or true positive rate) and false alarm probability (also called 1-specificity or false positive rate). Our goals are stated as follows: 1) Determining the values for $\mathfrak{D}_{Th}$ and $\mathfrak{R}_{Th}$ jointly so as to maximize the area under the curve (AUC) or the Youden index (sensitivity+specificity-1) [10], which are performance indices commonly used in this field, and comparing these performances with conventional algorithms. 2) Based on the determined values of thresholds, developing a statistic model that can closely fit the results. Consequently more insights can be gained and analysis can be conducted based on this model. All these goals are discussed separately in the following sections.

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3. PROPOSED ANALYTICAL MODEL

Since the proposed algorithm uses the difference D_u between consecutive dominant frequencies to predict the result of a defibrillation, if we treat D_u as a random variable, finding the distribution of D_u helps us gaining insights into the corresponding statistical performance.

We have evaluated the histogram of D_u and found that approximating D_u as a Gaussian random variable would be a reasonable suggestion, since the Gaussian approximation leads to results close to the experimental receiver operating characteristic (ROC), AUC and Youden index. In this section, we introduce how to approximate D_u as a Gaussian random variable and the corresponding performance.

Gaussian assumption for D_u. The statistic of a Gaussian random variable is characterized by its mean and variance. It is reasonable to assume that D_u has zero mean. Thus, once the variance is known, the complete statistic is known. For each of the ECG record, we approximate D_u as a Gaussian random variable with zero mean. We estimate the variance of D_u and obtain the complete PDF for this ECG record. Once the PDF for each ECG record is known, one can theoretically derive the ratio in (8), and obtain the corresponding ROC and AUC with this Gaussian approximation.

Let $\mathbf{D} = (D_0,\ D_1, \cdots,\ D_{U-1})$. Assume that $\mathbf{D} \sim \mathcal{N}(\mu_D, \sigma_D^2)$. Then by writing down the log likelihood function and using the procedure in [11], we can obtain the Minimum Variance Unbiased (MVU) estimator for σ_D^2 to be

$$g(\mathbf{D}) = \hat{\sigma}_D^2 = \frac{1}{U}\sum_{u=0}^{U-1}(D[u] - \mu_D)^2. \tag{9}$$

Using (9), one can estimate the variance and thus obtain the whole PDF of an ECG record. The probability that the value of $|D_u|$ falls inside $\mathfrak{D}_{Th}$ in (8) can be calculated theoretically by

$$\hat{R} = 1 - 2Q\left(\frac{\mathfrak{D}_{Th} - \mu_D}{\sqrt{\hat{\sigma}_D^2}}\right), \tag{10}$$

where

$$Q(x) = \frac{1}{\sqrt{2\pi}}\int_x^\infty e^{-\frac{u^2}{2}}du.$$

After finding out the estimated ratio for each ECG record, one can pass the estimated ratios for all ECG records into the tool IBM SPSS 22.0 [9], and obtain the ROC curve and AUC. We show this in next section.

4. EXPERIMENTAL RESULTS

Material preparation. The male Wistar rats at the age of 14 weeks old and weighing around 400 g were used and prepared as described previously [8]. Briefly, the animals were anesthetized with an intraperitoneal injection of sodium pentobarbital (50 mg/kg body weight). The tracheas were orally intubated with a PE 200 catheter and the animals were mechanically ventilated with a tidal volume of 0.65 mL/100 g body weight, a frequency of 100/min, and a FiO2 of 1.0. The saline-filled PE-50 tubes were inserted through the right femoral artery (FA) and through the right carotid artery and advanced into the left ventricle (LV), respectively, to measure arterial and LV pressures. Another PE-50 tube was inserted and placed in the right jugular vein for fluid administration and pressure monitoring. To monitor temperature changes, a thermodilution-tipped catheter (ADInstruments, Sydney, Australia) was inserted through the left FA and advanced into the abdominal aorta. A PC-based data-acquisition system (ADInstruments, Sydney, Australia) was used to record hemodynamics, temperature, and needle-probe electrocardiograms. Before the experiment, the animals were observed for 30 min to ensure hemodynamic stability. The body temperature was maintained at $37 \pm 0.5°C$.

Ventricular fibrillation cardiac arrest was induced in rats and maintained for 5 mins, followed by cardiopulmonary resuscitation for 1min and then defibrillation of 3 J. These steps are shown in Fig. 1. The first shock was considered to be successful if the animal regained organized cardiac rhythm with mean arterial pressure more than 60 mmHg after defibrillation. The electrocardiographic signals are 30 rats with first-shock success and 300 rats without first-shock success. The ventricular fibrillation waveform immediately before the first defibrillation was analyzed and compared between the animals with and without first-shock success.

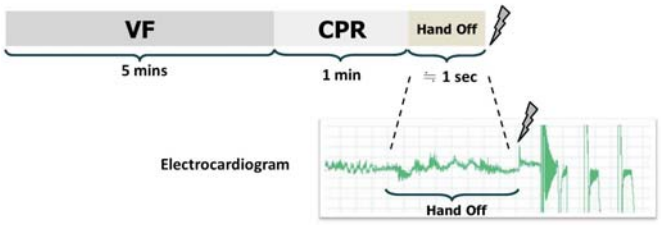

Fig. 1. Protocol of experiments.

Experiment 1: Performance comparison between proposed and conventional methods. In this experiment, we determine the threshold values for $\mathfrak{D}_{Th}$ and $\mathfrak{R}_{Th}$ in (8) that maximize the Youden index (sensitivity+specificity-1) [10]. The Youden index is usually used and is regarded as a good trade-off point. The SPSS was used to determine the threshold values, which were $\mathfrak{D}_{Th} = 9.5$ Hz and $\mathfrak{R}_{Th} = 87.43\%$. The corresponding results of the proposed FV method described in Sec. 2 using these threshold values are shown in the first row in Tab. 2. For comparison, the results for the AMSA and DFA are also shown in the second and third rows of this table. Observe that the proposed FV method outperforms the AMSA [2]-[4] and DFA [7] methods in terms of AUC and

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the Youden index.

Table 1. Performance comparison.

	AUC	Sensi.	Speci.	Sensi.+ Speci.−1
Pro. FV	0.708	0.8	0.583	0.383
AMSA	0.678	0.767	0.547	0.314
DFA	0.676	0.633	0.690	0.323
Comb. 1	0.732	0.933	0.493	0.426

During the experiments, the AMSA and the proposed method usually made different predictions in some ECG records, implying that both the proposed and the AMSA methods capture important but different characteristics of ECG records for making successful predictions. Therefore, we combine the proposed method with the AMSA method to integrate the advantages of the two methods to improve the predictability. The combination of the proposed and the AMSA method is shown below:

$$\beta \cdot AMSA + (1-\beta) \cdot R, \tag{11}$$

where $AMSA$ is the corresponding AMSA value obtained using the method in [2]-[4] and R is the value in (8) obtained using the obtained values of $\mathfrak{D}_{Th} = 9.5$ Hz and $\mathfrak{R}_{Th} = 87.43\%$. The value of β was determined to be $\beta = 0.105$ using grid search for maximizing the Youden index. The results are shown in the fourth row in Tab. 2. From the results, the combined FV and AMSA can significantly improve the performance than these stand-alone techniques.

Experiment 2: Accuracy of proposed statistic model. We evaluate the accuracy of the proposed approximation of D_u in Sec. 3, *i.e.,* as a Gaussian random variable. For comparison purpose, the results obtained by approximating D_u as a Cauchy random variable are also shown here. Tab. 2 shows the comparison among the simulation results, Gaussian and Cauchy approximations that maximize the Youden index. Meanwhile, since the best simulation result (maximum Youden index) occurs when the sensitivity is 0.8, we also obtain the corresponding results for the Gaussian and Cauchy approximations by fixing the sensitivity being 0.8. Observe from the table that the Gaussian approximation (with sensitivity 0.8) fits the simulation result quite well in terms of the AUC, the specificity and the applied value of threshold $\mathfrak{R}_{Th}$.

To be more specific, the corresponding ROC curves are shown in Fig. 2. We see that the ROC curves of the Gaussian assumption approximate the simulation result well. From these comparison results, we consider that the Gaussian approximation is suitable for D_u.

5. CONCLUSIONS

We have proposed a scheme to find suitable defibrillation timing during the ventricular fibrillation. From the simulation results, the proposed scheme has shown to outperform the conventional AMSA and DFA methods in terms of the AUC and Youden index. Moreover, we have proposed to approximate the difference of the dominant frequencies, an important parameter used to make decision in the proposed scheme, as a Gaussian random variable for theoretically model the proposed scheme. The corresponding results have shown that this proposed approximation achieves satisfactory accuracy. As a result, this proposed scheme can help in determining better defibrillation timing during ventricular fibrillation than the conventional methods, and its analysis also helps in gaining insights and forming a systematic decision rule.

Table 2. Approximation vs. simulation.

	AUC	Sensi.	Speci.	$\mathfrak{R}_{Th}$
Simulation	0.708	0.8	0.583	0.874
Gaussian (Youden index)	0.7	0.633	0.743	0.946
Gaussian (Sensi. 0.8)	0.7	0.8	0.533	0.878
Cauchy (Youden index)	0.647	0.567	0.7170	0.904
Cauchy (Sensi. 0.8)	0.647	0.8	0.427	0.851

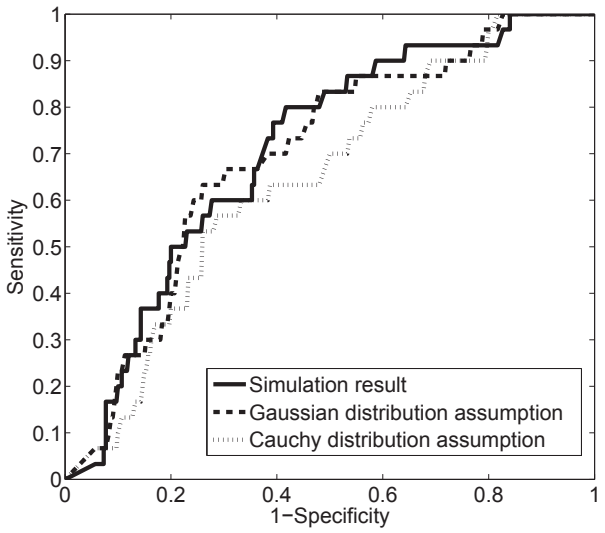

Fig. 2. The comparison of the ROC curves with simulation result and two distribution assumptions.

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