Signal Processing Subsystem Validation for T-wave Alternans Estimation

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Abstract

Since alternans phenomena in the cardiac repolarization have been shown to be related to arrhythmogenesis, a number of sophisticated methods have been proposed to detect and estimate microvolt T-Wave Alternans (TWA). However, their robustness with respect to the inclusion and tuning of the processing stages has not always been analyzed and quantified in detail. We propose a procedure based on bootstrap techniques to study the effect of some relevant preprocessing stages in a TWA estimation system. A controled data base was obtained by adding noise and TWA to control ECG signals. Several experiments were performed, each one to evaluate the influence of one characteristic of a processing stage in the whole TWA estimation system. For the analysis, different statistics (median, confidence interval width, and power) were obtained for the TWA amplitude estimation errors. It can be concluded that interactions among different preprocessing subsystems are complex, not always completely characterized, and small variations can affect significantly to the overall performance of the detection system.

1. Introduction

T-wave Alternans (TWA) can be defined as a beat-to-beat consistent fluctuation in the cardiac repolarization morphology. This phenomena can be observed in the Electrocardiogram (ECG) under adequate conditions, and TWA have been shown to be related to cardiac instability and increased arrhythmogenicity. Clinical studies suggest that there is a patent relationship between large amplitude microscopic (microvolt level) TWA and the risk of sudden cardiac arrest [1], therefore, TWA represents an important marker of cardiac electrical instability and have potential for arrhythmic risk stratification [2].

Though a number of methods have been proposed to detect and estimate the TWA, there is no definite method available to date, mostly due to the difficulties in the definition of a gold standard for the comparison and validation of the proposed algorithms [3].

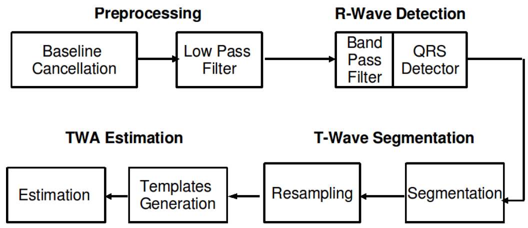


Figure 1. Processing stages diagram for TWA estimation.

The aim of this work is to analyze in detail the effect of some relevant signal processing stages in a TWA estimation system. For this purpose, a simple, yet operative, statistical test for system comparison is proposed, which uses the nonparametric bootstrap resampling for building confidence intervals. A general processing system for obtaining time-domain waveform-based decision statistics is used as demonstration of the capabilities of the method (see Fig 1).

The paper is structured as follows. In the next section, the processing blocks of the TWA estimation scheme are described, with emphasis in the preprocessing stages and in the nonparametric paired bootstrap test. Next, the semi-synthetic data base used for the experimental work is introduced. Results and benchmarks on the waveform-based TWA detection system are presented, and conclusions are briefly scrutinized.

2. Methods

The TWA estimation system considered in this paper is a waveform-based scheme, which consists of the following stages (Fig 1).

Preprocessing. The first stage consist of two preprocessing blocks: (1) a BaseLine Cancellation (BLC) block, to remove baseline fluctuations from the ECG by using a smoothing filter together with spline interpolation; and (2) a zero-phase distortion Low Pass Filter (LPF) block, to remove the high frequency noise. The convenience of including these blocks, as well as their parameters tuning, are studied in this work.

R-wave Detection. In this stage, a Band Pass Filter (BPF) [7.5-17.5] Hz is applied to remove those components not corresponding to the QRS complexes. Then, an adaptive threshold is used to isolate the QRS complexes, and the maximum of each QRS complex is selected as the R-wave.

T-wave Segmentation. This stage segments each T-wave by taking the signal segment between the R-wave and the 70% of the precedent cycle length. Then, each segment is resampled to a rate given by the ratio between the number of samples of the current segment and those of previous RR interval. The resampled T-wave is limited to the first 100 samples.

T-wave Alternan Estimation. The first block of this subsystem generates T wave templates separately for even and odd beats. The following block estimates the amplitude of the TWA as the maximum difference (absolute value) between the odd and the even templates.

In order to study the effect of each subsystem in Fig 1, we designed an evaluation procedure based on nonparametric bootstrap techniques [4], which are next summarized.

Model Comparison with Paired Bootstrap. Each experiment, which is a system robustness analysis, is here designed as the comparison between two data models, named *Model A* and *Model B*. Label *Model* represents a whole set of blocks used for the TWA estimation, together with the free parameters setting in all of them. A controlled approach consists on choosing both models being equal, except for a single feature that is the one to be benchmarked (such as including vs excluding a subsystem, or using two different values for a free parameter). To decide whether the difference between *Model A* and *Model B* is statistically relevant, we establish a decision statistic and a hypothesis test.

A suitable statistical hypothesis test is to contrast the null hypothesis (H_0) that *Model A* and *Model B* have the same unexplained variance against the alternative hypothesis (H_1) that both models have different unexplained variance. Let X_{MA} and X_{MB} denote the statistics obtained from the residuals using *Models A* and *B*, respectively, and define ΔX as:

$$\Delta X = X_{MB} - X_{MA} \tag{1}$$

Then, the hypothesis test can be stated as:

$$\begin{cases} H_0 : & \Delta X = 0 \\ H_1 : & \Delta X \neq 0 \end{cases} \tag{2}$$

In order to approximate the probability density function of X_{MA}, X_{MB}, and subsequently of ΔX, we used a paired bootstrap resampling method with B random resamplings. The paired bootstrap considers exactly the same resampling sets, $X^*_{MA}(b)$ and $X^*_{MB}(b)$, for computing $\Delta X^*(b)$, for $b = 1, ..., B$ ($B = 500$ for the experiments in this work). An estimation of the confidence interval for ΔX can be easily obtained from bootstrap resamples $\Delta X^*(b)$. We state that H_0 is fulfilled if the confidence interval contains the zero point, otherwise H_1 is accepted and we can state that the differences between both models are statistically relevant in terms of that statistic. Note that using the same resampling for estimating X_{MA}, X_{MB} from the residuals of both models, we are controlling the resampling variability of the ΔX estimate, and the variance of the estimator will be due only to the differences between both models. This approach is called a *paired bootstrap test*. A detailed discussion on bootstrap resampling for statistical hypothesis test can be found in [4].

In this work we compared two models in each experiment, differing just in one design block/parameter of the preprocessing stage. A set of 50 semi-synthetic signals were obtained (see Sec.3) for each experiment, and for each signal, the TWA amplitude was estimated.

The decision statistics chosen for the bootstrap hypothesis test comprise the Median (Med), a central tendency parameter, the 95% Interval Confidence Width (ICW), a dispersion tendency parameter, and the Power (P), which comprises both dispersion and central tendency effects.

3. Dataset

Three minutes records were generated by adding noise and TWA to a set of five control ECG signals from the MIT-BIH Arrhythmia Database ($f_s = 360Hz$) [5], using the first lead of the records. The criteria to take the control ECG signals were described in [6]. Physiological noise records from the MIT-BIH Noise Stress Test Database ($f_s = 360Hz$) [5] were used to obtain nonstationary ECG signals. Three possible noise sources were considered, namely, muscular activity artifact, electrode motion artifact, and baseline wandering, which are predominant in 'ma', 'em' and 'bw' records, respectively. To create every semi-synthetic signal, a three minutes segment of the noise records was added to the control ECG signal. The noise segment was extracted from a random position in the whole noise record. Experiments were conducted for the control ECGs with no added extra noise and for different Signal to Noise Ratio (SNR), namely, 25 dB and 15 dB. Finally, TWA episodes were included by adding an alternan waveform of $35\mu V$ amplitude to every other beat with different patterns: pattern1, with no TWA; pattern2, pattern3, and pattern4, with alternans in the 10%, 50%, and 100% of the signal, respectively. The inclusion pattern was randomly selected for each signal.

Table 1. Experiment 1. ΔX of the decision statistics (mean, [95% IC]) for TWA amplitude estimation errors.

Noise	SNR	Med	ICW	P
No		**-0.89,[-1.16,-0.75]**	**-0.78,[-0.81,-0.28]**	**-22.89,[-30.43,-15.50]**
bw	25 dB	**-0.96,[-1.36,-0.44]**	0.15, [-1.60,1.76]	-13.56,[-34.59,9.93]
	15 dB	-0.68,[-1.35,0.84]	**5.81,[0.12,14.94]**	28.25,[-26.69,94.25]
ma	25 dB	**-0.68,[-1.28,-0.04]**	-0.19,[-1.75, 0.67]	**-30.48,[-49.19-13.09]**
	15 dB	-0.08[-1.51,1.85]	**11.29, [3.04,25.15]**	129.75,[-18.63,295.55]
em	25 dB	**-0.81,[-1.50,-0.03]**	0.16,[-1.70,2.94]	**-35.62, [-65.54,-9.90]**
	15 dB	0.28,[-1.58,3.29]	2.17,[-6.25,14.18]	**277.74,[79.00,510.43]**

4. Results

The experiments in this work were focused in the pre-processing blocks (Fig. 1). Tables show the mean and 95% IC of the difference ΔX between the statistics X_{MB} and X_{MA} for TWA amplitude estimation errors. Results are highlighted when the 95% IC of ΔX does not overlap zero. In this case, a negative value in certain statistic means that *Model B* outperforms *Model A* for that statistic, since its residuals for *Model B* are significantly lower than those for *Model A*, while a positive value means that *Model A* outperforms *Model B*.

Experiment 1. The convenience of using the BLC block was studied, both for no extra noise and for three additive noise sources ('bw','ma','em') with SNR = 15 dB and 25 dB. In all cases *Model A* included the BLC block, while *Model B* did not. Tab. 1 shows that, with no extra noise, and for the three decision statistics, TWA amplitude estimation was significantly better for *Model B*. This means that the BLC block can introduce distortion when the input signal is not very noisy. For SNR = 25 dB, some of the statistics were still significantly better for *Model B*: Med for the three kind of noises, and P for 'ma' and 'em' noises. However, when the noise level was increased to get SNR = 15 dB, the trend changed and some of the statistics were significant in favor of *Model A*: ICW for 'bw' and 'ma' noises, and P for 'em' noise. We suspect that we did not find considerable differences between the three kind of noises when studying the BLC block, because noise was added to real ECGs which may already have baseline wandering.

Experiment 2. All stages in Fig. 1 were used. *Model A* included a median filter in the BLC block, while *Model B* included a mean filter. Tab. 2 shows the results with additive 'bw' noise and SNR = 25 dB. Note that, in terms of Med and P statistics, the median filter is preferable in the BLC block.

Table 2. Experiment2. ΔX of the decision statistics (mean, [95% IC]) for TWA amplitude estimation errors.

Decision statistic	mean, [95%IC]
Med	**1.78,[0.93,2.30]**
CIW	-0.15,[-0.87,0.50]
P	**46.82,[21.77,70.95]**

Experiment 3. This experiment analyzed the effect of the window length in the median filter of the BLC block (T_A for *Model A* and T_B for *Model B*) when all stages in Fig. 1 were considered. Tab. 3 shows the results with additive 'bw' noise and SNR = 25 dB. The first window length explored (500 ms) was selected shorter than the majority of the RR interval lengths in the control ECGs, and it was progressively increased until we found a length (1000 ms), from which further increase did not outperform the results. We did not find many significant differences in this experiment, maybe because the optimum window length is related to the RR interval length, which changes with the time evolution and the particular control ECG.

Experiment 4. The effect of including the LPF block was evaluated. *Model A* included all blocks in Fig. 1, while *Model B* did not include the LPF one. Taking into account the results from the previous experiments, a median filter of $T = 1000$ ms was set in the BLC block. Tab. 4 shows that, without extra noise, statistics were significant in favor of *Model B*, which means that the LPF block can introduce distortion when the signal is not noisy. For SNR = 25 dB, the test was just significant in favor of *Model A* for ICW statistic with 'ma' noise. For SNR = 15 dB, no significant differences were found for 'bw' noise (low frequency noise); for 'ma' and 'em' noises, the test showed a significantly better performance for *Model A* in all statistics except for ICW with 'em' noise, and this significancy was stronger for 'ma' noise. It seems reasonable that the LPF affects more to the signals with 'ma' noise, since the power of the 'em' noise is concetrated in lower frequencies than the power of the 'ma' noise.

Fig. 2 represents an example of a control ECG with semi-synthetic TWA episodes: (a) without additive noise; (b) with additive 'ma' noise (SNR = 15 dB). Top panels show the input signal in Fig 1, medium panels show the signals after the BLC block, and bottom panels after the LPF block.

5. Conclusion

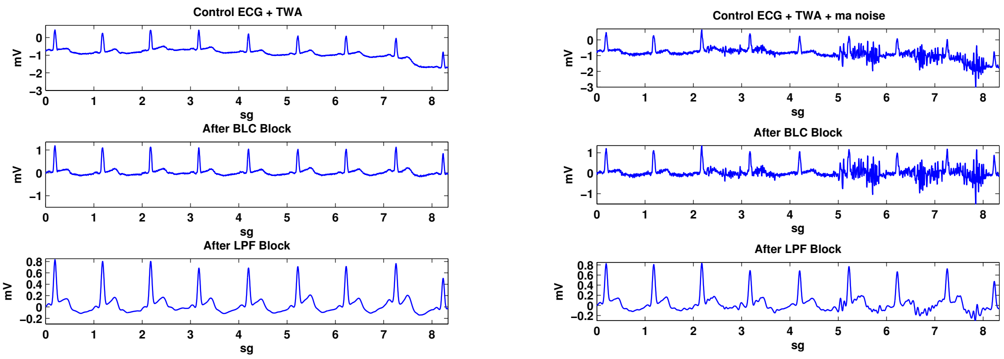
Interactions among processing blocks in TWA estimation can be complex and not obvious, and they can affect significantly the performance. Therefore, further work will be devoted in this direction.

Table 3. Experiment3. ΔX of the decision statistics (mean, [95% IC]) for TWA amplitude estimation errors.

T_A (ms); T_B (ms)	Med	ICW	P
500 ; 700	-0.80,[-1.86,0.22]	**2.18,[0.87,3.41]**	-24.01,[-53.49,3.89]
500 ; 1000	**-1.53,[-2.78,-0.06]**	0.87,[-0.08,1.98]	-32.85,[-69.12,1.88]
1000 ; 1500	-0.19,[-0.40,0.09]	0.29,[-0.40,1.07]	-6.34,[-15.81,3.05]
1000 ; 2000	0.72,[-1.12,2.30]	4.22,[-1.45,6.90]	24.76,[-24.91,79.41]
1000 ; 4000	1.48,[-0.36,3.17]	5.24,[-0.60,7.90]	50.85,[-5.66,113.90]
1000 ; 8000	1.56,[-0.51,3.25]	**5.74,[0.45,8.28]**	56.36,[-1.80,117.04]

Table 4. Experiment 4. ΔX of the decision statistics (mean, [95% IC]) for TWA amplitude estimation errors.

Noise	SNR	Med	ICW	P
No		**-2.35,[-4.39,-1.47]**	**-1.09,[-1.71,-0.23]**	**-57.83,[-95.70,-20.37]**
bw	25 dB	-1.86,[-3.56,0.40]	0.68,[-3.15,3.49]	-30.19[-74.39,21.20]
	15 dB	-2.31,[-4.48,1.45]	8.52,[-2.54,18.93]	26.71,[-43.80,109.68]
ma	25 dB	-2.14,[-8.02,3.21]	**12.88,[6.79, 15.94]**	15.72,[-115.68,154.68]
	15 dB	**22.89,[15.20,32.60]**	**55.26,[23.76,73.99]**	**2012.2,[1287.6,2835.3]**
em	25 dB	-2.86,[-6.63,3.65]	12.43,[-3.54,19.01]	15.25,[-112.83,141.92]
	15 dB	**15.95,[9.86,20.21]**	-5.38,[-38.69,47.92]	**1126.2,[56.9,2092.5]**



(a) (b)

Figure 2. Example of a control ECG with synthetic TWA episodes. (a) Without additive noise. (b) With ‘ma’ noise (SNR = 15 dB). Top panels show the input signal in diagram of Fig 1. Medium panels show the signals after the BLC block. Bottom panels show the signals after the LPF block.

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