# Multilead T-Wave Alternans Quantification Based on Spatial Filtering and the Laplacian Likelihood Ratio Method

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## Abstract

*T-wave alternans (TWA) is considered as an index of susceptibility of sudden cardiac death. The Physionet/CinC challenge 2008 encourages teams to automatically detect and quantify the magnitude of TWA in every record of a given database. A reference ordering based on all entries submitted to the challenge is used for evaluation of algorithms. We participated in the challenge using a multilead analysis scheme that combines principal component analysis with the Laplacian likelihood ratio method. TWA was detected in 41 records, and a final score of 0.633 was obtained.*

*In this study, the effect of several design parameters in the estimation of TWA amplitude is discussed, and the importance of measuring additional TWA parameters is emphasized.*

## 1. Introduction

TWA is defined as a consistent fluctuation in the repolarization morphology on an every-other-beat basis. It is presently regarded as a promising index of susceptibility to sudden cardiac death [1].

TWA amplitude is in the range of microvolts, and can be even below the noise level, making its detection a difficult task. Several signal processing methods exist to detect and estimate TWA [2]. The most widely used techniques are the spectral method [3] and the modified moving average method [4]. Alternative techniques are the complex demodulation method [5] and the recently proposed Laplacian likelihood ratio method (LLR) [6]. The main drawback of existing techniques is either their sensitivity to the presence of nonalternant components with high amplitude, or their low sensitivity to low-level TWA [1, 2]. Furthermore, some of those techniques measure TWA amplitude, but do not estimate the TWA waveform. An accurate waveform estimation is desirable because, in addition to the presence and magnitude of TWA, the distribution of TWA within the ST-T complex has been shown to indicate arrhytmic risk [7].

The Physionet/CinC challenge 2008 encourages participants to develop methods for automatic TWA quantification in a set of 100 ECG records. Results submitted by all participants are aggregated to derive a reference ordering, and then the agreement between each participant and the reference ordering is evaluated by calculating the Kendall rank correlation coefficient [8]. In this paper, we describe our participation in the challenge, using a previously developed multilead TWA analysis scheme [9].

## 2. Data sets

### 2.1. Challenge database

This database, available in www.physionet.org, contains 100 ECG records sampled at 500 Hz with an approximate duration of two minutes. QRS annotations for all records are provided. 32 of the 100 records are synthetic signals, generated with six model ECGs and with calibrated amounts of artificial TWA. The other 68 records belong to patients with different conditions, as well as healthy controls. 72 of the 100 records contain the standard 12-lead ECG, 12 records contain only 3 leads, and 16 records contain only 2 leads.

### 2.2. STAFF-III database

A set of 97 control records of the STAFF-III database [6] was selected to calculate the detection threshold for the TWA analysis scheme as described in Section 3. These records are sampled at 1 kHz, their duration is approximately five minutes, and they contain nine standard leads, from which only the eight independent leads were considered. According to previous studies [6], no TWA episodes are present in these signals.

## 3. TWA analysis

The block diagram of the analysis scheme is shown in Fig. 1. It consists of five stages: signal preprocessing, signal transformation with PCA, TWA detection, signal reconstruction, and TWA estimation.

The ECG signal is preprocessed as follows. Baseline wander is removed using a time-variant filtering technique [10]. The signal is then decimated to obtain a sampling frequency of $F_s = 125$ Hz, and low-pass filtered with a cut-off frequency of 15 Hz. On each beat, an interval of 300 ms is selected for TWA analysis (ST-T complexes). The starting point of each ST-T complex is located within a certain time from the QRS fiducial point, depending on the heart rate (HR): 70 ms if HR $\leq$ 100 beats per minute (bpm) and 60 ms if HR $>$ 100 bpm.

After the preprocessing stage, the signal is processed with a sliding window. In the case of 12-lead ECGs, only the eight independent leads (V1-V6, I, II) are considered for TWA analysis. Let $K$ be the number of beats in the analysis window, $N$ the number of samples of each ST-T complex, $L$ the number of leads, and $x_{k,l}(n)$ the ST-T complex of the $k$-th beat and the $l$-th lead. Each ST-T complex can be modeled as

$$x_{k,l}(n) = s_l(n) + \frac{1}{2}a_l(n)(-1)^k + v_{k,l}(n) \quad n = 0 \ldots N-1$$

where $s_l(n)$ is the background ST-T complex, which is periodically repeated in each beat, $a_l(n)$ is the alternans waveform, and $v_{k,l}(n)$ is additive random noise. For each beat $k$, complexes from all leads are put together into a matrix $\mathbf{X}_k$

$$\mathbf{X}_k = \begin{bmatrix} \mathbf{x}_{k,1} & \ldots & \mathbf{x}_{k,L} \end{bmatrix}^T \tag{1}$$

The $n$th column of $\mathbf{X}_k$ contains the amplitudes of the $L$ leads at a given sample $n$ of the $k$th beat. The $\mathbf{X}_k$ matrices are then concatenated to form the data matrix $\mathbb{X}$

$$\mathbb{X} = \begin{bmatrix} \mathbf{X}_0 & \mathbf{X}_1 & \ldots & \mathbf{X}_{K-1} \end{bmatrix} \tag{2}$$

The $l$th row of $\mathbb{X}$ contains the concatenated ST-T complexes corresponding to the $l$th lead.

A detrending filter is then applied to $\mathbb{X}$ to cancel the background ST-T complexes

$$\mathbf{x}'_{k,l} = \mathbf{x}_{k,l} - \mathbf{x}_{k-1,l}, \;\; k = 1 \ldots K-1$$

The resulting matrix $\mathbb{X}'$ has the same structure as $\mathbb{X}$ (this time with $K-1$ beats), that is, the $l$th row contains the concatenation of the detrended complexes corresponding to the $l$th lead. PCA basis is then calculated from matrix $\mathbb{X}'$. The detrended signal $\mathbb{X}'$ is a zero-mean random process with a spatial correlation matrix $\mathbf{R}_{\mathbb{X}'} = E\{\mathbb{X}'\mathbb{X}'^T\}$. In practice, $\mathbf{R}_{\mathbb{X}'}$ is replaced by the sample correlation matrix, defined as

$$\hat{\mathbf{R}}_{\mathbb{X}'} = \frac{1}{(K-1)N}\mathbb{X}'\mathbb{X}'^T. \tag{3}$$

To obtain the whole set of $L$ principal components of $\mathbb{X}'$, the eigenvector equation for $\hat{\mathbf{R}}_{\mathbb{X}'}$ must be solved

$$\hat{\mathbf{R}}_{\mathbb{X}'}\mathbf{\Psi} = \mathbf{\Psi}\mathbf{\Lambda} \tag{4}$$

where $\mathbf{\Lambda}$ denotes the eigenvalue matrix and $\mathbf{\Psi}$ denotes the eigenvector matrix. Matrix $\mathbf{\Psi}$ defines an orthonormal transformation, which is applied to the original data $\mathbb{X}$

$$\mathbb{Y} = \mathbf{\Psi}^T\mathbb{X}. \tag{5}$$

The $l$th row of $\mathbb{Y}$ contains the $l$th principal component of $\mathbb{X}$ (denoted as the $l$th transformed lead).

After PCA transformation, TWA detection is performed in the transformed data. The Generalized Likelihood Ratio Test (GLRT) for Laplacian noise is applied to each transformed lead (rows in $\mathbb{Y}$) as proposed in [6]. To decide whether alternans is present or not, the resulting value of the test is compared to a threshold $\gamma$. The result of this lead-by-lead detection is denoted as $d_l$: $d_l = 1$ if TWA is detected in the $l$th transformed lead, and $d_l = 0$ otherwise. The overall TWA detection is positive if TWA is detected at least in one transformed lead ('OR' block in Fig. 1).

The value of the threshold is calculated from the control records described in 2.2, considering a probability of false alarm $P_{\text{FA}} = 0.01$. To do so, control signals are processed, and for each beat the maximum GLRT value of the $L$ leads is kept. $\gamma$ is chosen so that it is exceeded only by 1% of those GLRT values.

After TWA detection, a new signal in the original lead set is reconstructed. This is necessary because TWA must be measured in the original leads. A diagonal matrix is defined from the lead-by-lead detection as

$$\mathbb{A} = \begin{bmatrix} d_1 & & 0 \\ & \ddots & \\ 0 & & d_L \end{bmatrix} \tag{6}$$

and the basis in $\mathbf{\Psi}$ is truncated,

$$\mathbf{\Psi}_{\text{TR}} = \mathbf{\Psi}\mathbb{A}. \tag{7}$$

Matrix $\mathbf{\Psi}_{\text{TR}}$ has zeros in columns corresponding to leads without TWA. A reconstructed signal is then obtained as

$$\tilde{\mathbb{X}} = \mathbf{\Psi}_{\text{TR}}\mathbb{Y}. \tag{8}$$

The reconstructed data matrix $\tilde{\mathbb{X}}$ consists of the concatenation of the multilead single-beat matrices $\tilde{\mathbf{X}}_k$:

$$\tilde{\mathbb{X}} = \begin{bmatrix} \tilde{\mathbf{X}}_0 & \tilde{\mathbf{X}}_1 & \ldots & \tilde{\mathbf{X}}_{K-1} \end{bmatrix} \tag{9}$$

where

$$\tilde{\mathbf{X}}_k = \begin{bmatrix} \tilde{\mathbf{x}}_{k,1} & \ldots & \tilde{\mathbf{x}}_{k,L} \end{bmatrix}^T \tag{10}$$

with $\tilde{\mathbf{x}}_{k,l}$ corresponding to the reconstructed ST-T complex of the $k$th beat in the $l$th lead. When no detection is obtained, $\tilde{\mathbb{X}} = 0$.

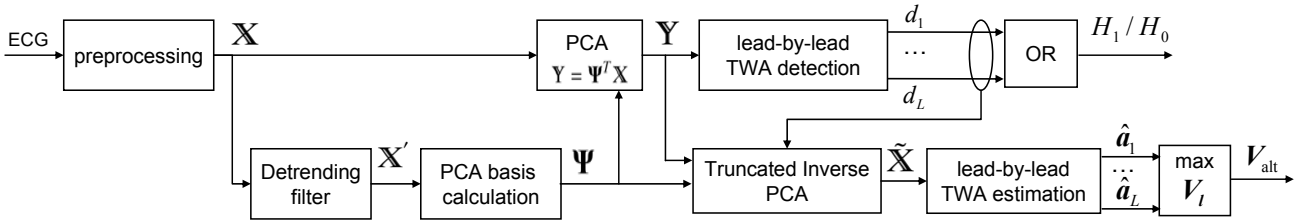


Figure 1. Block diagram of the analysis scheme

Then, the Maximum Likelihood Estimation (MLE) for Laplacian noise is applied to the reconstructed data as described in [6] to estimate the TWA waveform and amplitude. On each lead, TWA amplitude is calculated as the root mean square (RMS) value across the estimated TWA waveform $\hat{a}(n)$

$$V_l = \sqrt{\frac{1}{N}\sum_{n=0}^{N-1}\hat{a}_l^2(n)} \ (\mu V). \qquad (11)$$

A final TWA amplitude estimation $V_{alt}$ is calculated as the maximum $V_l$ in the $L$ leads.

## 4. Results

An entry was submitted to the Physionet/CinC challenge 2008 applying the analysis scheme previously described with an analysis window of $K = 32$ beats. 82 TWA episodes were detected in 41 records (52 episodes in 23 synthetic records and 30 episodes in 18 real records). The amplitude estimation for each record was taken as the maximum amplitude of all episodes found in that record. Fig. 2 shows the boxplot of the estimated amplitudes in real and synthetic records. The final score in the challenge was 0.633 in a range of [-1, 1].

Shortly after the deadline of the challenge, the reference TWA amplitudes added to synthetic records were published. In this synthetic set, the sensitivity of our scheme was 76.7%, detecting 100% of episodes with amplitudes > 6 $\mu$V. Fig. 3 shows the estimated amplitudes vs. the reference values. The relationship between our measurements and the references is approximately linear, the slope of the straight line fit is 0.4 and the correlation coefficient is 0.78. Two measurements, corresponding to records *twa28* and *twa69*, differed significantly from the reference. After visual inspection, they were considered erroneous measurements caused by the inestability of QRS annotations, and they were excluded from the linear fit calculation.

In addition to TWA amplitudes, we also measured the duration of the episodes detected in real records, and their onset heart rate (OHR). The duration was 17 ± 31 seconds (mean ± one standard deviation), and the OHR was 111 ± 23 bpm. Fig. 4 shows the cumulated histogram of the OHR.

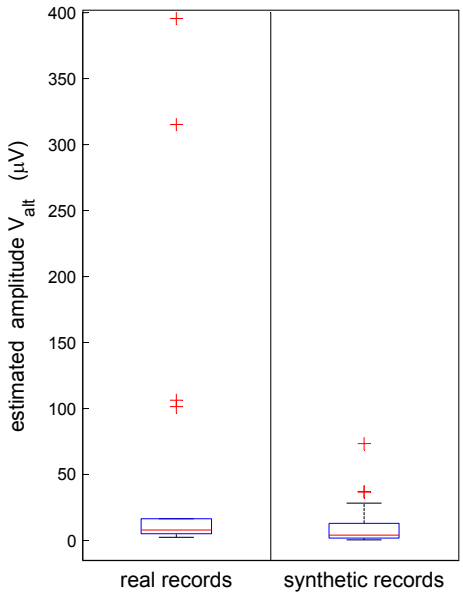


Figure 2. Boxplot of estimated TWA amplitudes in real records (left) and synthetic records (right)

## 5. Discussion and conclusions

The sensitivity of the analysis scheme is mainly determined by the detection threshold $\gamma$. Noise affects both TWA detection and estimation, so $\gamma$ must be carefully chosen to avoid false detections and obtain reliable TWA measurements, while maintaining a high sensitivity. This compromise exists for all TWA detection methods, although in some cases it is not adequately stressed. In our study, $\gamma$ was statistically calculated from a set of reference signals to obtain a theoretical probability of false alarm of 1%. In practice, the sensitivity in the synthetic dataset was high (76.7%) and no false episodes were detected.

According to the results of the synthetic set, our analysis scheme underestimates the amplitude of TWA. This could be due to the way of defining the TWA amplitude. We calculate the amplitude $V_{alt}$ along the entire ST-T complex (see (11)), and this measure is lower than the amplitude at the maximum of the TWA waveform, which might be another usual way of defining the TWA amplitude. More-

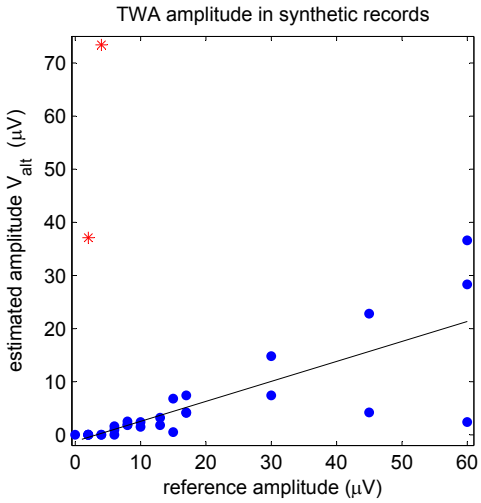


Figure 3. Scatterplot of TWA amplitudes in synthetic records. Outliers shown with asterisks. Straight line fit shown in black

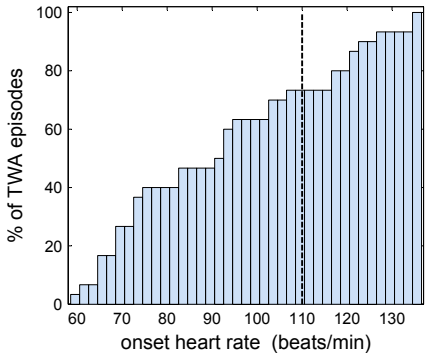


Figure 4. Cumulated distribution of the onset heart rate of TWA episodes detected in real records

over, as shown in a previous study [11], the truncation that is carried at the reconstruction stage may increase the bias, because only a subset of transformed leads is used to reconstruct the signal, and the discarded leads may still contain a small alternant component. There exists a trade-off between bias and variance of the estimation. A higher bias is compensated by a lower variance, making the study of the temporal distribution of TWA along the ST-T complex more reliable.

In addition to TWA amplitude, two more parameters need to be evaluated in a TWA analysis. One of them is the duration of the episodes, which has not been considered in the challenge. The minimum duration that the system can detect is mainly determined by the length of the analysis window. The other important parameter is the onset heart rate (OHR), because it provides additional prognostic value in risk stratification [1]. A cut-off point of 110 bpm is usually considered to distinguish between normal and abnormal TWA tests. In the real records set, 22 episodes (73.3%) belonging to 16 records (88.9%) have an OHR < 110 bpm, and therefore they would be considered abnormal.

The database and the TWA measurements obtained as a result of the Physionet challenge 2008 will be useful to evaluate TWA detectors from a methodological point of view. However, the clinical utility of the database as a "gold standard" is limited, since there is no information available about the follow-up of the patients.

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