Non-Linear Trend Estimation of Cardiac Repolarization using Wavelet Thresholding for Improved T-wave Alternans Analysis

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Abstract

The phenomenon of cardiac repolarization or T-wave alternans (TWA) has attracted tremendous attention after its acceptance as a marker of malignant ventricular arrhythmias leading to sudden cardiac death. TWA manifests subtle alternation in the ST-T segment of ECG, therefore, its detection and estimation is considerably affected by deteriorated signal conditions due to noise. In this paper, we evaluate the potential of discrete wavelet transform thresholding for accurate trend estimation of ECG repolarization segment. An exhaustive experimental approach is adopted to find the optimal parameter sets for accurate trend estimation, including mother wavelets, decomposition levels and other common thresholding parameters. Validation study is carried out after short-listing Coiflet\textsuperscript{4} and Symlet\textsuperscript{7} wavelets, subsequently applied to spectral method (SM) and modified moving average method (MMAM) for performance evaluation. For both the TWA analysis schemes, proposed method is inserted within the preprocessing stage after ST-T segmentation of ECG. When using wavelet based thresholding, SM achieves a detection gain of 3 dB in case of Gaussian and Laplacian noises. The estimation bias and error in Gaussian noise is also improved by 40\% and 62.5\%, respectively, for SNR \leq 5\text{dB}. Whereas, in case of MMAM, the estimation performance improves by more than 100\% for lower operating range of SNR.

Keywords: Detection, electrocardiography, estimation, T-wave alternan, wavelet transform

1. Introduction

Electrocardiography (ECG) is the most crucial clinical diagnostic tool for investigation of cardiac abnormalities. Surface ECG is measured by placing
the electrodes on a subject’s upper torso and recording the variation of cellular action potentials of cardiac muscles. The voltages measured by the electrodes are not absolute but obtained with reference to a 0 mV isoelectric baseline, and graphically plotted as a function of time. The resulting trace represents sequential depolarization of atria and ventricles (P-wave and QRS complex) and repolarization of ventricles (T-wave) in each heartbeat. A single such heartbeat is shown in Figure 1(a).

Microvolt T-wave alternans (TWA) is a phenomenon in which temporal and spatial characteristics of cardiac repolarization morphology periodically fluctuate in every other heartbeat, as shown Figure 1(c). Being peak to peak amplitudes in microvolts, this alternation is not visible through manual examination of surface ECGs in common clinical settings. Pathological significance of the phenomenon is established since first observations in 1910 [1], [2], however, the prognosis value is considerably enhanced since detection and estimation has become possible through advanced signal processing techniques [3], [4]. Since then, TWA has been increasingly linked with malignant ventricular arrhythmias [5], [6], [7] and recently included among the risk stratifiers for sudden cardiac death (SCD) [8], [9], [10].

Pathological TWA is manifested at higher heart rates which are commonly attained by subjecting the patient to stress tests. However, ECG signals acquired through exercise test have poor signal-to-noise ratio (SNR) due to various process noises, transient outliers and physiological artifacts. Short-time Fourier transform (STFT) based spectral methods are among the most widely used classical techniques [3], [5] applied on ECGs acquired during stress tests. These methods are highly dependent upon the stochastic nature of ECG signal and the estimates are susceptible to length of the estimation window. Secondly, the robustness of TWA estimation also depends upon the choice of noise reference band [11], [12] and estimation of noise levels within that window. Another class of spectral methods reduce the particular portion of ECG (e.g., ST-T complex) to a basis set and perform analysis on these reduced number of coefficients [13]. These techniques are now being applied on multi-lead ECGs and giving better estimation results [14]. To cater for the problem of non-stationarity as well as non-linearity, a recent innovative approach has utilized empirical mode decomposition (EMD) to estimate the trend of ST-T complex from high noise [15]. Consequently, the performance of classical spectral method (SM) has been improved by more than 2 dB.

Alternatively, various time domain approaches have also been proposed which are applied on holter ECG recordings. These approaches are usually based upon non-linear filtering [16], sign change counting [17], statistical tests [18] and phase space methods [19]. These techniques theoretically cater well for the ectopic beats, transient morphological changes and other non-stationarities. Among these techniques, modified moving average method (MMAM) has been clinically proved to be most significant [20]. It behaves linearly when the difference between consecutive beats is small [7] and responds non-linearly to transient beat to beat changes. Both SM and MMAM are implemented in the commercial diagnostic equipment (HearT wave II, Cambridge Heart Inc. and CASE-8000,
Wavelet transform has been extensively applied for signal encoding, denoising and multiresolution time-frequency analysis of ECG [21]. In the context of cardiac repolarization analysis, continuous wavelet transform (CWT) has been utilized to predict myocardial ischemia and detect TWA [22], [23], [24]. Alternatively, discrete wavelet transform (DWT) has emerged as a tool for ECG compression, classification and multiresolution analysis for detecting various abnormalities [21]. In discrete wavelet domain, thresholding methods have been proposed for shrinkage of noise components by [25]. Since then, the approach and its variants are applied for denoising high resolution ECGs [26], [27].

The clinical recognition of TWA phenomenon as a significant marker of SCD necessitates evaluation of all possible avenues which can contribute towards enhancing the efficiency of detection approaches. Few studies utilizing DWT denoising have recently been reported [28], however, it is considered that a complete performance validation of efficient TWA detection approaches from detection and estimation theoretic viewpoint is still open. In this paper, we present rigorous experimental analysis to evaluate the potential of cardiac repolarization trend estimation from noisy ECGs, using DWT coefficients thresholding and detection and estimation of TWA. The study incorporates vital parameters effecting thresholding performance, i.e., optimal wavelet basis, decomposition levels, thresholding strategies, threshold types and noise rescaling approaches. Subsequently, the analysis leads to the evolution of optimal parameter sets, achieving accurate trend estimation of ventricular repolarization. Consequently, a significant improvement in TWA assessment is achieved. Detection performance with the proposed strategy is validated using SM and estimation accuracy is evaluated using both SM and MMAM.

In the following section, we briefly review the wavelet theory and establish the theoretical basis of our proposed scheme. Experimental methodology and materials are described in section 3 and section 4, respectively. Validation results and related discussion are presented in section 5, followed by important conclusions.

2. Theoretical Basis

2.1. Continuous Wavelet Transform

Development of Wavelet theory is motivated by an important implication of the uncertainty principle, i.e., information in a signal cannot be localized at arbitrary small time-frequency scales using STFT analysis. Consequently, STFT dictates Gabor atoms of rigid dimensions across the time frequency plane, even when the area of time-frequency boxes is compressed to minimum [29]. In contrast, wavelet transform provides a mapping (through associated wavelet functions) which allows great flexibility to study transient features of the signal in time-frequency plane. An energy normalized wavelet function is defined as [30]
Figure 1: ECG morphology and TWA presence; (a) a single heart beat of 0.6 sec at paced heart rate of 110 bpm exhibiting PQRST cycle, (b) a normal sinus rhythm ECG segment of 5 seconds in a clean ECG signal with heart rate 110 bpm, and (c) simulating TWA presence in the same signal with peak to peak amplitude of alternan waveform set at 100 µV with uniform spatial distribution to simulate stationary characteristics for 5 seconds. Red line traces the alternan waveform and green squares mark the peak of T-wave where alternan amplitude is maximum.
\begin{align}
\psi_{a,b}(t) &= \frac{1}{\sqrt{a}} \psi \left( \frac{t-b}{a} \right) \quad (1)
\end{align}

where \( a \) and \( b \) are dilation and translation parameters, respectively. In order for a function \( \psi_{a,b}(t) \) to qualify as a wavelet, it must have finite energy, i.e., \( \int_{-\infty}^{\infty} |\psi(t)|^2 dt < \infty \) and zero mean, i.e., \( \int_{-\infty}^{\infty} \psi(t) dt = 0 \). CWT of a signal \( f(t) \) is obtained by convolving it with the complex conjugate of the mother wavelet \( \psi^*(t) \), as

\begin{align}
T(a, b) &= \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} f(t) \psi^* \left( \frac{t-b}{a} \right) dt \quad (2)
\end{align}

where the choice of \( \psi(t) \) usually depends upon the nature of \( f(t) \) as well as analysis considerations.

2.2. Discrete Wavelet Transform

The most common concern while dealing with real signals is processing their discretely sampled finite versions. For efficient time frequency analysis of such practical signals, implementation of (1) involves a dyadic grid of scale and position parameters with orthonormal basis to achieve zero redundancy. The resulting wavelet function follows from (1) as

\begin{align}
\psi_{j,k}(t) &= \frac{1}{\sqrt{2^j}} \psi \left( \frac{t-k2^j}{2^j} \right) \quad (3)
\end{align}

where \( j, k \) are indices defining the scale-location grid and the DWT coefficients are given by \( T_{j,k} = \int_{-\infty}^{\infty} f(t) \psi_{j,k}(t) dt \). If \( \psi_{j,k}(t) \) are the orthonormal basis, then \( f(t) \) can be reconstructed by summation over all \( j \) and \( k \) as \( f(t) = \sum_j \sum_k T_{j,k} \psi_{j,k}(t) \).

2.3. Multiresolution Representation

The orthonormal dyadic wavelets are associated with scaling functions \( \phi_{j,k}(t) \), having the same form as \( \psi_{j,k}(t) \) and exhibiting \( \int_{-\infty}^{\infty} \phi(t) dt = 1 \). Convolution of scaling function with \( f(t) \) produces approximation coefficients, \( U_{j,k}(t) \), given by

\begin{align}
U_{j,k} &= \int_{-\infty}^{\infty} f(t) \phi_{j,k}(t) dt \quad (4)
\end{align}

which collectively form a discrete approximation of \( f(t) \) at scale \( j \). A continuous approximation \( f_{j_0}(t) = \sum_k U_{j_0,k}(t) \phi_{j_0,k}(t) \) of \( f(t) \) at scale \( j_0 \) can be obtained by summing a sequence of scaling functions at scale \( j_0 \), and weighted by the approximation coefficients. Consequently, \( f(t) \) can be represented by combining \( T_{j,k} \) and \( U_{j,k} \) from (2) and (4), as

\begin{align}
f(t) &= f_{j_0}(t) + \sum_{j=-\infty}^{j_0} d_j(t) \quad (5)
\end{align}
where \( f_{j_0}(t) \) is referred as signal approximation at an arbitrary scale \( j_0 \) and \( d_j(t) = \sum_k T_{j,k} \psi_{j,k}(t) \) is called the signal detail at scale \( j \). The signal representation through (5) is called multiresolution decomposition as it entails \( f_{j-1}(t) = f_j(t) + d_j(t) \), which means that a signal can be approximated at higher resolution (or lower scale) by adding a signal detail and approximation at some arbitrary scale.

### 2.4. Wavelet Thresholding

An obvious implication of multiresolution representation in (5) is the potential to conveniently reconstruct an approximation of the input signal after altering the wavelet transform coefficients before computing the inverse transform. The coefficients can be manipulated in variety of ways depending upon the desired objective, e.g., denoising, smoothing or trend estimation. Two common ways of thresholding coefficients are hard and soft thresholding, which involve setting of a threshold \( \lambda \) and removing or reducing the coefficients which are below this threshold \([30]\).

Hard thresholding is formulated as

\[
c_{n}^{\text{hard}} \equiv \begin{cases} 
0, & |c_n| < \lambda \\
\frac{c_n}{|c_n|}, & |c_n| \geq \lambda
\end{cases}
\]  

(6)

where \( c_n \) are the sequentially indexed DWT coefficients \( T_{j,k} \), which are simply kept or removed during hard thresholding. Soft thresholding does not just keep the coefficient above (or equal to) a certain threshold but reduces it according to some analytical shrinkage rule. A common form of a shrinkage rule is when the coefficients are reduced by an amount \( \lambda \), i.e.,

\[
c_{n}^{\text{soft}} = \begin{cases} 
0, & |c_n| < \lambda \\
\text{sign}(c_n) \left( |c_n| - \lambda \right), & |c_n| \geq \lambda
\end{cases}
\]  

(7)

where the choice of \( \lambda \) varies according to the adopted threshold strategy. There are various thresholding methods reported in the literature \([31], [25], [32], [33]\), e.g., universal thresholding, Stein’s unbiased risk estimate (SURE) and its variants, cross validation method and Bayesian approaches.

### 3. Methodology

#### 3.1. ECG Signal Preprocessing and Segmentation

Generalized framework for TWA analysis is shown in Figure 2. An \( M \) beat digitized ECG signal is fed as input to the analysis system, whose outputs include a decision statistics regarding the TWA presence or absence and the magnitude estimate. The aim of the preprocessing stage is to condition the digitized ECG for analysis in subsequent stages \([34]\). As TWA is a localized phenomenon only manifested during the repolarization phase of beat to beat ECG signal, it is convenient to adopt a segmentation procedure to extract the relevant portion from the complete ECG signal before analysis.
QRS and T-wave peak detection is performed using the waveform locator of Laguna et al [35], available at Physionet [36]. Fiducial points are selected using the scheme proposed by [37] and validated beats are aligned over these fiducial points. ST-T Segmentation is then carried out by selecting an interval of 300 ms from QRS fiducial points. The onset for the l-th beat $b_l$ is set using [38],

$$b_l = 40 + 1.3RR^{1/2}(ms)$$

where $RR$ is the interval (in milliseconds) between two consecutive R peaks.

### 3.2. Trend Estimation of ST-T Complex

The output $X \in \mathbb{R}^{N \times M}$ of the preprocessing stage contains preprocessed ECG repolarization segments $X = [x_0 \ldots x_{M-1}]$, where $x_l = [x_l[0], \ldots, x_l[N-1]]^T$ is the segment corresponding to l-th beat, having $N$ samples. TWA is essentially a non-stationary phenomenon and analysis has to be performed on a limited number of beats. Therefore, an analysis window $B \in \mathbb{R}^{L \times N}$ comprising of $L$ beats is defined, such that if the window is shifted $r$ times it covers the entire signal length $M$. At $r = 1$, the analysis window is centered at beat $\frac{l}{2} - 1$, such that $B = [b_0 \ldots b_{\frac{l}{2}-1} \ldots b_{L-1}]$. The segmented ST-T complexes in the $L$ beat analysis window can be written in matrix notation as,

$$X = S + W$$

where $X \in \mathbb{R}^{N \times L}$ contains the aligned ST-T segments and $S, W \in \mathbb{R}^{N \times L}$ represent signal, i.e., $S = [s_0 \ldots s_{L-1}]$ and noise samples, $W = [w_0 \ldots w_{L-1}]$, respectively. We assume $s_l$ to be an unknown deterministic signal and the elements of $w_l$ are assumed to come from an uncorrelated random process and distributed as $\mathcal{N}(0, \sigma^2)$.
Table 1: Pseudocode for Implementing ST-T Complex Trend Estimation.

For \( l = 0 \) to \( L - 1 \)

- Use (5) to compute multiresolution decomposition of \( x_l \) (desired wavelet basis)
- Set a threshold value of \( \lambda \) (desired thresholding strategy)
- Use (6) and (7) to remove the coefficients below \( \lambda \)
- Obtain \( \hat{s}_l \) through inverse DWT computation
- Increment counter

End For

The proposed methodology to estimate the trend of cardiac repolarization segment is conceived to be a three step process, as depicted by the dotted block in Figure 2. We characterize a single ST-T segment corresponding to \( l \)-th beat \( x_l \) as the observation vector to render multiresolution computation using (5).

Such that \( x_l = x_{lj_0} + \sum_{j=-\infty}^{j_0} d_{lj} \), where \( x_{lj_0} \) is the discrete approximation of ST-T segment at scale \( j_0 \) and \( d_{lj} = \sum_k T_{lj,k} I_N \bar{\psi}_{j,k} \) is the detail at \( j \)-th level of decomposition, and \( I_N \) is an \( N \) dimensional identity matrix. \( T_{lj,k} \) are DWT coefficients corresponding to \( l \)-th ST-T segment and \( \bar{\psi}_{j,k} \) is the vector representation of discrete wavelet function. The DWT coefficients \( c_{l,j,k} = T_{lj,k} \) corresponding to \( x_l \) are effectively understood to be obtained through DWT mapping over signal \( s_l \) and noise \( w_l \), respectively. If we assume \( W \) to be the DWT operator, then \( c_{l,j,k} = Wx \) represents DWT of the ST-T segment containing both signal and noise samples and \( g = Ws_l \) represents DWT of the signal. We define \( h(c, \lambda) \) as a thresholding function according to hard or soft thresholding strategy given in (6) and (7), respectively. The threshold \( \lambda \) is set according to the selected threshold type, for instance, \( \lambda = \sigma \sqrt{2 \log n} \) for the universal threshold [25] or the optimal minimax threshold in terms of \( L^2 \) risk [33]. After performing the requisite thresholding of coefficients, the estimated coefficients are obtained as \( \hat{g}_{j,k} = h(c_{l,j,k}, \lambda) \) and the ST-T trend can be estimated by taking the inverse DWT as \( \hat{s}_l = W^T \hat{g} \). The Pseudocode delineating implementation steps for estimating the ST-T complex trend is given in Table 1.

3.3. Choice of Estimation Parameters

Trend estimation of ST-T complex in wavelet domain is dictated by the choice of different parameters, i.e., the optimal wavelet basis, appropriate decomposition level, thresholding method, threshold type and noise rescaling approach. Analytical basis guiding choice of these parameters vary and depends upon various assumption regarding signal of interest, e.g., the data model and characterization of noises contaminating the signal. Cardiac repolarization morphology has not yet been characterized conclusively through analytical models and choice of mother wavelets are diverse. Moreover, it is established that even small noise levels can mask the TWA phenomenon or considerably effect the magnitude estimates. Therefore, it is difficult to decide regarding the best combination of these parameters which give the accurate estimate of ventricular
repolarization trend, and it is appropriate to adopt and exhaustive search with all possible combinations.

Table 2 lists the parameters, i.e., thresholding method, threshold type and noise rescaling approach, which are tested over the experimental dataset (section 4) with different combinations and $10^3$ realizations using Monte Carlo method.

### 3.3.1. Optimal Wavelet Basis

Using a sequential approach, in first step, the optimal wavelet basis and the decomposition level is shortlisted. An ST-T complex $x_l$ is decomposed with different wavelet basis (given in Table 2) at scale $j_0$ and reconstruction is performed using only the approximation coefficient at that scale. The cross correlation coefficient of the reconstructed approximation $\hat{x}_{j_0}$ with the original clean signal $s_l$ is computed as

$$\rho_{j_0} = \frac{[\hat{x}_{j_0} - \mu_{\hat{x}_l}]^T [s_l - \mu_{s_l}]}{\sigma_{\hat{x}_l} \sigma_{s_l}}$$

where $\mu_{s_l}, \sigma_{s_l}$ and $\mu_{\hat{x}_l}, \sigma_{\hat{x}_l}$ duple represent (mean, standard deviation) of original signal and approximated trend at scale $m_0$ respectively.

Figure 3 depicts the trend of $\rho_{j_0}$ for approximated trend of cardiac repolarization obtained through reconstruction using only the approximation coefficients at different scales. Out of 53 wavelet basis, the ones giving the best results within their respective families are chosen as optimal.

### 3.3.2. Appropriate Decomposition Level

It is observed that all mother wavelets maximize the correlation coefficient with the original ST-T complex at decomposition level 4. An example reconstruction using Symlet8 as mother wavelet is shown in Figure 4 to confirm the deduction that correlation is maximized at fourth decomposition level. It is observed that higher scales not only remove the presumed noisy components, but also extract the useful morphological information. Therefore, Daubechies8, Discrete Meyer, Symlet7, Symlet8, Coiflet4, Coiflet5, Biorthogonal3.3, Biorthogonal6.8, Reverse Biorthogonal6.8 are chosen as candidate wavelets basis with fourth decomposition level as optimum.

### 3.3.3. Threshold Selection

The nine shortlisted mother wavelets at decomposition level 4 for all possible thresholding combinations are tested over the experimental dataset for multiple realizations of synthetic noises and real physiological artifacts. Mean squared error (MSE) is used as a performance measure to comparatively characterize each parameter set. There are marginal differences between MSE of all parameter sets, however, Coiflet4 and Symlet7 with corresponding parameters for each noise type are generally the best in terms of MSE. It is also observed that switching between hard and soft thresholding strategy does not have great impact in improving the repolarization trend estimates. Among the applied threshold types, Stein’s unbiased risk estimate (SURE) and Heuristic SURE are
Table 2: Different parameters tested over the experimental dataset.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Possible Choices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother wavelet function</td>
<td>Daubechies 1,...,10, Symlet 2,...,8,</td>
</tr>
<tr>
<td></td>
<td>Discrete Meyer, Coiflet 1,...,5,</td>
</tr>
<tr>
<td></td>
<td>Biorthogonal, Reverse Biorthogonal</td>
</tr>
<tr>
<td>Decomposition level</td>
<td>1,...,6</td>
</tr>
<tr>
<td>Thresholding method</td>
<td>Hard, Soft</td>
</tr>
<tr>
<td>Threshold type</td>
<td>SURE, Heuristic SURE, Universal, Minimax</td>
</tr>
<tr>
<td>Noise level rescaling</td>
<td>No scaling, Single level, Multiple level</td>
</tr>
</tbody>
</table>

preferred over other types. Lastly, it is confirmed that noise scaling approach can be accordingly chosen if *a priori* knowledge regarding noise statistics are available. For electrode movement and muscular activity artifacts, single or multiple level scaling generally gives better results than no scaling, which is an appropriate choice when noise is white Gaussian or Laplacian. Table 3, 4 and 5 lists the parameter sets with least MSE among the shortlisted wavelet basis for Gaussian noise, electrode movement and muscular activity, respectively. The results for Laplacian noise are observed to be generally similar to the Gaussian case.

3.3.4. Simulations Results

Figure 5 presents an example of ST-T segment trend estimation using the proposed method. An ST-T complex contaminated by Gaussian noise with 5 dB signal-to-noise ratio (SNR) is shown in dashed line. *Coiflet4* is used as the mother wavelet with soft thresholding and Heuristic SURE rule. The estimated trend is superimposed over the noisy and original ST-T segment. Wavelet thresholding with arbitrary choice of parameters or simple scale-dependent thresholding sometimes adds distortion into the signal or reduces the magnitude of coefficients corresponding to useful information, i.e., pathological TWA in our case. It can be assessed from the example that proposed parameters accurately estimate the repolarization trend from high noise and closely trace the original morphology while preserving the important pathological information.
Figure 3: Comparison of normalized correlation coefficient for various wavelet filters at different decomposition levels.

Figure 4: Reconstruction of a single ST-T complex from approximation coefficients at six different scales using Symlet8 as mother wavelet. Dashed lines show the approximated trends at decomposition levels 1, \ldots, 6 (from bottom to top) and solid line is the original signal.
Table 3: Parameter sets with least mean square errors among all shortlisted mother wavelets for Gaussian noise. Wavelet functions are denoted by their Matlab conventions.

<table>
<thead>
<tr>
<th>Mother wavelet</th>
<th>Threshold method</th>
<th>Threshold type</th>
<th>Noise scaling</th>
<th>MSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>db8</td>
<td>Soft</td>
<td>Heuristic SURE</td>
<td>No scaling</td>
<td>0.001448</td>
</tr>
<tr>
<td>dmey</td>
<td>Hard</td>
<td>Heuristic SURE</td>
<td>No scaling</td>
<td>0.001563</td>
</tr>
<tr>
<td>sym7</td>
<td>Hard</td>
<td>Heuristic SURE</td>
<td>No scaling</td>
<td>0.00136</td>
</tr>
<tr>
<td>sym8</td>
<td>Soft</td>
<td>Universal</td>
<td>No scaling</td>
<td>0.001481</td>
</tr>
<tr>
<td>coif4</td>
<td>Soft</td>
<td>Heuristic SURE</td>
<td>Single level</td>
<td>0.001261</td>
</tr>
<tr>
<td>coif5</td>
<td>Hard</td>
<td>Heuristic SURE</td>
<td>No scaling</td>
<td>0.00142</td>
</tr>
<tr>
<td>bior3.3</td>
<td>Hard</td>
<td>SURE</td>
<td>No scaling</td>
<td>0.001952</td>
</tr>
<tr>
<td>bior6.8</td>
<td>Soft</td>
<td>SURE</td>
<td>No scaling</td>
<td>0.001421</td>
</tr>
<tr>
<td>rbio 6.8</td>
<td>Hard</td>
<td>Universal</td>
<td>No scaling</td>
<td>0.001406</td>
</tr>
</tbody>
</table>

Figure 5: Noisy ST-T complex at 5 dB SNR, original complex and estimated trend using Coiflet4 with associated parameters, as given in Table 3.
Table 4: Parameter sets with least mean square errors among all shortlisted mother wavelets for electrode movement. Wavelet functions are denoted by their Matlab conventions.

<table>
<thead>
<tr>
<th>Mother wavelet</th>
<th>Threshold method</th>
<th>Threshold type</th>
<th>Noise scaling</th>
<th>MSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>db8</td>
<td>Soft</td>
<td>SURE</td>
<td>No scaling</td>
<td>0.015967</td>
</tr>
<tr>
<td>dmey</td>
<td>Hard</td>
<td>Minimax</td>
<td>Multiple level</td>
<td>0.016598</td>
</tr>
<tr>
<td>sym7</td>
<td>Hard</td>
<td>SURE</td>
<td>Multiple level</td>
<td>0.015429</td>
</tr>
<tr>
<td>sym8</td>
<td>Soft</td>
<td>SURE</td>
<td>Multiple level</td>
<td>0.016073</td>
</tr>
<tr>
<td>coif4</td>
<td>Soft</td>
<td>Heuristic SURE</td>
<td>Single level</td>
<td>0.015839</td>
</tr>
<tr>
<td>coif5</td>
<td>Hard</td>
<td>Universal</td>
<td>Multiple level</td>
<td>0.017139</td>
</tr>
<tr>
<td>bior3.3</td>
<td>Hard</td>
<td>Universal</td>
<td>Multiple level</td>
<td>0.015626</td>
</tr>
<tr>
<td>bior6.8</td>
<td>Soft</td>
<td>Minimax</td>
<td>Multiple level</td>
<td>0.016257</td>
</tr>
<tr>
<td>rbio6.8</td>
<td>Hard</td>
<td>Minimax</td>
<td>No scaling</td>
<td>0.016161</td>
</tr>
</tbody>
</table>

Table 5: Parameter sets with least mean square errors among all shortlisted mother wavelets for muscular activity. Wavelet functions are denoted by their Matlab conventions.

<table>
<thead>
<tr>
<th>Mother wavelet</th>
<th>Threshold method</th>
<th>Threshold type</th>
<th>Noise scaling</th>
<th>MSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>db8</td>
<td>Soft</td>
<td>Heuristic SURE</td>
<td>No scaling</td>
<td>0.004184</td>
</tr>
<tr>
<td>dmey</td>
<td>Hard</td>
<td>Universal</td>
<td>No scaling</td>
<td>0.004093</td>
</tr>
<tr>
<td>sym7</td>
<td>Hard</td>
<td>SURE</td>
<td>No scaling</td>
<td>0.004336</td>
</tr>
<tr>
<td>sym8</td>
<td>Soft</td>
<td>SURE</td>
<td>Multiple level</td>
<td>0.004228</td>
</tr>
<tr>
<td>coif4</td>
<td>Hard</td>
<td>Heuristic SURE</td>
<td>Multiple level</td>
<td>0.003639</td>
</tr>
<tr>
<td>coif5</td>
<td>Hard</td>
<td>Heuristic SURE</td>
<td>No scaling</td>
<td>0.004405</td>
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3.4. T-wave Alternans Detection and Estimation

Two detectors are implemented with the proposed scheme to achieve robust detection of TWA in noisy conditions. Both these detectors, i.e., spectral method (SM) and modified moving average method (MMAM), have been implemented in the commercial equipment (HearTwave II, Cambridge Heart Inc. and CASE-8000, GE Medical Systems) and have been extensively employed in clinical studies [20].

3.4.1. Spectral Method (SM)

The spectral FFT-based method defines TWA magnitude as the peak at 0.5 cpb point in aggregate T-wave energy spectrum [5]. After preprocessing and segmentation, \( L \) individual beats \((L=128)\) are aligned over fiducial points and a \( B \in \mathbb{R}^{L \times N} \) analysis window comprising of only ST-T complexes (having \( N \) samples) is extracted for alternan estimation. Power spectral estimate of the \( n \)-th time series \( b_n = [b_n[0], b_n[1], \ldots, b_n[L]]^T \) is computed, where \( b_n \) is the \( n \)-th column of matrix \( B \) and the TWA magnitude at 0.5 cpb \((E_{0.5})\) is computed by averaging the \( N \) power estimates. The cumulative alternan voltage estimate \( \hat{V}_{SM} \) for the complete analysis window is given by \( \hat{V}_{SM} = [(E_{0.5} - \mu)/N]^{1/2} (\mu V) \) where \( \mu \) is the sample mean of noise measured in a properly chosen spectral window around 0.5 cpb point. Another parameter T-wave alternan ratio (TWAR) is defined as \( TWAR_l = \hat{V}_{SM} l / \sigma_n \) to quantify the significance of estimation relative to signal quality.

The estimated magnitude \( \hat{V}_{SM} \) and the significance measure \( TWAR_l \) are combined to give the joint decision rule for SM

\[
Z_{1SM} = \frac{\hat{V}_{SM}}{H_1} \geq \gamma_1 \\
Z_{2SM} = \frac{TWAR_l}{H_1} \geq \gamma_2
\]  

where \( \gamma_1 = 1.9 \mu V \) and \( \gamma_2 = 3.0 \) according to the recent consensus guidelines for TWA measurement [20]. The test statistics in (11) and (12) is computed when the analysis window is centered on \( l \)-th beat and conditions in both statistics have to be fulfilled in order to decide in favor of the hypothesis.

3.4.2. Modified Moving Average Method (MMAM)

MMAM involves computation of recursive averages of even \((A)\) and odd \((B)\) ECG beats in parallel [16], defined as \( A_l(n) = ECG \text{ Beat}_{2l}(n) \) and \( B_l(n) = ECG \text{ Beat}_{2l-1}(n) \), where \( n \) is number of samples in a beat \((n=1,2,\ldots,N)\) and \( l \) is the analyzed beat \((l=1,2,\ldots,L/2)\). An update factor \( \triangle \) initialized with \( \triangle = 1/8 \) is used to modify the computed averages to incorporate small as well as large amplitude differences, thus adding robustness for common non-linearities. The algorithm computes average beats using the present MMA beat and the
next beat in respective even or odd series. The alternan magnitude is finally estimated as the maximum absolute difference within the JT segment of any two computed averages of even and odd beats, i.e., $V_{\text{MMAM}} = |\bar{B}(n) - \bar{A}(n)|$, where $\bar{A}$ and $\bar{B}$ are computed averages of even and odd beats, respectively. The global detection statistics is subsequently computed as

$$Z_{\text{MMAM}} = \frac{T_{\text{end}}}{\max_{n=j\text{point}}} \left( |\bar{B}(n) - \bar{A}(n)| \right)$$ (13)

No decision rule is given by Nearing and Verrier [16], as the proposed method implements dynamic estimation of TWA magnitude and not deciding formally about its presence of absence, thereby implying allowance in decision threshold according to clinical considerations.

4. Materials

No gold standard dataset is available to validate the performance of TWA detection and estimation schemes against reference annotations since TWA is usually masked by noise. Therefore, an accepted procedure is to design simulated ECG signal datasets to facilitate performance assessment with prior knowledge of various TWA parameters [34]. We have induced synthetic alternan waveforms in real ECG signals to achieve physiological realism and inter-beat cardiac variability. Test signals are simulated with an a priori knowledge of alternan magnitude, and distribution and level of noise.

Figure 6 depicts the scheme implemented to synthesize ECG signals. Background ECG signal is synthesized using concatenation of heartbeat streams, arbitrarily extracted from two different ECG signals (mitdb101 and mitdb103) of MIT-BIH Arrhythmia Database, publicly accessible from MIT Physionet [36]. These records are selected because most of the beats contained in both the records are annotated as normal (denoted by ‘N’ in the database), and therefore considered reasonable candidates for ECG synthesis. Random and out of rhythm beat selection from two different records ensures inter-beat physiological variability as well rhythmic non-stationarity.

An alternan waveform obtained through ST-T extraction of the same signal is added in each alternative beat with varying scales to obtain the final ECG signals with added TWA. An alternan episode $e_{ij}[.]$ is realized as $e_{ij}[.] = \{u_1[n], \ldots, u_L[n]\}$, where $i$ denotes the episode index and $j$ denotes the particular beat pair in the $i$-th episode. Figure 7 shows an example of simulating TWA presence in the synthesized ECG.

Detectors’ performance is evaluated in different scenarios involving variety of noise realizations. Two different types of synthetic noises, i.e., Gaussian and Laplacian with two 30 minutes recordings of electrode movement (“em”) and muscular activity (“ma”), provided by MIT BIH noise stress database [39], [36] are included in the study. These noises are used to contaminate the ECG signals and analyze estimation performance in response to process noises as well as physiological artifacts. Monte Carlo approach is adopted to evaluate
detection performance and estimation accuracy under varying levels of noise by controlling the SNR of signals.

5. Validation Study

5.1. Performance Metrics

ECG signals are simulated with SNR levels ranging between -15 dB to 35 dB and TWA magnitude ranging between 0 to 100µV. For each parameter set (noise type, alternan amplitude and SNR level), $10^3$ realizations are generated. Experiments are performed with four different schemes included in the study,
i.e., original SM, SM with wavelet based estimation (SM-W), original MMAM and MMAM with wavelet based estimation (MMAM-W). Results are compared in terms of detection performance and estimation accuracy.

Detection performance is evaluated with 32, 64 and 128 beat analysis windows in terms of detection probability $P_d$, i.e., the total number of detections over total number of statistics. Subsequently, any value of $P_d > 0$ for a true alternan magnitude $V_{alt} = 0$ is interpreted as probability of false alarm $P_{fa}$. Detection results for MMAM are not shown as no decision rule (with fixed or adaptive threshold) is given by [16] to discriminate TWA from noise. MMAM's global estimation statistics in (13), if compared against a fixed amplitude threshold (like $1.9 \mu V$ in case of SM), gives $P_d = 1$ for all SNR values with very high bias from true value, especially when the SNR is low. Therefore, MMAM is only included in evaluation of estimation accuracy.

The estimation accuracy is evaluated using bias ($b$), standard deviation ($\sigma$) and mean squared error (MSE). For each SNR level, the estimation bias and MSE is calculated as

$$b = E \left\{ \hat{V}_{alt} \right\} - V_{alt} \quad (14)$$

$$MSE = E \left\{ (\hat{V}_{alt} - V_{alt})^2 \right\} \quad (15)$$

where the expected values are estimated as the mean of $10^3$ realizations.

5.2. Detection Performance

Detection performance for $10 \mu V$ TWA is presented in Figure 8 for all the studied noise types. Such a small amplitude is chosen to enable comparison under stringent conditions as higher alternan magnitudes are more easily discriminated from noise and consequently the probability of detection improves. Conversely, a lower alternan amplitude (such as $10 \mu V$) can be masked with significantly lower noise levels.

For Gaussian noise, under very low operating range of SNR (SNR < -5 dB), both traditional SM and SM-W behave robustly and give negligible detection probability. SM-W shows an improvement of 5.85 dB over traditional SM when the sensitivity of both schemes is between 25% and 60%. Finally, SM-W achieves a detection gain of 3 dB when sensitivity of both algorithms is maximized, i.e., $P_d = 1$. Results for Laplacian noise are observed generally similar to the Gaussian noise. Both traditional SM and SM-W perform similar against electrode movement and muscular activity artifacts, and $P_d$ is maximized at 23 dB and 24 dB, respectively.

Detection performance under two different Gaussian noise levels, i.e., SNR = 0 dB and SNR = 20 dB, for increasing alternan amplitudes is shown in Figure 9. At higher noise levels (SNR = 0 dB), SM-W maximizes detection performance for $50 \mu V$ TWA amplitude, whereas SM achieves the same performance at higher amplitudes of $75 \mu V$. As the signal conditions improve (SNR = 20 dB), SM and
SM-W achieve $P_d = 1$ at $V_{alt} = 10\mu V$ and $V_{alt} = 5\mu V$, respectively. It is deduced that SM-W is especially suitable for detecting lower TWA magnitudes than traditional SM under higher noise levels.

5.3. Estimation Accuracy

Figure 10 shows the trend of bias and error of all estimators under various noise types with respect to SNR. Once again, the alternan amplitude of $10\mu V$ is chosen to compare estimation accuracy under rigorous conditions when the alternan amplitude is sufficiently low with respect to noise levels. Under Gaussian noise for lower operating range of SNR, SM-W outperforms traditional SM by 40% in terms of bias and 62.5% in terms of MSE, whereas improvement in case of MMAM-W is greater than 100%. For Laplacian noise, the results are observed to be slightly better and not shown for sake of brevity, as they follow the same trend as in Gaussian noise. The performance of both SM and SM-W remain same for electrode movement and muscular activity artifacts, whereas, MMAM-W performs better than MMAM for the case of muscular activity at high noise levels.
Figure 9: Detection performance for two different Gaussian noise levels and increasing alternan amplitudes.

Following the detection performance results, 20 dB SNR is assumed to represent good signal quality as both SM and SM-W achieve $P_d = 1$ for $V_{alt} \geq 10\mu V$ for both synthetic noises, and $P_d > 0.9$ for the electrode movement and muscular activity artifacts (Figure 8). Conversely, we assume 0 dB SNR as a reasonable representation of sufficiently deteriorated signal conditions for detecting $V_{alt} \geq 10\mu V$, as $P_d < 0.2$ for both SM and SM-W for all noise types.

Estimators’ bias and error for 0 dB and 20 dB SNR is shown in Figure 11(a) and Figure 11(b), respectively. Under higher noise level (SNR = 0 dB), the estimation bias of SM-W is consistently less than traditional SM for $V_{alt} \leq 80\mu V$. Alternan magnitudes higher than 80µV are discriminated accurately from noise by both versions of SM. Moreover, standard deviation of SM-W is less than SM as the latter overestimates the alternan waveforms with $V_{alt} \leq 15\mu V$ and underestimates the higher TWA magnitudes till $V_{alt} = 80\mu V$. The estimation error of SM-W is considerably less than SM for complete range of TWA magnitude, i.e., $V_{alt} \leq 100\mu V$. The bias and error of MMAM-W is considerably less than MMAM, however, both have similar trend in terms of standard deviation.

Under improved signal conditions (SNR = 20 dB), both versions of MMAM improve while maintaining the same performance gap as in low SNR case. The bias and error of SM-W is less than SM for $V_{alt} \leq 10\mu V$ and $V_{alt} \leq 20\mu V$, respectively.

6. Conclusion

In this paper, a new nonlinear approach is evaluated to discriminate ECG ventricular repolarization segment from noise and artifacts. Repolarization
Figure 10: Bias and error for 100 µV TWA amplitudes for entire operating range of SNR. Plots for SM and MMAM are shown separately for better visualization as SM significantly outperforms MMAM in terms of both bias and error.
Figure 11: Estimation bias and error for two different Gaussian noise levels and increasing alternan amplitudes.
trend is estimated through thresholding of DWT coefficients, obtained from optimal wavelet basis functions. The exhaustive experimental analysis reveals various parameter sets including mother wavelets, decomposition levels, thresholding strategies, threshold types and noise scaling approaches. Among the shortlisted parameters sets, Coiflet4 and Symlet7 appear to be most suitable for reconstruction, in terms of minimum MSE as well as maximizing of cross correlation with the original repolarization segment.

The study is conceived to augment and improve detection and estimation of TWA which is a major risk stratifier for sudden cardiac death. The validation study is carried out using a physiologically realistic dataset with a priori knowledge of alternan magnitude and noise power. A wide set of experiments are performed with TWA magnitude ranging from 0 to 100µV and an SNR from -15 to 35 dB. In the context of generalized framework of TWA analysis, proposed wavelet thresholding is incorporated after the preprocessing stage. No other filtration or smoothing during the preprocessing stage is required when the implementation is carried out with the proposed method.

Detection performance is validated by observing improvement in detection probability of SM when proposed repolarization trend estimation strategy is incorporated. Estimation accuracy is evaluated using SM and MMAM, and estimation bias, standard deviation and MSE are used for performance comparisons. Results show that these classical algorithms, while using the proposed strategy, achieve a considerable improvement in TWA detection and estimation.

References


