Improved Estimation of V-Index Based on Analytic Forms of Dominant T-Wave

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Abstract

Spatial heterogeneity of ventricular repolarization (SHVR) is related to the development of arrhythmias. To assess SHVR, we introduced the $\mathcal{V}$-index, a metric which needs computation of the Dominant T-Wave (DTW) and its derivatives. Theoretically, the larger the number of derivatives, the better the adherence to the modelled T-wave. In practice, only the first derivative is included, as the numerical computation of higher derivatives is corrupted by computation noise. Here, we introduce a parametric method (PM), based on analytic definitions of the DTW, to allow analytical computation of its derivatives. Three analytic forms, based of combination of sigmoidal (S), Gaussian (G) or exponentials (E) functions, were considered.

A set of simulated ECGs were generated using a forward ECG model (Matlab version of ECGSIM). SHVR was varied from 5 to 40 ms (5 ms-steps). To simulate real recordings, noise available from the MIT-BIH Noise Stress Test Database was added with different peak-to-peak amplitudes (30, 60, 120 and $180\mu V$). The use of PM allowed the inclusion of a larger number of derivatives in the model and reduced the difference between actual and estimated T-waves, especially for larger SHVR. This reduction was more pronounced for model S and G. However, the model E resulted in a lower estimation bias of $\mathcal{V}$-index with respect to the actual SHVR.

1. Introduction

Spatial heterogeneity of ventricular repolarization (SHVR) is a property of the human heart, due to the electrophysiological heterogeneity in action potential repolarization times in different regions of the ventricles, and it is responsible for the genesis of the T-wave on the ECG. The clinical interest in studying the SHVR is due to the fact that its pathological increase could bring to the onset of cardiac arrhythmia, some of them potentially life-threatening (e.g. ventricular fibrillation) [1, 2]. There has thus been a growing interest in finding new metrics for estimating SHVR, non-invasively, from the ECG [3, 4]. In this perspective, we recently introduced the $\mathcal{V}$-index [5], a metric based on a biophysical model of the ECG, according to which the T-waves on the different leads derive from a projection of a main waveform, called Dominant T-Wave (DTW), and its derivatives:

$$\mathbf{\Psi} = \boldsymbol{w}_1 \mathbf{T}_d + \boldsymbol{w}_2 \dot{\mathbf{T}}_d + \dots. \quad (1)$$

where $\mathbf{\Psi}$ is a $[LxN]$ matrix containing the N T-wave samples on L different leads, $\mathbf{T_d}$ is the vector containing the DTW, $\dot{\mathbf{T}}$ the DTW first derivative and $\boldsymbol{w}_1$ and $\boldsymbol{w}_2$ are $[L \times 1]$ vector of *lead factors*, one for each lead. The DTW has a fundamental electrophisological interpretation being the first derivative of the average shape of the repolarization part of the Transmembrane potential (TMP) of myocites.

The dots in equation (1) refer to the fact that the approximation of ψ could be improved through the use of higher order derivatives of the DTW, weighted by the corresponding lead factors. Specifically, the $\mathcal{V}$-index estimates the dispersion of ventricular repolarization, s_ϑ, through the ratio of the standard deviations of the lead factors measured across successive beats on the i-th lead:

$$\mathcal{V}_i = \frac{\mathrm{std}\,[w_2(i)]}{\mathrm{std}\,[w_1(i)]} \approx s_\vartheta. \quad (2)$$

The algorithm for estimating the lead factors is based on a minimization of the difference between the potential measured on the ECG, $\psi(t)$, and its estimate by equation (1), which requires the computation of the DTW and its derivatives. The approach described in [5] is based on a numerical calculation of these quantities: despite simulations showed a linear increase of the $\mathcal{V}$-index with increasing SHVR, it was also demonstrated that a bias in the estimation of the heterogeneity was introduced.

The aim of this article is to introduce some analytic approximations of the DTW and of its derivatives, in analogy to [6]: this approach was developed to investigate whether it was possible to improve the estimate of the lead factors (and thus of the $\mathcal{V}$-index), based on the assumption that this approach could be more resilient to the noise present in real ECGs. Noise in fact dramatically affects the numerical estimate of the DTW derivatives.

2. Method

2.1. Analytical models of DTW

We consider three analytical models of the DTW. They are based on different functions, namely sigmoidal, Gaussian or exponential functions as described in the following.

2.1.1. Model S: sigmoidal function

This model employs a sigmoidal (S) description of DTW according to the T–wave model introduced by [6]. It is based on the following expression

$$T_d(t) = a\left[b + L_{\alpha_1}(t - T_r)\, L_{(-\alpha_2)}(t - T_r)\right] \quad (3)$$

where T_r is the average repolarization time across ventricle and the L_α's are two sigmoidal functions, namely

$$L_\alpha = \frac{1}{1 + e^{-\alpha t}} \quad (4)$$

where α_1 and α_2 are proportional to the maximal slopes (positive and negative, respectively) of the DTW.

2.1.2. Model G: bi-Gaussian function

The DTW is modeled by two Gaussian functions according to [7]

$$T_d(t) = \begin{cases} Be^{\frac{(t-T_r)^2}{2\sigma_1}} & t < T_r \\ Be^{\frac{(t-T_r)^2}{2\sigma_2}} & t > T_r \end{cases} \quad (5)$$

where B is the maximum amplitude (either positive or negative) of the DTW and were σ_1 and σ_2 control the width of the early and late part of the DTW.

2.1.3. Model E: exponential function

Differently from the previous ones, this model describes the repolarization part of the TMP according to the formulation employed in *et al.* [8]

$$TMP(t) = K_2 \frac{\left[(1 - K_3)e^{K_4 t} + K_3\right] e^{-K_5 t}}{1 + e^{K_6 (t - K_7)}} \quad (6)$$

where the K's are the coefficient of the model. The DTW is obtained as the first derivative of equation (6).

2.2. Data analysis and DTW computation

The computation of DTW, its derivative and the associated lead factors are obtained by minimization of the Frobenius norm of the difference between the ECG signal and its approximation by DTWs

$$\epsilon = \left\| \boldsymbol{\Psi} - \hat{\boldsymbol{\Psi}} \right\|_F = \left\| \boldsymbol{\Psi} - \boldsymbol{w}_1 \mathbf{T}_d - \boldsymbol{w}_2 \dot{\mathbf{T}}_d - \ldots \right\|_F. \quad (7)$$

The way the minimization is realized varies if the analytic or numerical form of DTW are employed.

2.2.1. Numerical approach

The algorithm is an extension of the one we previously introduced in the appendix of [5] and it takes into account an higher number of derivatives. Basically, when up to the second derivative of DTW is considered, it can be shown that the DTW which minimizes equation (7) satisfies

$$\begin{aligned}
&T_d(j)[\|\boldsymbol{w}_1\|^2 - 4\boldsymbol{w}_1\boldsymbol{w}_3/(\Delta t)^2 + \\
&\quad 2\|\boldsymbol{w}_2\|^2/(\Delta t)^2 + 6\|\boldsymbol{w}_2\|^2/(\Delta t)^2] + \\
&\quad [T_d(j+1) + T_d(j-1)]\left[2\boldsymbol{w}_1\boldsymbol{w}_3/(\Delta t)^2 - |\boldsymbol{w}_2\|^2/(\Delta t)^2\right] \\
&\quad - 4\|\boldsymbol{w}_3\|^2/(\Delta t)^4 + \qquad (8)\\
&\quad [T_d(j+2) + T_d(j-2)]\,\|\boldsymbol{w}_3\|^2/(\Delta t)^4 = \\
&\quad \sum_{i=1}^{L} \{\Psi_{i,j} w_1(i) - [\Psi_{i,j+1} - \Psi_{i,j-1}]\, w_2(i)/(2\Delta t) - \\
&\quad [\Psi_{i,j+1} - 2\Psi_{i,j} + \Psi_{i,j-1}]\, w_2(i)/(\Delta t)^2\}
\end{aligned}$$

where Δt is the inverse of the sampling rate, while the lead factors are estimated by solving the linear system introduced in [6] and expressed by the equation:

$$\mathbf{W} = \boldsymbol{\Psi}\mathbf{U}^{\mathbf{T}}(\mathbf{U}\mathbf{U}^T)^{-1} \quad (9)$$

where the rows of $\mathbf{U}$ contain the DTW and its derivatives up to the desired order, while the columns of $\mathbf{W}$ are the lead factors. The identification is performed by iteration: the estimate of the lead factors is obtained by solving (9) which are inserted into (8) to obtain DTW, whose derivatives are then computed numerically. The procedure is iterated until the desired convergence is reached: in this paper when the Frobenius norm is below an opportune threshold. The initial estimate of DTW was obtained by Singular Value Decomposition (SVD) [9].

Although the above procedure can be extended to any number of DTW derivative, the high–sensitivity of the computed derivative to noise, makes the use of third DTW derivative (or higher) unpractical.

2.2.2. Analytic models

Also in the parametric approach, the estimation is performed by an iterative method. After having initialized the estimate of DTW by SVD, the approximation is fitted by the desired model function (S, G or E) and then the derivative analytically computed.

After DTW initialization, the lead factor are estimated by solving the linear system previously introduced in Equation (9). The estimated lead factors are inserted in equation (7) and the parameter of the parametric forms adjusted using a non–linear optimization procedure (Levemberg–Marquard) to minimize ϵ. The procedure is iterated between (9) and (7) until the desired convergence (or a maximum number of iteration) is reached.

2.3. Simulated data

Simulated ECGs were obtained using Matlab (The MathWorks, Natick, MA) through the re-implementation of the forward ECG model of ECGSIM [10]. In details, the heart surface is discretized in 257 nodes, in each of which the myocytes are lumped together and share the same TMP. Spatial repolarization heterogeneity across nodes was simulated at different extent ranging from 5 to 40 ms (5 ms-steps). From the TMP, simulated ECG were obtained through the forward transfer matrix $\mathbf{A}$ of ECGSIM (version 1.3). To simulate real recordings, noise available from the MIT-BIH Noise Stress Test Database was added with different peak-to-peak amplitudes $(30, 60, 120$ and 180μV).

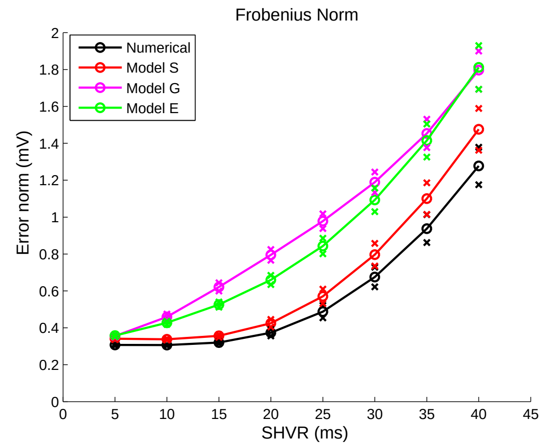
3. Results

The simulations were planned to compare the performance of the three parametric forms of DTW with the numerical approach. Two aspects are mainly investigated: i) the minimization of equation (7), i.e. the capability to fit the ECG for different SHVR; ii) the bias in the estimation of SHVR by the $\mathcal{V}$-index in respect to the one observed with numerical approach.

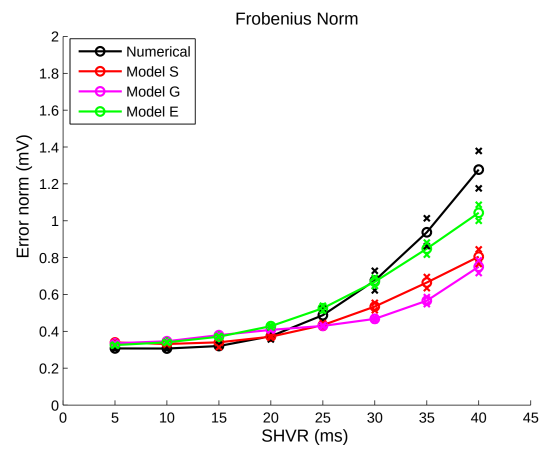
Figure 1 shows the trend of Frobenius norm of ϵ as function of the SHVR values. A common trend is observed for both the numerical and the parametric methods: the norm increases for increasing values of SHVR. Two observations can explain this behavior: the first one is that the validity of the approximation in equation (1) does to not necessarily hold when SHVR increases and higher and higher order derivatives should be included. The second one is that, when SHVR increases, a concomitant increase in the T–wave amplitude is observable and thus the absolute error increases.

The advantages of including a larger number of DTW derivatives in the approximation is well documented by comparison of Figure 1(a) and Figure 1(b), which evidence a drop in the value of the norm when three DTW derivatives are included. Such reduction is more pronounced by model S and model G and is achievable by parametric methods only. In fact, the numerical method could not reach convergence when, at higher SHVR, more than two derivatives are included in the model

Figure 2 shows the performance of parametric methods in the computation of $\mathcal{V}$-index and thus on the estimation of SHVR. In general, the performance of the parametric methods are similar to those of the numerical approach



(a)



(b)

Figure 1. Comparison between the numerical method and the parametric models in the minimization of the Frobenius norm of equation (7). Results obtained using (a) the first DTW derivative only and (b) three DTW derivatives. The black line is repeated in graph (b) for the sake of comparison.

(data not shown), with the exception of model E which showed a lower bias (the curve is closer to black line, representing the true SHVR values).

Concerning the robustness to noise, when SNR is very low, the fitting of the parametric forms becomes more difficult, especially for lower SHR values. In general the performance of the parametric methods was better when three derivatives where used in the approximation of the surface potential Ψ. Figure 3 shows the estimated $\mathcal{V}$-index using model E at various levels of noise and shows the robustness of the approach to the added noise. The performances of each parametric method are summarized in Table 1. Four main issues are considered: the number of DTW derivatives, used in the approximation, which provides the best

Models	DTW deriv.	Noise Robustness	Bias	Norm
S	3	Good	Comparable	Lower
G	3	Very good	Comparable	Lower
E	3	Good	Slightly Lower	Comparable

Table 1. Comparison among the analytic models.

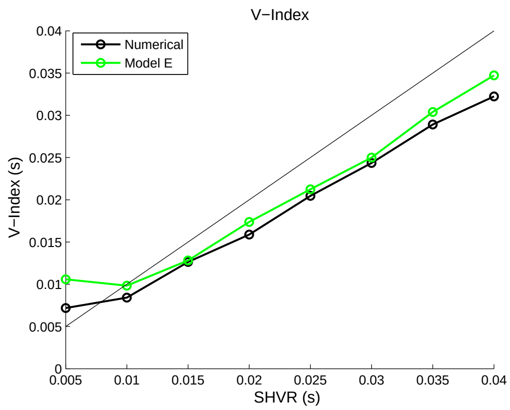


Figure 2. Comparison between the $\mathcal{V}$-index computed with the numerical method and with the model E using three DTW derivatives.

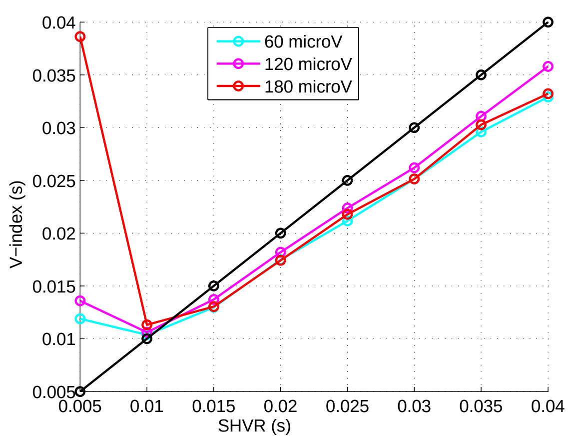


Figure 3. $\mathcal{V}$-index computed for increasing levels of added noise using three DTW derivatives for the model E.

results; the robustness to noise; the bias in the $\mathcal{V}$-index estimation; and finally the capacity of minimizing the Frobenius norm. In Table 1 the latter two columns are expressed as comparison with the numerical method.

4. Conclusions

The use of parametric DTW allowed the inclusion of a larger number of derivatives in the model and reduced the difference between actual and estimated T–waves. This reduction was more pronounced for model S and model G. However, the model E resulted in a lower estimation bias of $\mathcal{V}$-index with respect to the actual SHVR. Finally all the three considered parametric forms proved resistant to noise addition, being model G the most robust.

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