T-Wave Alternans Estimation with Manifold Learning

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Abstract

T-wave Alternans (TWA) measures the differences between consecutive T-waves in Electrocardiographic (ECG) studies, serving as an index for identifying high-risk sudden cardiac death patients. In this study, ECG Imaging (ECGI) is employed to assess the spatial distribution of alternans across the subject's epicardium. ECGI signals were acquired from the torsos of eight patients with Long QT syndrome and three control subjects, while epicardial signals were estimated through the inverse problem of ECG. Conventional TWA estimation methods have limitations in harnessing the spatial and temporal richness of ECGI simultaneously, and to overcome this limitation, we propose using manifold learning (MnL). In this work, we compare linear and non-linear MnL approaches with conventional methods, evaluating the reconstruction error of MnL outputs, reaching minimum values of $0.55\mu V$ *and* $4.22\mu V$ *with linear and non-linear methods, respectively. Our findings suggest that MnL methods can effectively leverage all the information provided by ECGI, facilitating the localization of areas that may exhibit higher levels of TWA.*

1. Introduction

T-wave alternans (TWA) is a high-risk sudden cardiac death (SCD) indicator, which measures the changes in amplitude or morphology of consecutive T-waves in electrocardiographic (ECG) studies [1]. Reducing SCD incidence should be a priority, but TWA assessment is not commonly performed in medical practice, mainly because there exist technical issues such as the lack of consensus on appropriate signal processing and TWA estimation procedures that could yield clinically relevant results [2, 3].

TWA typically manifests as variations of the order of microvolts in consecutive T-waves. These variations can overlap with the spectral range of noise, making it crucial to apply meticulous noise removal techniques to ECG signals to avoid losing physiological information [4]. Furthermore, multiple TWA estimation methods exist, but none of them could be considered the gold standard [3]. The temporal method (TM) is one of the most common TWA estimation methods, which analyzes TWA in the time domain.

The relevance of a combined spatial-temporal study has been demonstrated to be significant in our research context [5]. Taking advantage of an imaging technique such as ECG Imaging (ECGI) allows the study of alternans not only from a temporal perspective, as achieved using conventional ECG, but also from a spatial point of view [6]. However, conventional estimation approaches evaluate each signal individually, disregarding part of the relevant information provided by ECGI [5]. To overcome this limitation, we propose using manifold learning (MnL) techniques to estimate TWA, which can harness both the temporal and spatial information that ECGI data contain. In this work, we use principal component analysis (PCA), a linear method, and an autoencoder (AE) architecture, a non-linear method, to estimate TWA. We aim to compare both techniques with each other and with the TM to determine the advantages of leveraging the temporal and spatial information provided by ECGI simultaneously.

The work is organized as follows. TWA estimation methods are explained in Section 2. Experiments performed and results obtained are described in Section 3. Finally, the conclusions are presented in Section 4.

2. TWA Estimation

In the pre-processing stage, a spline interpolator is used for baseline wander removal, and a zero-phase distortion low-pass filter is applied to eliminate high-frequency noise. In the TWA estimation process step, T-waves are first segmented with the Single Reference Segmentation method [7], which is tailored for ECGI data. After that, even and odd templates for each mesh point are generated by averaging their even and odd T-waves. Finally, TWA

Table 1. Mean of the RE for each subject in the test set, as the original data is reduced to latent spaces of dimensions one to nine. Units are μV.

	C 2	P 5	P 6	P 7	P 8
PCA					
1D	19.92	10.91	5.59	19.37	12.25
2D	11.20	4.88	5.78	10.81	3.36
3D	11.21	3.72	5.73	10.14	3.59
4D	1.92	1.84	1.42	2.82	1.05
5D	1.99	1.90	1.38	2.90	0.98
6D	1.87	1.86	1.38	2.82	0.86
7D	1.87	1.86	1.38	2.82	0.86
8D	1.58	1.86	1.20	2.45	0.85
9D	0.67	1.47	1.05	0.89	0.55
AE					
1D	56.51	24.70	86.26	45.62	138.36
2D	20.43	7.39	19.02	21.78	11.16
3D	15.56	7.43	5.59	9.09	4.99
4D	16.56	7.64	9.51	18.67	10.67
5D	9.62	5.08	8.52	8.86	7.49
6D	7.91	4.22	5.41	7.30	6.31
7D	10.78	6.83	5.51	12.16	7.42
8D	16.34	5.55	5.03	22.20	9.33
9D	20.18	9.55	14.20	10.27	15.56

is estimated with the TM or with MnL. The difference between the even and odd templates is calculated for each mesh point individually to estimate TWA with the TM. On the other hand, we propose two approaches for TWA estimation with MnL.

First, PCA involves linearly transforming the variables in the original dataset into a new set of uncorrelated variables known as principal components (PC). The data are projected in the directions of maximum variance in the original dataset, and the PCs are ordered based on their corresponding variances. The first PC in the list contains the most information about the original space, while the latter may contain information that can be discarded. In this work, the PC is computed by linearly combining a set of signals obtained by the TM TWA estimation, which form the training set, and the obtained transformation is applied to the test set.

Second, an AE gradually compresses the data into a lower-dimensional (encoder) space and then reconstructs it to the original (decoder) space. The encoder in this work contains six fully connected layers, each followed by a leaky rectified linear unit layer with a scalar multiplier of 0.75 for negative inputs, serving as the activation function. The bottleneck layer has an output size of one to nine, indicating the dimensions to which the data have been reduced. The decoder consists of the opposite configuration of the encoder, allowing the data to recover their original size.

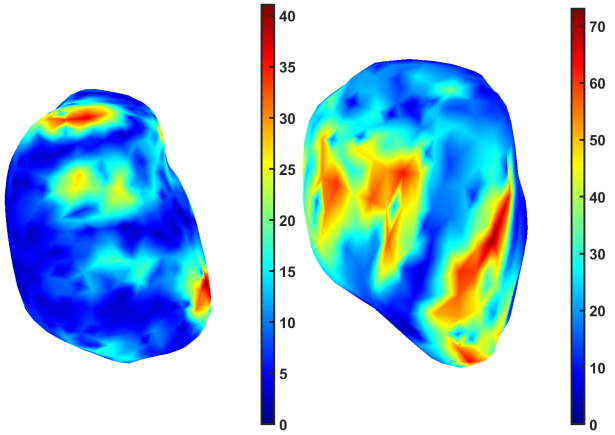

Figure 1. TWA estimated with the TM in control subject 2 (left) and LQTS patient 8 (right). Units are μV.

However, before the last fully connected layer, a dropout layer with a probability of dropping out input elements of 0.2 is included. Finally, a regression layer is added as the last layer. The Adam optimizer is utilized to train the AE. Minibatches of size 100 are used, and a maximum of 500 epochs is set. The training is stopped if no improvement is observed within six epochs. Like PCA, the AE is trained with the training set and then tested with the test set.

These two dimensionality reduction methods enable the reconstruction of the original space, thus allowing the reconstruction error (RE) calculation. Therefore, they will help us leverage all the information provided by ECGI and assess the lower-dimensional space representation quality. To visualize spaces exceeding three dimensions, we employ t-distributed Stochastic Neighbor Embedding, another MnL technique that can reveal hidden patterns and structures in complex datasets.

3. Experiments and Results

The ECGI database includes recordings from eight patients with Long QT Syndrome (LQTS) and three control subjects. The data were acquired at the Cardiac Bioelectricity and Arrhythmia Center, Yoram Rudy Lab at Washington University in St. Louis, from a previous study [8]. Torso measurements were extracted from body surface potential mapping, and epicardial potentials were estimated by solving the inverse problem of electrocardiography and using other imaging modalities [6]. Control subject 1 and LQTS patients 1, 2, 3, and 4 form the training set, and control subject 2 and LQTS patients 5, 6, 7, and 8 belong to the test set.

Table 1 displays the mean REs for all signals belonging to each subject, with each error computed over the maximum of the signal utilized as input in the MnL method. As expected, using more PCs to generate the embedded space

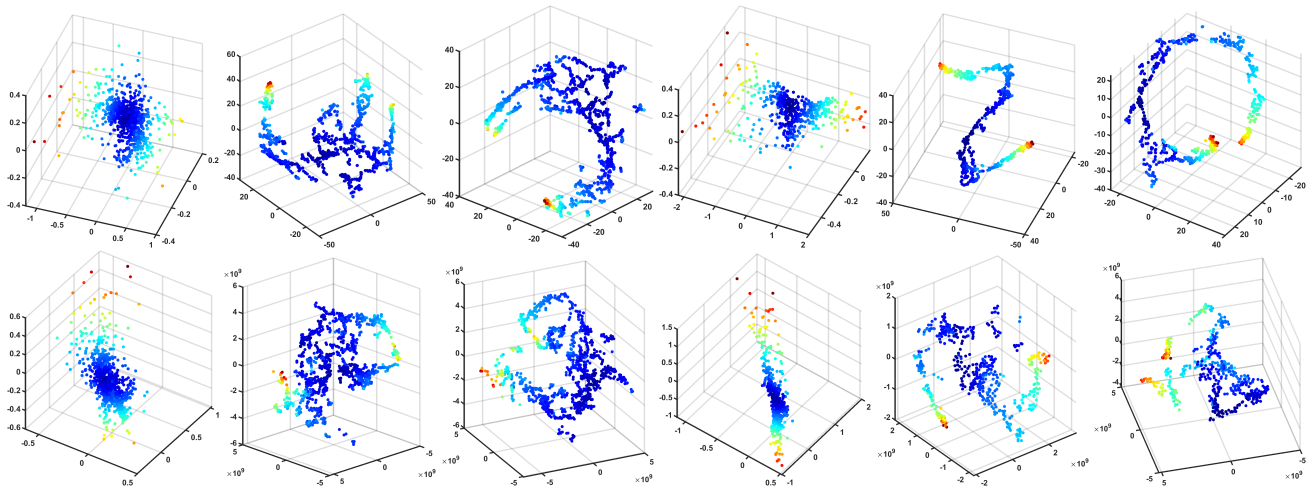

Figure 2. Latent spaces generated by PCA (row 1) and the AE (row 2) in control subject 2 (columns 1, 2, and 3) and LQTS patient 8 (columns 4, 5, and 6), with original data reduced to three (columns 1 and 4), six (columns 2 and 5), and nine (columns 3 and 6) dimensions. Colors correspond to the TM TWA estimation specified in Figure 1.

in PCA decreases the RE. However, in the case of the AE, higher-dimensional spaces do not always result in smaller errors. For instance, in control 2, a latent space of six dimensions yields an error of $7.9\mu V$, while a space of nine dimensions results in an error of $20.2\mu V$. In general, PCA REs tend to be smaller than AE REs.

Figure 1 displays the epicardial meshes of control 2 and patient LQTS 8, colored according to the TM TWA estimation. Figure 2 presents the lower-dimensional spaces that PCA and the AE generated for these two subjects, with colors corresponding to those in Figure 1. In Figure 2, specifically, in columns 1 and 4, the yellow to red areas are sparser, as these panels represent cases where the original data dimensions are reduced to three. When data are reduced to six and nine dimensions (columns 2 and 5, and 3 and 6, respectively), the yellow to red areas are more localized in the embedded space and are separable from blue regions in almost all cases.

Figure 3 represents the meshes and latent spaces colored according to the RE. In the case of PCA, the RE decreases as the data are reduced to higher dimensions, as illustrated in rows 1 and 3. Specifically, the data are reduced to three, six, and nine dimensions in columns 1 and 2, 3 and 4, and 5 and 6, respectively. However, as previously noted, this trend does not always apply to the AE (even rows). For example, in the second row, the RE is smaller in the six-dimensional space than in the nine-dimensional space.

4. Conclusions

This work addressed the estimation of TWA in ECGI recordings with MnL. Our results suggest that those signals with a higher level of TWA according to a well-known conventional method, i.e., the TM, are localized in specific areas of the latent space when using any of the MnL methods tested. Additionally, REs remained small in most cases, indicating the good quality of the embedded spaces. In this scenario, a new research direction for exploring alternans emerges. Further studies will aim to understand the embeddings better and make them more accurate complements to conventional TWA estimation methods.

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References

[1] Cutler MJ, Rosenbaum DS. Explaining the clinical manifestations of T wave alternans in patients at risk for sudden cardiac death. Heart Rhythm 2009;6(3):S22–S28.

[2] Gimeno-Blanes FJ, et al. Sudden cardiac risk stratification with electrocardiographic indices - a review on computational processing, technology transfer, and scientific evidence. Frontiers in Physiology 2016;7(82):1–17.

[3] Martinez JP, Olmos S. Methodological principles of T wave alternans analysis: a unified framework. IEEE Transactions on Biomedical Engineering 2005;52(4):599–613.

[4] Caulier-Cisterna R, et al. Spatial-temporal signals and clin-

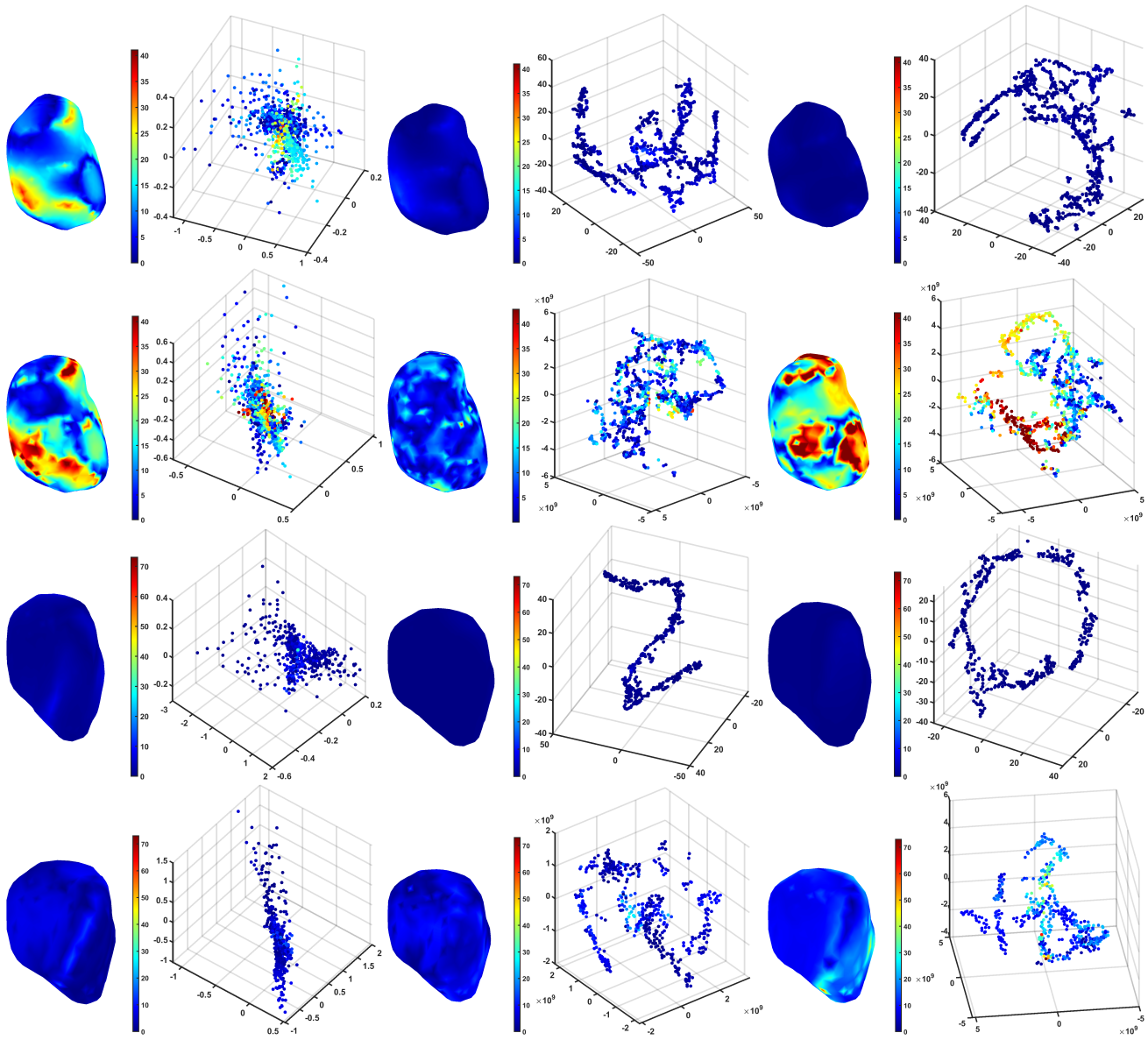

Figure 3. Epicardium meshes (odd columns) of control subject 2 (rows 1 and 2) and LQTS patient 8 (rows 3 and 4), and PCA (odd rows) and AE (even row) embedded spaces when the original data has been reduced to three (columns 1 and 2), six (columns 3 and 4) and nine (columns 5 and 6) dimensions. Colors are according to the RE (μV).

ical indices in electrocardiographic imaging (I): Preprocessing and bipolar potentials. Sensors 2020;20(22):1–28.

[5] Caulier-Cisterna R, et al. Spatial-temporal signals and clinical indices in electrocardiographic imaging (II): Electrogram clustering and t-wave alternans. Sensors 2020;20(11):1–24.

[6] Ramanathan C, et al. Noninvasive electrocardiographic imaging for cardiac electrophysiology and arrhythmia. Nature Medicine 2004;10(4):422–428.

[7] Sánchez-Carballo E, et al. Single reference segmentation to estimate t-wave alternans. In 2023 Computing in Cardiology (CinC), volume 50. 2023; 1–4.

[8] Vijayakumar R, et al. Electrophysiologic substrate in congenital long QT syndrome: Noninvasive mapping with electrocardiographic imaging (ECGI). Circulation 2014; 130(32):1936–1943.

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