Novel Metric Using Laplacian Eigenmaps to Evaluate Ischemic Stress on the Torso Surface

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Abstract

The underlying pathophysiology of myocardial ischemia is incompletely understood, resulting in persistent difficulty of diagnosis. This limited understanding of underlying mechanisms encourages a data driven approach, which seeks to identify patterns in the ECG data that can be linked statistically to disease states. Laplacian Eigenmaps (LE) is a dimensionality reduction method popularized in machine learning that we have shown in large animal experiments to identify underlying ischemic stress both earlier in an ischemic episode, and more robustly, than typical clinical markers from signal space. We have now extended this approach to body surface potential mapping (BSPM) recordings acquired during acute, transient ischemia episodes from animal experiments following graded heart rate increase and to human recordings acquired during percutaneous transluminal coronary angioplasty (PTCA).

The LE algorithm has been previously described. Here we decompose the entire collection of BSPM's and represent them in a low-order coordinate system as trajectories that represent all leads together, one trajectory for each beat. The shape of the trajectory reflects morphological features in the input signals and changes in shape have been previously reported to reflect injury conditions such as ischemia.

Our preliminary results suggest that the LE approach is sensitive to the spatiotemporal electrocardiographic consequences of ischemia-induced stress within the heart and on the epicardial surface. In this study, we expand this technique to the body surface of animals and humans. Across 10 episodes of induced ischemia in animals and 200 human recordings during PTCA, the LE algorithm was able to detect ischemic events from BSPM as changes in the morphology of the resulting trajectories.

The sensitivity of this method on BSPM, and its ability to leverage a predefined LE space, suggests that its performance on experimental data may be transferable to the clinical setting and could support novel approaches during, for example, clinical stress testing.

1. Introduction

Myocardial ischemia occurs when the coronary perfusion in the heart is outstripped by the metabolic demand of the cardiac tissue. This perfusion deficit results in a series of electrical changes that can be measured on the body surface. This electrical response is a reflection of the ischemic stress being induced on the heart and can be used as a non-invasive means of diagnosis. Diagnosis based on the ECG has both a long history and a compelling rationale; ischemia generates changes in cardiac electrical behavior that should be visible in the ECG. However, identification of robust markers of ischemia remains challenging. Traditional biomarkers of ischemia, such as upward or downward shifts in the ST segment, are thought to be driven by the differences in transmembrane potentials between healthy and ischemic regions. This potential difference gives rise to injury currents which drive diagnostic ST-segment shifts. However, ischemia affects more than the plateau of the action potential, suggesting that additional metrics could reveal ischemic stress earlier and with a greater robustness than current clinical standards. [1] To leverage the changes across the entire QRST we employed a machine learning technique known as Laplacian Eigenmaps (LE)[2]. LE is an algorithm that utilizes the entire QRST over all available leads nonlinearly projected onto a lower dimensional parameter space from which differentiating features can be extracted. We applied LE to quantify changes in this lower dimensional space, or LE

space, to produce what we call the LE metric. Our previous work with LE showed that LE based metrics could detect ischemia earlier in an ischemic episode than traditional signal space metrics. [3] This work extends the capability of LE to the body surface in both our closed chest animal experiments and BSPM data collected during PTCA where the LE space can be defined ahead of time. With this predefined LE space new subjects can be mapped into the space and the deviation away from the training manifold may be able to gauge the level of ischemic stress in the new subject using the deviation in the LE space.

2. Methods

2.1. Experimental Data Collection

The experimental cardiac electrograms and electrocardiograms used for this study were collected over a series of canine and porcine experiments during which we induced episodes of acute myocardial ischemia. Each ischemic episode, or intervention, lasted 15 minutes with a 30-minute downtime to allow the tissue to recover before subsequent episodes. Anywhere from 3-8 interventions were performed per animal, using ischemic protocols designed to produce a graded ischemia in the tissue perfused by the left anterior descending (LAD) artery. Electrograms were captured during experiment using 20 -30 plunge needles with ten electrodes along the shaft that measures the transmural potentials in addition to an epicardial sock with 247 electrodes. Body surface potentials were then captured using 72 - 100 electrodes across the anterior surface of the torso surface. Signals were captured simultaneously using a 1024 channel multiplexor at 1kHz. The signals were the processed and fiducialized using the PFEIFER signal processing platform. [4]

2.2. BSPM Collection

During acute episodes of percutaneous transluminal coronary angioplasty (PTCA) 120 unipolar leads were placed on the body surface during 200 episodes of complete coronary occlusion. During each of these episodes a baseline recording was taken and another recording was taken at the peak of the inflation. These recordings were captured using the Dalhousie leadset which allowed the 120 recordings to be mapped to to a 352 electrode leadset encompassing the entire torso surface. Some subjects have multiple inflations within the same vessel included in the dataset.

2.3. Laplacian Eigenmaps

Laplacian Eigenmaps (LE) is a dimensionality reduction method that is capable of reducing many simultaneous time signals into a trajectory on a manifold of lower dimensionality. In both implementations, as described in detail in Erem *et al.*[2], each time point measured across the entire set of electrodes corresponds to a single location on the manifold. These trajectories were obtained by computing a matrix of inverse exponentials of pairwise Euclidean distances between all input points, and then taking its singular value decomposition (SVD). The inverse exponentials are scaled to emphasize local relationships in the data. The SVD determined and ranks the significance of the coordinates in the lower dimensional space. We defined three relevant coordinates to be the second through fourth columns of the right singular vector matrix (the first column was ignored because it is constant.) [5] [2]

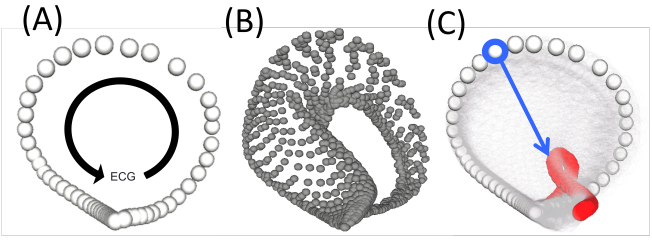

Figure 1. Laplacian Eigenmap manifolds. A.) This manifold consists of a single trajectory corresponding to a run during the rest period, before the induction of ischemia. The progression of the ECG and its relation to the trajectory are shown by the black arrow. B.) This manifold shows several runs mapped into the same manifold space. Each trajectory corresponds to a single run during the intervention. C.) This final manifold shows the trajectory of the run taken at rest (white) and the final run of the intervention (red) with all other trajectories set to be transparent. The blue arrow corresponded to the point on the trajectory that showed the greatest sensitivity to the underlying ischemic stress.

2.3.1. LE from Experimental Recordings

For the experimental recordings the manifold coordinates were learned using the beats recorded during the initial rest period before the first intervention was induced. Once the coordinate space was identified, it was populated with subsequent beats over repeated episodes of induced ischemia, as seen in Fig. 1B. The manifold produced by this analysis consisted of a single trajectory for every run in the experiment. As progressively ischemic runs were mapped into the manifold space, large regions of the trajectories responded to the underlying stress state. To determine which point on the trajectory responded most robustly, we measured the Euclidean distance between each point on the healthy trajectory and its corresponding point on each subsequent trajectory for each run in the exper-

iment. The trajectory point that showed the greatest CR was chosen as the LE metric for that intervention. The magnitude of movement along the blue arrow, seen in Fig. 1C, was used as the LE metric. [6] [3]

2.3.2. LE using BSPMs

The manifold coordinates for the BSPMs were learned using a control dataset. Once the LE space was defined all other ischemic episodes were then mapped into the predefined LE space. However, due to the limited temporal sampling we have of the ischemic event in this dataset t is not possible to perform the same analysis as was done on the experiment recordings. As a preliminary result we quantified the summed euclidean distance between the training manifold to both the control and peak trajectories. Figure 2 shows the training manifold (A.)) and the two trajectories B.) and C.) corresponding to the BSPMs in D.) and E.). These BSPMs were visualized using the *map3d* platform. [7]

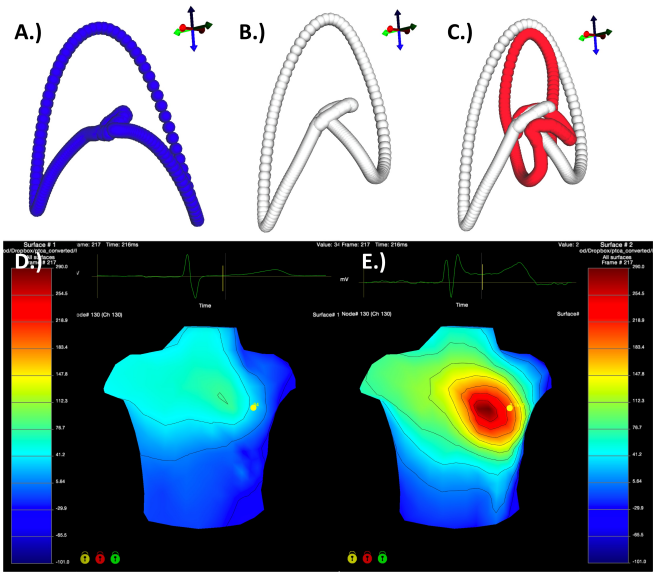

Figure 2. LE manifolds and the corresponding BSPMs. A.) The trajectory of the BSPM used to learn the LE space. B.) The baseline manifold mapped into the predefined LE space. C.) The baseline and peak manifold mapped into the predefined LE space. D.) The baseline BSPM with a selected electrode and corresponding time signal. E.) The peak BSPM with a selected electrode and corresponding time signal.

2.4. Signal Space Metrics

In order to establish the relative performance of the LE metric in our previous work we employed a series of signal space metrics. Two ST-segment based metrics were employed, the ST40% and the ST60 metric. [8] We also looked at the Twave integral, the peak of the Twave, and the integral of the QRS. We will be performing a similar analysis

2.5. Measures of Metric Quality

In order to compare the performance of the LE metric against the signal space metrics two measures were developed to quantify how early each metric was able to detect ischemia and the robustness with which each metric responded using the experimental recordings. These metrics were calculated on the representative beats we extracted over the course of the experiments. We will refer to each extracted beat as a 'run", defined here as the first representative beat per continuous recording (typically 3 s in duration taken every 15 seconds during the ischemic interventions and every ten minutes during the rest periods). We captured 80–300 such runs over the course of each experiment. To follow the progression of metrics over the experiments, we defined "run-metric plots", continuous plots of each metric over one or more intentions (see Figure 3). We also defined the Time to Threshold (TTT) as a measure of how early each metric responds and the Contrast Ratio (CR) as the magnitude of the response with respect to the mean amplitude at rest extracted from the run-metric plots. We hope to now extend these same measures to the torso surface from our animal and human recordings.

$$\textbf{TTT} = \overline{A_r} + \frac{A_m - \overline{A_r}}{3}$$
$$\textbf{Contrast Ratio (CR)}: = \frac{A_m}{A_r},$$

where $\overline{A_r}$ is the mean value at rest or control of any metric and A_m is the maximum value of the metric.

3. Results

3.1. Time to Threshold and Contrast Ratio

Table 1 shows the values of TTT and CR for all the metrics we compared in a previous study using LE. Of the 51 interventions evaluated, the LE metrics detected ischemia earlier than the ST40% metric in 42 of the episodes with a mean decrease in detection time of 36.4 s. The ST40% metric detected ischemia earlier than the CV metric in 38 of the episodes with an average difference of 32.7 s. A comparison of the two traditional metrics showed no meaningful differences in performance. The results for CR, showed that both LE and CV metrics exhibited a greater degree of contrast from baseline levels (5.5 and 5.9 for LE and CV, respectively) than the two ST segment based metrics (3.5 and 3.6 for ST60 and ST40%).

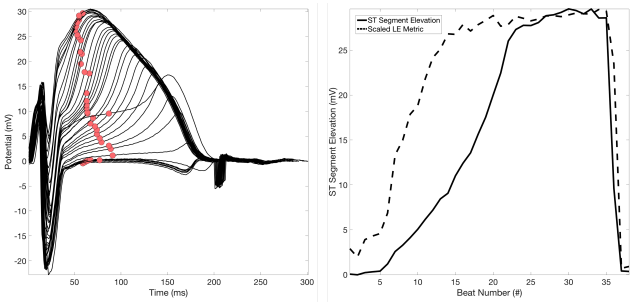

Figure 3. ST Segment Elevation vs. the LE Metric. LEFT: A single electrode with consecutive runs overlaid over a single episode of ischemia. The red circles are tracking the ST40% metric. RIGHT: The ST40% run-metric (solid) overlaid with the LE run-metric(dashed).

Table 1. Evaluating the TTT and CR of Four Metrics Designed to Detect Ischemic Stress

Metric	TTT (s)	CR
ST40%	262.8	3.6
ST60	264.2	3.5
LE	226.5	5.5

3.2. Human BSPM stratification

The LE algorithm was able to distinguish between the baseline and peak recordings in both the animal and human ischemic episodes. The delineation between the baseline and peak recordings proved to be statistically significant. While preliminary, this performance on the body surface is promising going forward.

4. Discussion and Conclusions

The sensitivity of the LE approach to ischemic stress regardless of the anatomical origin of the signals shows great utility in using metrics derived from this low-order space. While our results on the torso surface are preliminary, in both animals and humans, the ability to detect ischemia from the torso surface suggests that the heightened performance of the LE metric on the cardiac surface versus traditional metrics may be transferable to the clinical setting.

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