Realistic Training Data Improve Noninvasive Reconstruction of Heart-Surface Potentials

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Abstract—**The inverse problem of electrocardiography is to noninvasively reconstruct electrical heart activity from body-surface electrocardiograms. Solving this problem is beneficial to clinical practice. However, reconstructions cannot be obtained straightforwardly due to the ill-posed nature of this problem. Therefore, regularization schemes are necessary to arrive at realistic solutions. To date, no electrophysiological data have been used in reconstruction methods and regularization schemes. In this study, we used a training set of simulated heart-surface potentials to create a realistic basis for reconstructions of electrical cardiac activity. We tested this method in computer simulations and in one patient. The quality of reconstruction improved significantly after projection of the results of traditional regularization methods on this new basis, both *in silico* (p<0.01) and *in vivo* (p<0.05). Thus, we demonstrate that the novel concept of applying electrophysiological data might be useful to improve noninvasive reconstruction of electrical heart activity.**

I. Introduction

HEART rhythm disorders kill 7 million people worldwide each year. Body-surface electrocardiograms (ECGs) are widely used to assess cardiac arrhythmias. However, these only reflect the attenuated and dispersed electromagnetic propagation of the heart's electrical activity to the body surface. Direct, noninvasive assessment of electrical processes at the level of the heart muscle would be of great benefit to clinical practice. This can be achieved by solving the *inverse problem of electrocardiography*, which would yield electrical heart activity in terms of body-surface ECGs and the corresponding patient-specific torso-heart geometry.

During the last decades, much progress has been made in tackling the inverse problem of electrocardiography [6] and applications in humans appear with increasing frequency. [9] However, reconstruction of cardiac electrical activity remains imperfect. This is partly due to the ill-posedness of the inverse problem, meaning that little variation (noise) in the input data will yield unique but unrealistic variations in the reconstructions. To cope with this problem, regularization is applied, incorporating additional knowledge to arrive at more realistic solutions. Until now, additional constraints have been based mainly on physical or mathematical properties of the problem. [6, 8] It might be beneficial to also include electrophysiological knowledge in the reconstruction process. In this paper, we investigate whether the use of a training set of cardiac electrical activity can improve the quality of reconstructions.

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II. The Inverse Problem of Electrocardiography

The goal of the inverse problem of electrocardiography is to reconstruct electrical heart activity in terms of body-surface ECGs and the patient-specific geometry. The electrical activity of the heart can be represented by different models. Most often, models are chosen that reconstruct heart-surface potentials (epicardial potentials) or activation sequences. In this paper, we use a potential-based formulation. This is represented by the following *forward* problem:

$$\Phi_B = Z \cdot \Phi_H$$

in which Φ_B represents the vector of body-surface potentials, Φ_H is the vector of heart-surface potentials, and Z is the *transfer matrix* that describes the electromagnetic relation between those potential vectors. The transfer matrix is based solely on geometrical and conductivity properties of the torso. Usually, the transfer matrix is determined from a patient-specific Computed Tomography (CT) scan.

In the inverse problem, the body-surface potentials Φ_B and the transfer matrix Z are known. Due to the ill-posedness of the problem, direct solutions are very sensitive to noise, even when Z would be invertible. By applying regularization schemes, the ill-posed nature of this problem can be restricted. In this paper, we use four different regularization methods that are commonly applied:

- Truncated Singular Value Decomposition (tSVD), which solves the problem with a least-squares solution based on truncation of the less important components of the decomposed problem. [4]
- Tikhonov regularization, in which a constraint is placed on the amplitude of the potentials. [7]
- Greensite Singular Value Decomposition, in which both spatial and temporal regularization are used to arrive at a better solution. [5]
- Generalized Minimal Residual (GMRes) method, an application of iterative Krylov subspace methods. [10]

Every method has a *regularization parameter* that balances the influence of the regularization and the ill-posed nature of the problem. For example, in tSVD the regularization parameter is the truncation number: truncating more rigorously will reduce the influence of the ill-posed nature of the inverse problem, but will ultimately also reduce the solution space to unrealistic results. In other regularization schemes, the regularization parameters aim at finding a similar balance.

III. PROJECTING ON A REALISTIC BASIS

Traditional regularization methods incorporate mathematical or physical information to arrive at a better solution, but do not take advantage of biological properties. A novel approach of dealing with the ill-posed nature of the inverse problem would be to use electrophysiological knowledge. In this study, we investigate the use of a training set of heart-surface potentials to create a new basis for the reconstructions of electrical heart activity.

A. Including Training Data of Heart-Surface Potentials

If a time-series of realistic heart-surface potentials $\Phi_H^{\#}$ is available, Singular Value Decomposition (SVD) yields:

$$\Phi_H^{\#} = U \cdot D \cdot V^T$$

in which the columns of U represent a spatial basis for that set of realistic heart-surface potentials, the columns of V represent a temporal basis, and the diagonal matrix D presents the corresponding singular values. It is common to order these diagonal entries in non-increasing order; thus, the largest singular value is presented as first. The first singular value can be interpreted as a weight, connecting the first temporal pattern (first column of V) with the first spatial pattern (first column of U). The last singular values will be very small and correspond to patterns that hardly contribute to spanning the space of training potentials, such that truncation may be applied to arrive at smaller spatial and temporal bases. Condensed bases might be beneficial as they leave fewer possibilities for ill-posed influences that could result in unrealistic solutions.

Application of SVD on a set of realistic heart-surface potentials $\Phi_H^{\#}$ should be distinguished from application of SVD as a regularization method as described in the previous section. There, truncated SVD is applied to the transfer matrix Z and yields a spatial basis for potentials on the body surface, a spatial basis for potentials on the heart surface, and their corresponding singular values. [2] However, these bases and their singular values are determined by transferability properties of the torso and do not incorporate any electrophysiological cardiac properties.

In contrast, applying SVD on a set of realistic heart-surface potentials $\Phi_H^{\#}$ provides a spatial basis U that represents the electrophysiological knowledge that could be used for improving reconstruction quality. By projecting the (perhaps less strictly) regularized results of traditional regularization methods on this realistic basis, a preference for more realistic solutions could be introduced.

B. Obtaining or Generating Training Data

Obtaining a set of training potentials on the heart-surface $\Phi_H^{\#}$ that represents realistic electrical cardiac activity is essential for applying the method described above. One way to obtain such a set is to measure heart-surface potentials in humans or animals. However, ethical and practical problems limit availability of these data. A whole-heart model, based on coupled electrochemical models of heart muscle cells, would provide a detailed and realistic set of training data. Unfortunately, this is not yet possible due to computational issues. However, a simpler and more macroscopic model might already provide realistic data and was used in this study.

IV. IN SILICO EXPERIMENTS

A realistic geometry and transfer matrix were used to perform simulations to investigate the advantages of using a realistic basis for heart-surface potentials.

A. Methods

In a patient, we measured body-surface ECGs simultaneously at 256 locations. A CT scan was performed to extract the locations of the body-surface electrodes and to extract the exterior heart surface. From the digitized geometry, a transfer matrix was computed with methods available from the SCIrun software repository. [1] For the *in silico* experiments, the body-surface ECGs were not used, as no reference for corresponding heart-surface potentials was available. Instead, testing potentials on the heart surface were generated with a FitzHugh-Nagumo (FH-N) model, which models excitable systems in general, not specifically of cardiac origin. [3] Also a training set of heart-surface potentials was generated with this model. For realism, locations of first activation, as well as model parameters, were varied. The random locations not only represent normal (sinus rhythm) heart beats, but also spontaneous beats (extrasystolic activity). In some training beats, multiple random locations of first activation were used, to represent simultaneous extrasystolic activity or biventricular pacing. We generated a training set of heart-surface potentials consisting of 35 beats and a test set of 12 beats. Subsequently, SVD was applied to the set of training data to get the realistic spatial basis U for heart-surface potentials.

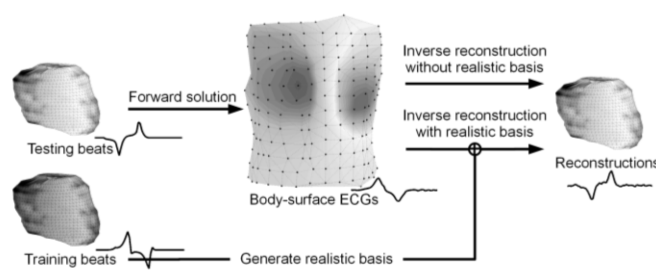

Figure 1. The setup for *in silico* experiments. Testing and training potentials are generated on the heart surface (left) and are used for forward computation of testing body-surface potentials and creation of a realistic heart-surface potential basis, respectively (middle). Subsequently, reconstructions of heart-surface potentials are performed (with and without projection on the realistic basis) and compared to the original testing potentials on the heart surface (right).

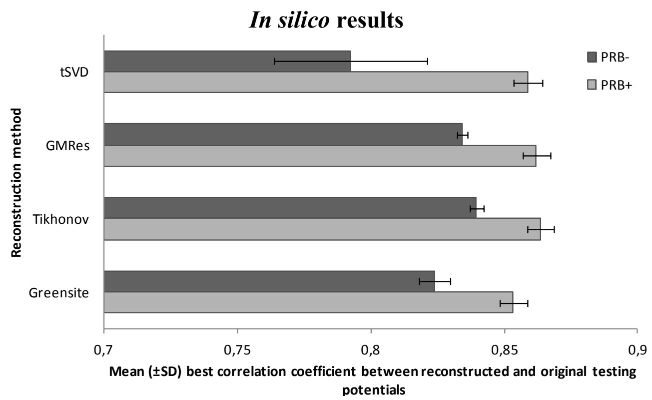

Figure 2. Correlation coefficients (average over 8 tests with each 12 beats) for reconstructed and original testing potentials for different regularization schemes, with and without projecting on a realistic basis for heart-surface potentials. Reconstructions significantly improve when projecting on a realistic basis (PRB+) compared with not projecting on a realistic basis (PRB-). Abbreviations: tSVD: truncated Singular Value Decomposition; GMRes: Generalized Minimal Residual method; Tikhonov: Tikhonov regularization; Greensite: Greensite SVD regularization.

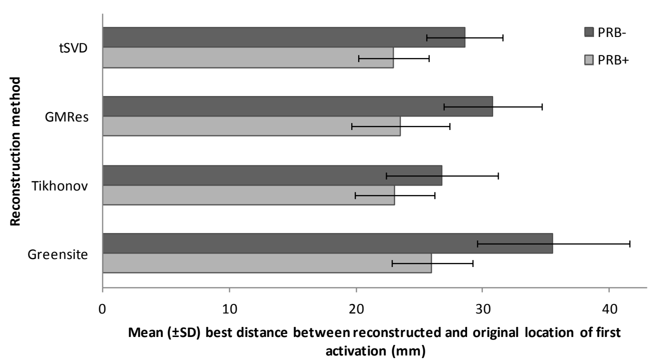

Figure 3. Average distances between reconstructed and original location of first activation on the heart surface. The distance significantly decreases when projecting on a realistic basis (PRB+) compared with not projecting on a realistic basis (PRB-). Abbreviations and methods equal to Figure 2.

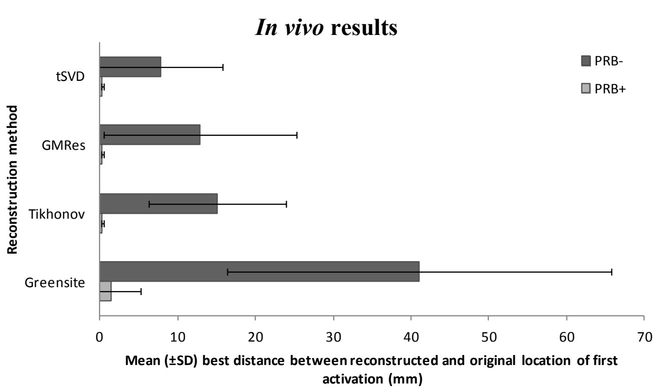

Figure 4. Average distances between reconstructed and known location of first activation in a patient's heart over 7 beats. Note that as with previous experiments, optimal results are selected for comparison. Abbreviations and methods as shown in Figure 2.

The test set of heart-surface potentials, together with the transfer matrix, was used to generate test body-surface potentials, to which some noise was added for realism. Additionally, noise was added to the geometry. Next, traditional regularization methods with and without projection onto the realistic basis were used to reconstruct the corresponding heart-surface potentials. Quality of reconstruction is expressed in correlation coefficients or in distance between the reconstructed and original location of first activation. The location of first activation is determined as the location with the earliest minimum derivative (earliest max –dV/dt) during a QRS complex.

Methods exist for automatically selecting regularization parameters. However, these do not always perform consistently or optimally. Therefore, in this study, reconstructions were made for all (or a large set of) possible reconstruction parameters. By doing so, it is possible to genuinely investigate the potential influence of training data, without artifacts resulting from inadequate parameter selection methods. When projection onto the realistic basis was applied, also the size of the new basis was varied. Truncating the realistic basis represents a more condensed solution space, allowing less ill-posed influences and more guidance by the training set. For all possible regularization parameters and (if applicable) basis sizes, the reconstruction with the highest correlation or lowest distance to location of first activation was selected.

In silico experiments were repeated eight times to confirm consistent results. Figure 1 outlines the *in silico* setup.

B. Results

Correlation coefficients (Figure 2) show that reconstructing with projection on a realistic basis of heart-surface potentials significantly improves the reconstruction quality *in silico* ($p<0.01$ for all reconstruction methods). Similarly, distance to location of first activation (Figure 3) decreases significantly ($p<0.01$ for all methods).

Although not shown, optimal regularization parameters did not significantly differ when afterward projection on the realistic basis was applied compared with the regularization parameter without afterward projection. Thus, projecting on a realistic basis does not result in less need for strict regularization. Apparently, projecting on a realistic basis improves the reconstruction quality on itself.

V. In vivo experiments

A. Methods

For the real geometry used for the *in silico* experiments, also real body-surface measurements were available, making it possible to reconstruct heart-surface potentials from patient-specific data. Although no heart-surface potentials were available as reference, it was known that the patient was biventricularly paced. The pacing leads could be detected in the CT scan and provided the known location of first activation, which provided a reference to compare to the reconstructed location of earliest activation. Body-surface measurements were selected that represented QRS complexes of paced beats. Regularization with and without projection on the realistic basis was performed for all possible regularization parameters and all possible sizes of the realistic basis; reconstructions with a minimal distance between reconstructed and known locations of first activation were selected for comparison.

B. Results

Figure 4 shows the results of the *in vivo* reconstructions for seven representative heart beats. Projecting on a realistic basis significantly improves the accuracy of detection of first-activation location ($p<0.05$ for all reconstruction methods). Note that almost perfect reconstruction of location of first activation is achieved after projection on the realistic basis.

VI. Discussion

In this study, we aimed at improving noninvasive reconstructions of electrical cardiac activity by including electrophysiological information. Therefore, we used a training set of simulated heart-surface potentials to create a realistic basis for reconstructions of electrical cardiac activity. We tested this method in computer simulations and in one patient. The quality of reconstruction improved significantly after projection of the results of traditional regularization methods on this new basis, both *in silico* ($p<0.01$) and *in vivo* ($p<0.05$).

It is fascinating that the very simple training set generated with a FitzHugh-Nagumo model already improves quality of reconstruction of heart-surface potentials in one patient. The FH-N model represents action potentials of nerves; it thus lacks the plateau phase of a cardiac action potential. It is to be expected that a more realistic training set introduces even more improvements. However, obtaining more realistic training data will be difficult. Representative and detailed epicardial measurements in animals and humans are difficult to obtain. Whole-heart models might provide a useful alternative when computational issues are resolved.

A limitation of the current study is that automatized selection of regularization parameters was not used, which would be necessary for practical application. However, by searching the whole space of possible regularization parameters, the true potential of projection on a realistic basis could be evaluated.

Another limitation is that in the *in silico* experiments the same model is used for both the forward solution (for generating testing body-surface potentials) and the inverse solution (for reconstructing corresponding heart-surface potentials). This neglects modeling error in the forward/inverse model and is an inherent limitation of *in silico* studies. Nevertheless, we have demonstrated that consistent results are achieved when applying our methods *in vivo*, although in only one patient and with only the pacing locations as available reference.

Apart from general improvement of reconstruction quality, a training set of heart-surface potentials might provide other benefits. For example, it might be useful to apply a disease-specific training set, to focus on a specific electrical abnormality.

Nevertheless, it remains to be investigated to which extent a training set can corrupt reconstructions. A measure for the projection error might provide a useful tool to quantify the amount of bias that is introduced by projecting on a realistic basis. Whether that bias is useful or corruptive will be difficult to assess. A trained cardiologist should assess both the reconstruction with and without projection to estimate the influence and usefulness of the projection bias.

In this paper we have introduced the novel concept of incorporating electrophysiological knowledge to tackle the ill-posed nature of the inverse problem of electrocardiography. This restricts the solution space to physiologically and pathologically relevant possibilities. We have demonstrated that the use of a training set of heart-surface potentials improves reconstruction quality *in silico*. Our expectation that similar results will hold in humans is encouraged by consistent results in one patient.

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