SOME SPATIO-TEMPORAL APPROACHES TO INVERSE ELECTROCARDIOGRAPHY

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ABSTRACT

In inverse electrocardiography one tries to accurately and meaningfully characterize cardiac electrical activity from electrical potential measurements on the body surface and a volume model of the torso. This is a typical ill-posed bioelectric field problem requiring constraints (regularization). One source of constraints is the strongly spatio-temporal nature of cardiac electrical activity. However formulating such constraints in a tractable fashion can be challenging. We review the major approaches used for this problem, and present work on a middle ground between simple non-electrophysiological constraints and strong electrophysiological constraints that eliminate useful complexity in solutions.

Index Terms— dynamic inverse problems, inverse electrocardiography, spatio-temporal regularization

1. INTRODUCTION

Characterizing cardiac electrical activity based on recordings on the body surface is already common clinical practice, in the form of the ubiquitous electrocardiogram (ECG). The standard clinical 12-lead ECG uses a relatively small number of electrodes (9) and relies on the clinicians ability to identify abnormalities based on training and heuristic pattern recognition. Although a tremendously valuable part of current practice, there remain significant limitations in the diagnostic ability of ECG's, leading to a significant degree of both missed detections and false positives. One approach to improve our ability to extract information from such body surface recordings, which has by now been the subject of over 30 years of research, is to record from a significantly larger number of sites on the body and then, using a mathematical model of the torso interior, attempt to synthesize a representation of the cardiac electrical activity which could have produced those recordings. In other words, one takes the measurements and a forward model and attempts to invert it, thus solving what is known as the inverse problem of electrocardiography[1].

However there are some intrinsic difficulties in solving this problem accurately and reliably. The most critical is that the inverse problem, due to superposition and attenuation in the torso volume, is quite ill-posed. Small errors in modeling and measurements can cause large errors in estimated cardiac activity, so much so that simply finding the answer that best matches the data, without additional constraints, leads to wildly oscillatory and thus useless results. Thus, despite 30 years of effort, there have been relatively few attempts to transition these methods into clinical practice. This situation has begun to change in the last half-decade or so, in response to continued advances in methodology. Nonetheless, there remain considerable limitations that, in turn, continue to spur on-going research.

The need to combat the ill-posedness of the inverse problem requires imposition of *a priori* constraints on the solutions. Thus a significant fraction of the effort in this field has gone into discovering physiologically effective and mathematically tractable constraints. As we describe in some detail below, the types of constraints available turns out to be strongly tied to the choice of model of cardiac electrical activity. In particular, we concentrate in this paper on approaches that attempt to include information about the temporal behavior of the solution into the constraint set. The basic idea is that the electrophysiology of cardiac propagation dramatically reduces the space of realistic solutions; currents flow in the heart as determined by a complex but highly structured interaction of cell morphology, tissue structure, and the electrophysiology and biophysics that link structure to function. The result, especially during the activation phase of the cardiac cycle, which is the direct trigger of the pattern of mechanical contraction, is a wavefront-like behavior. That is to say, there is a strong spatio-temporal coherence, or correlation, in the pattern of spread of electrical activation in the heart.

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[1]We note that this methodology currently has a number of other names including Cardiac Electrical Imaging (CEI), ElectroCardioGraphic Imaging (ECGI), and Noninvasive Imaging of Cardiac Electrophysiology (NICE).

2. CARDIAC SOURCE MODELS FOR THE INVERSE PROBLEM

The physics of current flow between the heart and body surface can be well represented by Laplace's equation, with Dirichlet boundary conditions on the heart and Neumann on the body surface. In a realistic geometry, forward models are typically built using techniques such as the Boundary Element or Finite Element method. We note that propagation from heart to body surface is essentially instantaneous as the quasi-static approximation is valid. This model gives a mathematical prediction of the potentials on the body given the sources. The exact nature of the Dirichlet boundary depends on the source model used.

Perhaps the simplest representation of the sources is to treat the heart as a closed surface: for instance, the epicardium, the outer surface of the ventricles, can be mathematically considered to be capped, or the ventricular epicardium and endocardium (the inner surface) can be mathematically joined at the base (where the ventricles meet the atria), at least during the part of the cardiac cycle when the atria are electrically inactive. Then the potentials on this surface can be considered an equivalent source model, and the body surface potentials are linearly related to the heart surface potentials via the forward model at each time instant, as in

$$\mathbf{y}(k) = \mathbf{A}\mathbf{x}(k). \tag{1}$$

$\mathbf{A}$ is a transfer operator, a discretized matrix representation containing transfer coefficients which link heart surface source potentials $\mathbf{x}(k)$ to the remote body surface potentials $\mathbf{y}(k)$.

The ill-posedness is then typically dealt with through Tikhonov regularization, leading to

$$\hat{\mathbf{x}}(k) = \text{argmin}\|\mathbf{A}\mathbf{x} - \mathbf{y}\| + \lambda|\mathbf{R}\mathbf{x}\|, \tag{2}$$

where $\|\cdot\|$ represents the 2-norm. $\mathbf{R}$ is typically a smoothing operator used to control the oscillatory effect of ill-posedness. An explicit form of the solution to Eq. 2 can be written as

$$\hat{\mathbf{x}}(k) = (\mathbf{A}^T\mathbf{A} + \mathbf{R}^T\mathbf{R})^{-1}\mathbf{A}^T\mathbf{y}(k). \tag{3}$$

These methods can be called "potential imaging". However since spatially sharp wavefronts characterize the actual potential distribution, this approach reconstructs such phenomena poorly. Moreover, the propagating wavefronts imply significant temporal correlation in the source but in this approach the source is treated as temporally uncorrelated.

There have been several expansions of this approach to allow incorporation of temporal correlation. Most of them start with an augmented model in which multiple time instants are dealt with jointly. Mathematically this can be accomplished by solving Eq. 1 jointly over those time instants. We briefly describe three examples of such approaches. In the first, joint regularization [1], one forms an augmented model by creating block vectors of the heart surface and body surface potentials and a block diagonal forward matrix to relate them. Then a spatial regularizer and a temporal regularizer are both employed, one of which operates separately on spatial nodes at each time instant, while the other operates on each node separately across time. A second approach, using a state-space model [2, 3], is to treat the source in Eq. 1 as the unobserved *state* of a system, and augment that equation with an explicit state evolution equation. The inverse problem can then be found via the Kalman filter or smoother. A third approach is based on what is known as the separability or isotropy assumption [4]. In this approach one assumes that the temporal statistics of the measurements have the same eigenstructure as those of the data. (Greensite, in [5] and other publications, showed that this is true if the source is "separable", that is if its spatio-temporal correlation can be written as the product of a space-only correlation and a time-only correlation.) Details on these models and an analysis of how they are related to making different structural assumptions about the underlying spatio-temporal correlation matrix can be found in [6].

A quite different approach to imposing temporal constraints on the source model, known as activation-time imaging (see [7, 8, 9], among many others), represents the source as a double layer of dipoles located where the wavefront intersects the heart surface, or equivalently as the trans-membrane potentials of the cardiac cells on that surface. If assumptions of isotropy and homogeneity are made, then the temporal waveforms can be assumed to have the same shape, but are simply shifted in time to represent the different arrival times of the wavefront at each location on the heart surface. Thus the unknowns are time instants of arrival as a function of space, generally denoted $\tau(s)$, and the forward equation becomes

$$\mathbf{y}(k) = \int A f(k - \tau(s))ds, \tag{4}$$

where $f(\cdot)$ is a step function or a smooth approximation to a step. Thus the number of degrees of freedom is dramatically reduced compared to potential imaging, and a physiologically-based temporal model is imposed. However this model is a significantly oversimplified representation of reality. We note that the remaining problem is still ill-posed, although considerably better-posed than the potential imaging formulation due to the constrained solution space. The inverse problem is also now non-linear, and is typically solved via iterative solutions. Such solutions tend to be sensitive to the initial starting point, and much recent work has been devoted to devising effective initializations. (Perhaps the most interesting from a signal processing standpoint is a MUSIC-like algorithm proposed by Huiskamp and Greensite [10].)

Recently, our group introduced a pair of approaches which attempt to combine virtues of both potential and activation-time imaging [11]. Both of these approaches use a three-level model of the potential surface; the surface is divided into flat regions of activated and non-activated tissue, separated by a transition region where the wavefront is located. The transi-

tion region is modeled by combinations of exponential curves. The first of these methods, Wavefront-Based Curve Reconstruction (WBCR), models the source as a propagating curve on the epicardium. Anisotropic propagation models and an approximate potential-from-wavefront model were built from a phenomenological study of recorded data. A non-linear state-space model used the curve location at each time instant as the state, and the solution was calculated via an extended Kalman filter. The second approach, Wavefront-Based Potential Reconstruction (WBPR), uses a wavefront-based approximation of the potential reconstruction at each time instant as a prior mean, or regularization term. In the WBPR method, this prior guess is formed by a non-linear transformation of the current solution, but the inverse problem itself is linear. The wavefront is "propagated" by using each time instant for the prior in the inverse solution at the subsequent (or, in backwards mode, the previous) time sample.

3. RESULTS

In order to effectively compare various types of electrocardiographic inverse solutions, we have constructed geometric models which have a combined endocardial/epicardial heart surface (which is a theoretical requirement of the activation-time imaging methods), with given source potentials on that surface. We have been working to build such a computational model. The results presented here use a geometry and source potentials based on the program ECGSim [12], a free cardiac modeling program available from `http://www.ecgsim.org`. We note that the only other published results we are aware of which report potential reconstructions on a combined epicardial and endocardial surface are in [13].

We used the geometric model of the heart and torso surfaces extracted from ECGSim, together with the default dataset distributed by ECGSim, itself based on a measured set of human body surface potentials. ECGSim performs an activation-time based solution, and from those activation times it can calculate the corresponding potentials on the heart surface using a Boundary Element Method (BEM) solution relating the transmembrane and heart surface potentials. We used the recorded body surface potentials generated by ECGSim as our data in the results presented here and compared results to the heart surface potentials generated by ECGSim from its activation-based solution. The forward model used in our simulations was a BEM matrix generated by our own BEM code from the ECGSim geometry. We then performed reconstructions using the Tikhonov regularization of Eq. 2, with $\mathbf{R}$ equal to an identity matrix and using the WBPR method in both the forward and backward directions.

Figures 1 and 2 report results from two different time instants during the cycle. The results are shown as visualizations of potentials color-mapped onto the heart surface. In addition to the color mapping, isopotential lines (contours of constant potential) are shown on the figures. All visualizations were performed using map3d [14], a free program distributed by the Center for Integrative Biomedical Computing.

Fig. 1 shows results very early in the cardiac cycle. The heart is oriented in the visualization so as to display the ventricular cavities down to the lower parts of the endocardium, because this is where the earliest activations take place in the ECGSim reconstruction. In the figure, the upper left panel shows the original ECGSim data, while the upper right panel shows a standard Tikhonov reconstruction with the regularization matrix $\mathbf{R}$ from Eq. 2 set equal to an identity matrix (thus constraining the amplitude of the reconstruction at each time instant). The two lower panels show WBPR reconstructions, with the results of a forward (in time) recursion shown on the left and a backward recursion on the right. The Tikhonov solution completely misses the early endocardial activations, as illustrated in the figure. This is not surprising because, of course, the endocardial surface is much more difficult to "see" in the body surface potentials. The WBPR reconstructions, because they use a prior model which "expects" to find a wavefront, is able to find this phenomenon in the data. We note that the backward WBPR recursion is able to localize the early activation much more precisely than the forward WBPR. This is not surprising as the forward recursion needs the phenomenon to be large enough to overcome the threshold by which the wavefront is detected, while the backward recursion can follow the wavefront as it reduces in area and amplitude in the anti-causal direction.

Fig. 2 shows results from the same simulation later in time, as the activation wavefront progresses through the heart wall and begins to break through onto the epicardium. In this image the heart is oriented so as to present this breakthrough. We note that the ECGSim data reveals the breakthrough with great fidelity, sharp boundaries, and little activity away from the wavefront, because it was synthesized directly from an activation-time model. In reality the potentials on the epicardial surface would not be nearly as well-defined and focused, and would have more variability way from the breakthrough, compared to the ECGSim solution used for comparison here. Fig. 2 also shows that the WBPR methods captured the wavefront-like behavior of the cardiac potentials much more clearly than the Tikhonov reconstruction. The two breakthrough foci were visible in the Tikhonov reconstruction, but with much lower contrast and greater spatial extent, or smearing, than either the WBPR reconstructions or the ECGSim data. We also note here that the two WBPR methods perform about equally.

4. DISCUSSION

The potentials used as the original cardiac sources in the simulations reported here were based, as described, on an activation-time solution. Thus they may show an undetectable bias that makes any potential-based reconstruction look less accurate.

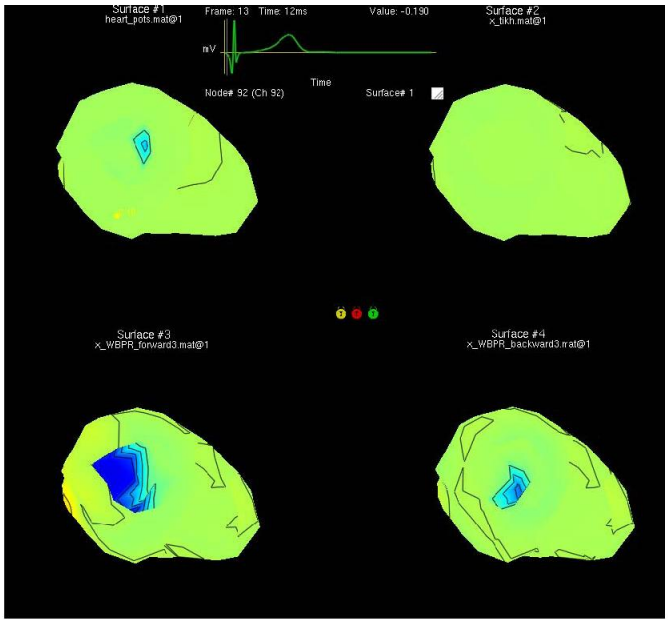

Fig. 1. The original ECGSim data is shown in the upper left panel. The upper right panel shows a Tikhonov reconstruction, while the lower left shows a forward WBPR and the lower right panel a backward WBPR reconstruction. The colormap is the same for all four panels, using blue to represent the most negative potentials and red the most positive, with green representing zero. The heart is oriented so that the earliest activations, which appear on the lower endocardial surface, are visible when the reconstruction method finds them. A sample temporal waveform from the ECGSim "original" data is show at the center top of the entire figure.

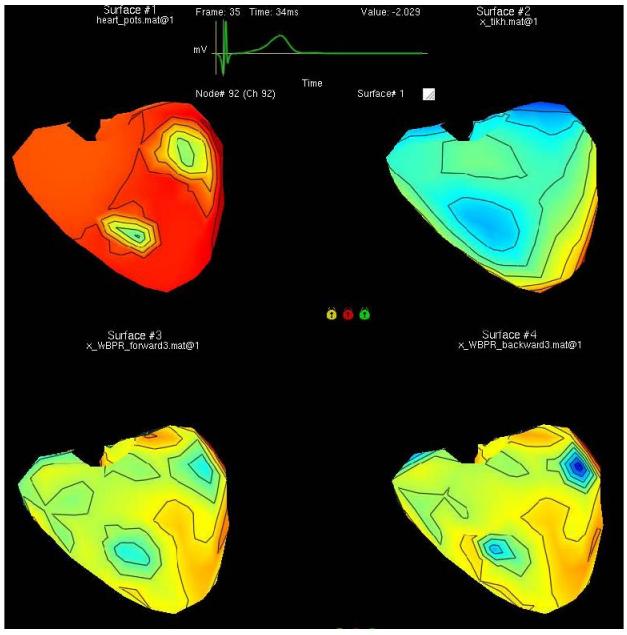

Fig. 2. Reconstructions showing the earliest breakthrough of the activation wavefront onto the epicardium. Format is the same as the previous figure.

Given that bias, the ability of the WBPR methods to find events that are difficult to reconstruct, such as early endocardial activations, is encouraging.

The role of the initial guess in the WBPR reconstruction is analogous to that of a prior mean in a statistical setting. To be more specific, we note that the reconstruction equation for WBPR was

$$\hat{\mathbf{x}}(k) = \bar{\mathbf{x}}(k) + (\mathbf{A}^T\mathbf{A} + \sigma^2\mathbf{I})^{-1}\mathbf{A}^T(\mathbf{y}(k) - \mathbf{A}\bar{\mathbf{x}}(k)), \quad (5)$$

where $\bar{\mathbf{x}}(k)$ is the prior guess at time k, formed by thresholding and interpolating the reconstruction $\hat{\mathbf{x}}(k)$ at time $k-1$ or $k+1$ depending on the direction of the recursion. Comparing Eq. 5 to Eq. 3, it is clear that the regularization is applied to the part of the data that is not explained by the wavefront-based estimate $\bar{\mathbf{x}}(k)$. The identity matrix in Eq. 5, in this context, plays the role of an inverse spatial covariance of the solution. It is interesting to note that considerable effort, by our group and others, has been spent in exploring the utility of a more accurate spatial covariance matrix in Tikhonov-regularized inverse electrocardiographic solutions, that is, replacing $\mathbf{R}$ in Eq. 3 with the inverse of a realistically estimated covariance matrix. The importance of the mean, as represented by our $\bar{\mathbf{x}}(k)$, has not been explored. We have tested the advantages of using a wavefront-based estimate of the covariance in this equation, but we found that it had little effect and that, indeed, it was the prior mean which played a much more important role.

5. CONCLUSION AND FUTURE WORK

The various methods that have been introduced to solve the inverse problem of electrocardiography take contrasting approaches to incorporating spatio-temporal assumptions about the behavior of the cardiac sources. On the one extreme are the standard potential-based solutions which treat each time sample independently and concentrate only on regularizing spatial behavior. At the other extreme are the activation-based imaging methods which reduce the problem to the estimation of the timing, but not the shape, of the same temporal waveform at each point on the heart surface. In between are modifications of the potential-based methods which attempt to regularize in time or impose temporal constraints on the solutions. Our recent addition to this suite of methods, the WBCR and WBPR approaches, use an explicit characterization of wavefront behavior. The goal is to allow much of the flexibility and freedom of the potential-based methods while retaining the physiological insight behind the activation-based methods. Initial results with the WBPR method, in particular, are quite promising. We plan to test the method further, compar-

ing to activation-based methods using common sets of synthesized and measured body surface potentials.

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