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INVERSE ELECTROCARDIOGRAPHY IN THE FRAMEWORK OF DYNAMIC IMAGING PROBLEMS

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ABSTRACT

We describe several current approaches which include temporal information into the inverse problem of electrocardiography. Some of these approaches operate directly on potential-based source models, and we show how three recent methods, introduced with rather distinct assumptions, can be placed in a common framework and compared. Others operate on parameterized models of the cardiac sources, and we discuss briefly how recent developments in curve evolution methods for inverse problems may allow more physiologically complex parametric models to be employed.

1. INTRODUCTION

The quasi-static electromagnetics (Laplace's or Poisson's equation) that describe quite accurately the relationship between cardiac electrical activity and heart surface potentials imply that the inverse problem of electrocardiography can be solved one time instant at a time—there is no temporal "memory" in the volume conductor at frequencies even many orders of magnitude higher than those of the ECG. On the other hand, any reasonable model of cardiac electrical sources takes into account the spatio-temporal correlation of cardiac depolarization and repolarization. Since the inverse problem is ill-posed, uncorrelated components of the measured potentials will tend to be amplified in the inverse solutions. Thus it makes sense to model this correlation of the sources and impose it on inverse solutions as one means to combat ill-posedness and make solutions more accurate and more robust. This approach to inverse electrocardiography falls within a category of inverse solutions frequently known as "dynamic imaging" or "dynamic inverse problems."

Although interest in using temporal information in inverse electrocardiography goes back at least as far as the work of Martin *et al.* [1], there has been increasing interest in recent years in this area. Indeed, there has been significant work in other application areas of biomedical (and other) inverse problems along the same lines, including not only other bioelectric field problems such as EEG and MEG, but also problems with quite different physics such as SPECT and Diffuse Optical Tomography. The nature of any such inverse solution depends heavily on the type of source model adopted; generally investigators in this field divide source models, and their associated inverse solutions, into two major categories: pixel-based, or non-parameterized, models, and parametric models. In inverse electrocardiography, pixel-based solutions generally correspond, for instance, to solutions in terms of epicardial or trans-membrane potentials, while parametric models would include activation-time approaches.

In this paper, we attempt to accomplish two objectives while discussing inverse electrocardiography in the context of dynamic imaging problems; first we review some recent non-parametric approaches and show how three of these methods can be placed in a common framework, and, second, we discuss the possibility of parametric approaches with a more complex source model than standard activation-time approaches. Given space constraints, of necessity both objectives will be treated rather tersely, and we will concentrate on describing these relationships while leaving mathematical detail for presentation elsewhere.

2. A COMMON FRAMEWORK FOR NON-PARAMETRIC DYNAMIC INVERSE ECG SOLUTIONS

A number of approaches have been introduced in recent years for this problem, including Kalman filtering methods [2, 3, 4, 5], combined spatial and temporal regularization [6], structurally-constrained statistical methods [7, 8], and convex optimization methods with linear [9] or non-linear [10] temporal constraints. (We note that this list of citations is not complete, but rather just a space-limited sampling.) Here we show how the first three of these approaches can be put in a common statistical regularization framework and, based on this understanding, make some observations on their relationships and possible relative advantages and disadvantages. More detail can be found in [11]

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We model body surface potential measurements as a space-by-time matrix $\mathbf{Y}$ which is related to a similar space-by-time matrix of epicardial potentials $\mathbf{X}$ as follows:

$$\mathbf{Y} = \mathbf{A}\mathbf{X} + \mathbf{N} \tag{1}$$

where $\mathbf{Y} \in R^{M\times L}$, $\mathbf{X} \in R^{N\times L}$, and $\mathbf{N} \in R^{M\times L}$ is a zero-mean random noise matrix which is uncorrelated with $\mathbf{X}$. M, N, L are the number of body surface measurements, modeled epicardial potentials, and time instants, respectively. $\mathbf{A} \in R^{M\times N}$ is a time-invariant forward solution matrix. The goal is to estimate $\mathbf{X}$ given $\mathbf{Y}$ and $\mathbf{A}$. Eq. (1) can be equivalently written as

$$\underbrace{vec(\mathbf{Y})}_{\bar{\mathbf{Y}}} = \underbrace{(\mathbf{I}_L \otimes \mathbf{A})}_{\bar{\mathbf{A}}} \cdot \underbrace{vec(\mathbf{X})}_{\bar{\mathbf{X}}} + \underbrace{vec(\mathbf{N})}_{\bar{\mathbf{N}}} \tag{2}$$

If we assume that the unknown matrix $\mathbf{X}$ is random, we can apply the LMMSE solution to Eq.(2) [12]:

$$\begin{aligned}\hat{\bar{\mathbf{X}}} &= E(\bar{\mathbf{X}}) + (\mathbf{C}_{\bar{\mathbf{X}}}{}^{-1} + \bar{\mathbf{A}}^T \mathbf{C}_{\bar{\mathbf{N}}}{}^{-1} \bar{\mathbf{A}})^{-1} \\ &\quad \bar{\mathbf{A}}^T \mathbf{C}_{\bar{\mathbf{N}}}{}^{-1} (\bar{\mathbf{Y}} - E(\bar{\mathbf{Y}})),\end{aligned} \tag{3}$$

where $\mathbf{C}_{\bar{\mathbf{X}}}$ is the spatiotemporal epicardial autocovariance matrix, whose (i, j) block is the spatial cross-covariance between the epicardial potentials at the i-th and j-th time instants, and $\mathbf{C}_{\bar{\mathbf{N}}}$ is defined similarly for the noise.

Kalman filtering, especially variants of Rauch-Tung-Striebel (RTS) fixed-interval Kalman smoothing [13], has been used extensively in recent years for inverse problems (see [4] as an example). It solves Eq. (3 by imposing structure on the evolution of the unknown potentials, which in turn leads to a particular structure for $\mathbf{C}_{\bar{\mathbf{X}}}{}^{-1}$. The deterministic joint spatial and temporal regularization method of Brooks *et al.* [6] can also be seen as a solution of this equation with distinct assumptions about the structure of $\mathbf{C}_{\bar{\mathbf{X}}}{}^{-1}$. Greensite's method [7, 8] starts from explicit assumptions about $\mathbf{C}_{\bar{\mathbf{X}}}$. In the rest of this section we briefly describe the assumptions these approaches make and comment on their relationships.

2.1. State-space Model for Kalman Smoothing

Suppose we assume the following state-space model to describe the source-measurement relationship in space and time:

$$\begin{aligned} \mathbf{x}[l] &= \mathbf{H}\mathbf{x}[l-1] + \mathbf{B}\mathbf{u}[l] \\ \begin{bmatrix} \mathbf{y}[l] \\ \mathbf{0} \end{bmatrix} &= \begin{bmatrix} \mathbf{A} \\ \lambda \mathbf{R} \end{bmatrix} \cdot \mathbf{x}[l] + \begin{bmatrix} \mathbf{n}[l] \\ \mathbf{0} \end{bmatrix}, \end{aligned} \tag{4}$$

where $\mathbf{y}[l], \mathbf{x}[l], \mathbf{n}[l]$ are the l-th columns of $\mathbf{Y}, \mathbf{X}, \mathbf{N}$, respectively at time index $l = 1, 2, \ldots, L$. $\mathbf{H} \in R^{N\times N}$ is a known state transition matrix; $\mathbf{B} \in R^{N\times N}$ is called a "control" matrix and $\mathbf{u}$ is state prediction noise. $\mathbf{R}$ is a spatial regularization matrix and λ a fixed spatial regularization parameter. We assume $\mathbf{u}[l] \sim N(\mathbf{0}, \mathbf{Q})$, $\mathbf{n}[l] \sim N(\mathbf{0}, \mathbf{C_N})$ are Gaussian noise, independent in time and from each other. We make some standard statistical assumptions about the intial state of $\mathbf{x}$. The key assumption here is that we know $\mathbf{H}$, which models assumptions about the spatio-temporal behavior of the epicardial potentials.

The consequence of this state-space model is that $\mathbf{C}_{\bar{\mathbf{X}}}{}^{-1}$ is a symmetric block tri-diagonal matrix which has a nice $\mathbf{LDL^T}$ factorization in terms of the matrices in the state-space model. In fact, the forward filtering pass of the RTS algorithm is simply block Gaussian elimination and the backward smoothing pass is block back-substitution.

2.2. Joint Regularization Model

Using spatial regularization jointly with temporal regularization in a determinsitic framework, Brooks *et al.* in [6] proposed a straightforward formulation to find $\mathbf{X}$:

$$\hat{\bar{\mathbf{X}}} = \operatorname{argmin}\{||\bar{\mathbf{A}}\bar{\mathbf{X}} - \bar{\mathbf{Y}}||^2 + \lambda^2||\bar{\mathbf{R}}\bar{\mathbf{X}}||^2 + \eta^2||\bar{\mathbf{T}}\bar{\mathbf{X}}||^2\} \tag{5}$$

where $\otimes$ is the matrix Kronecker product, λ, η are spatial and temporal regularization parameters, $\bar{\mathbf{A}} = \mathbf{I}_L \otimes \mathbf{A}$ is the block diagonal augmented forward matrix, $\bar{\mathbf{R}}$ has the same structure as $\bar{\mathbf{A}}$ and is a Tikhonov spatial regularization matrix, and $\bar{\mathbf{T}} = \mathbf{T}\otimes\mathbf{I}_N$ is a temporal regularization matrix. Note that $\bar{\mathbf{T}}$ picks out the same spatial measurement from all time instants and constrains temporal behavior according to the rows of $\mathbf{T}$. The solution can be written as

$$\begin{aligned}\hat{\bar{\mathbf{X}}} &= \left(\bar{\mathbf{A}}^T\bar{\mathbf{A}} + \lambda^2\bar{\mathbf{R}}^T\bar{\mathbf{R}} + \eta^2\bar{\mathbf{T}}^T\bar{\mathbf{T}}\right)^{-1}\bar{\mathbf{A}}^T\bar{\mathbf{Y}} \\ &= \left[\mathbf{I}_L \otimes (\mathbf{A}^T\mathbf{A} + \lambda^2\mathbf{R}^T\mathbf{R}) + \eta^2\mathbf{T}^T\mathbf{T}\otimes\mathbf{I}_N\right]^{-1} \cdot \\ &\quad \left(\mathbf{I}_L \otimes \mathbf{A}^T\right)\bar{\mathbf{Y}}\end{aligned} \tag{6}$$

Although formulated in the context of deterministic regularization, this approach can be re-interpreted in the LMMSE estimator by setting $\mathbf{C}_{\bar{\mathbf{X}}}{}^{-1} = \lambda^2\mathbf{I}_L \otimes \mathbf{R}^T\mathbf{R} + \eta^2\mathbf{T}^T\mathbf{T} \otimes \mathbf{I}_N$. This can be described as a *Kronecker sum* structure for $\mathbf{C}_{\bar{\mathbf{X}}}{}^{-1}$. Thus for this method *a priori* information about expected temporal behavior of $\bar{\mathbf{X}}$ is captured in the temporal filter matrix $\mathbf{T}$, similar to the way in which expected temporal behavior is captured in the state transition matrix of the state-space model.

Brooks *et al.* suggested two efficient algorithms: one used a block Jacobi iterative scheme, while the other one took advantage of Kronecker product properties and is especially efficient when $\mathbf{R} = \mathbf{I}$. We note that the method requires joint determination of two regularization parameters.

2.3. Separability Condition

From a quite distinct viewpoint, Greensite in [7, 8] approached Eq.(3) directly, suggesting three possible statistical assumptions on $\mathbf{X}$, such that the structure of $\mathbf{C}_{\bar{\mathbf{X}}}$ could be significantly simplified and, to a greater or lesser extent, its temporal correlation structure could effectively be estimated from the measurements $\mathbf{Y}$. Among these three, here we discuss one, which Greensite called "isotropy".

Greensite's isotropy condition corresponds to what is called "separability" in random field theory (P82 in [14]): separability occurs when the cross-covariance of any two spatial-temporal random variables can be decomposed as the product of a spatial covariance function by a temporal covariance function. It is easy to show that under the separability assumption, $\mathbf{C}_{\bar{\mathbf{X}}}$ has a *Kronecker product* form:

$$\mathbf{C}_{\bar{\mathbf{X}}} = \frac{E\widetilde{\mathbf{X}}^T\widetilde{\mathbf{X}} \otimes E\widetilde{\mathbf{X}}\widetilde{\mathbf{X}}^T}{E(||\widetilde{\mathbf{X}}||_F{}^2)} \tag{7}$$

where $\widetilde{\mathbf{X}}$ denotes the mean-removed unknown matrix and $||\cdot||_F$ is the matrix Frobenius norm.

Under separability, the orthogonal transform which diagonalizes the total temporal covariance matrix of the measurements, $E\widetilde{\mathbf{Y}}^T\widetilde{\mathbf{Y}}$ ($\widetilde{\mathbf{Y}}$ denotes the mean-removed measurement matrix), also diagonalizes $E\widetilde{\mathbf{X}}^T\widetilde{\mathbf{X}}$, and thus temporally whitens the entire problem. This happens because linear combinations of separable random variables are separable, and white noise will not affect separability.

Thus under separability, one can calculate the orthogonal matrix $\mathbf{Z}$ which diagonalizes $\widetilde{\mathbf{Y}}^T\widetilde{\mathbf{Y}}$ as an estimate of the matrix which diagonalizes $E\widetilde{\mathbf{Y}}^T\widetilde{\mathbf{Y}}$, and then solve a rotated problem separately at each time instant:

$$(\mathbf{YZ})_i = \mathbf{A}(\mathbf{XZ})_i + (\mathbf{NZ})_i, \tag{8}$$

where the subscript i means i^{th} column of a matrix. After that, the optimal estimate of original unknowns can be obtained by rotating back with $\mathbf{Z}^T$.

2.4. Comments on the Relationships Among These Approaches

First, we note none of the methods is a subset of any of the others; all three have degrees of freedom not shared by the other two, as can be seen in their implications on the structure of $\mathbf{C}_{\bar{\mathbf{X}}}{}^{-1}$ [11]. In fact, one can construct specific restrictions on each method to make it match either of the others, which space precludes us from illustrating here.

In terms of actually constructing the required matrices, the state-space model allows us to implicitly model the spatio-temporal correlation structure in terms of smaller matrices with physically meaningful interpretations and to implicitly solve it efficiently via the RTS algorithm. The joint regularization model similarly allows a direct physical interpretation of the quantities required and has its own computationally efficient solution. The separability model is more difficult to interpret; on the other hand it does not require the assumption of any specific temporal operators—one simply estimates the required temporal decorrelation matrix out of the data and then solves an equivalent sequence of space-only problems.

To be more specific, the state-space model restricts the temporal memory structure to first-order (unless one "lifts" the model by expanding the state space) but allows explicit modeling of temporal correlation across different epicardial nodes (*i.e.* spatio-temporal mixing) . The joint regularization model (unless one relaxes the constraints on the structure of $\bar{\mathbf{R}}$ and $\bar{\mathbf{T}}$), on the other hand, is restricted to separate imposition of spatial and temporal constraints, but has no particular restriction on the length of temporal memory in the constraints. The separability structure implies that there is no strong spatio-temporally coherent correlation structure—one way to view this assumption is that all the spatial covariance matrices, at every pair of time instants, has the same *shape*; they differ from each other only by a scalar that can vary from one time pair to another.

Thus one would imagine, for instance, that the separability model would have difficulty modeling a propagating wave, where spatio-temporal coherence is strong, but would do well at modeling a problem where each region in space has similar temporal dynamics (or equivalently each time instant has similar spatial dynamics).

3. SOME COMMENTS ON PARAMETRIC DYNAMIC INVERSE ECG SOLUTIONS

Besides the linear framework for spatial-temporal regularization introduced above, there has been considerable recent work in dynamic PET/SPECT, MRI, CT, and other medical inverse problems on parameterized methods for incorporating temporal information with spatial regularization. Some of these approaches model the temporal evolution with a parameterized model, such as sums of exponentials [15], and others model the evolution as monotonically increasing, decreasing, or even an increase followed by a decrease [16]. However of particular interest here are methods which use a parameterization of the *spatial* structure as well as the temporal structure. One approach which has been recently presented uses curve-evolution models [17] which lend themselves to level-set-based inverse solutions [18].

The level-set inverse solution idea is to assume that the spatial region of interest can be divided into a small number of distinct regions (usually only two such "regions", although they can each be disjoint), and then to reconstruct only the boundary between these regions and perhaps the value of the unknown quantity in each region as well. The extension to dynamic imaging seeks to impose reasonable temporal evolution of the region boundaries.

The activation-based approach to inverse solutions [19] can be seen as an extreme form of such models. One internal boundary curve (the activation isochrone) is reconstructed at each time instant. In addition, simplifications are made which reduce the equivalent source to the intersection of the wavefront with the epicardial and endocardial surfaces, which allows joint reconstruction over all time instants. One of the drawbacks of such methods, however, is that the required assumptions ignore known and important physiological structure such as the presence of fiber anisotropy. With the recent development of sophisticated methods for modeling and reconstructing curve evolution behavior, many of them based on diffusion-equation PDE methods which fit nicely with cardiac electrical behavior, it would appear possible to develop new approaches which lie in the space between the lack of physiological constraints implied by reconstruction epicardial potentials or trans-membrane potentials, even in a spatio-temporal fashion, on one hand, and the inability to incorporate important physiology which characterizes activation-based solutions, on the other.

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