A BAYESIAN APPROACH TO INCLUSION AND PERFORMANCE ANALYSIS OF USING EXTRA INFORMATION IN BIOELECTRIC INVERSE PROBLEMS

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ABSTRACT

Due to attenuation and spatial smoothing that occurs in the conducting media, the bioelectric inverse problem of estimating sources from remote measurements is ill-posed and solution requires regularization. Recent studies showed that employing Bayesian methods could help increase accuracy. The basic limitations are the availability of good *a priori* information about the solution, and the lack of a "good" error metric. In this paper, we employ Bayesian methods, and present the mathematical framework for incorporating additional information in the form of prior statistics, and extra measurements. We also use Bayesian error metrics to evaluate the reconstructions, and select prior models. We apply the methods to inverse electrocardiography problem. The results show that we can improve the reconstructions by including extra information, and Bayesian error metrics are useful in evaluating the results.

1. INTRODUCTION

The primary goal in bioelectric inverse problems is to retrieve a bioelectric source distribution in space given a set of remote measurements and a mathematical model that relates the desired spatial source distribution to the measurement data distribution. Examples include inverse electrocardiography (ECG) or magnetocardiography (MCG) problems in which the measurements are the potential distributions or magnetic field distributions on the body surface, and the solution is in terms of the cardiac electrical source distributions, and inverse electroencephalography (EEG) or magnetoencephalography (MEG) problems in which one seeks to reconstruct the distribution of sources in the brain given electrical or magnetic measurements outside the head. Traditional reconstruction methods such as least squares estimation fail due to the ill-posed nature of this problem; small disturbances in the measured data may yield large variations in the reconstructed source distribution. The most common approach to this problem is deterministic "regularization" (also known as Tikhonov regularization), where the solution is a trade-off between the estimate that best represents the data and fidelity to an *a priori* regularization constraint imposed on the solution [1]. Recent studies have described Bayesian inverse approaches to inverse bioelectric problems [2, 3]. In addition to providing a more general way to look for regularization constraints, the Bayesian models offer additional statistical performance evaluation tools. These tools have been applied to certain aspects of some problems (*eg.,* inverse EEG/MEG [3]), but not at all to others (*eg.,* inverse ECG/MCG problem). Specific interpretation of measures such as error covariance and "evidence" (marginal probability density function of the measurements) can differ in various applications, therefore it is worth the effort to study Bayesian framework applied to different types of problems.

The basic limitation on performance of the reconstruction methods for ill-posed problems is the availability of good *a priori* information about the solution, and available independent measurements. One possible way to achieve improved performance would be to acquire better *a priori* information about the desired source distribution and try to incorporate this information into the reconstruction scheme. For example, using training datasets of previously recorded bioelectric source distributions, one can estimate the prior statistics. The "evidence", which is one of the tools for Bayesian estimation, could be used as a criterion to select among many candidate models. Another approach to increase the reliability of the reconstructions is incorporating one or more types of measurements. For example, in the reconstruction of cardiac source distribution problem, one can combine ECG and MCG recordings or ECG recordings and catheter measurements through coronary veins [4]. In the reconstruction of brain sources problem, EEG and MEG data could be used together [5]. There are also other applications that have the possibility of combining different measurements. For example, one can measure potential distribution remotely from the inner chambers of the heart and through contact electrodes from the inner walls of the heart [6] and combine them to reconstruct the potential distribution on the inner surfaces of the heart. Huiskamp measured potential distribution on the cortex (outer surface of the brain) on a small region in addition to EEG and MEG measurements [7]. Extra measurements in these studies were used for validation purposes, but it is possible to combine them in the reconstruction. The questions in including *a priori* information and, if available, different types of measurements, include how to include this information, and how to decide before-hand what improvement can be expected by including such additional information.

We report here a study that looked at using Bayesian techniques both to include one or both types of additional information – a priori and independent measurements – and to quantify expected performance improvements when using them. Although we have framed the work in terms of inverse bioelectric source problems, we believe the ideas can be applicable to a wider range of medical imaging problems where, for instance, sparse but highly reliable measurements could be obtained to include along with more complete but much more blurred and attenuated data.

2. PROBLEM DEFINITION

The standard linear inverse bioelectric source distribution problem is to estimate the original spatial source distribution, $\mathbf{x}$, of length N, obtained by stacking the values at each pixel into a column vector, given the remote measurements, $\mathbf{y}$, also a column vector similarly obtained, of length M, and the forward matrix representing the mathematical model, $\mathbf{A}$, of size $M \times N$ in the equation:

$$\mathbf{y} = \mathbf{A}\,\mathbf{x} + \mathbf{n} \tag{1}$$

where $\mathbf{n}$ is measurement noise.

In addition to $\mathbf{y}$, we have available a second set of measurements, denoted as $\mathbf{z}$, of length K, and are related to the desired source distribution via equation:

$$\mathbf{z} = \mathbf{B}\,\mathbf{x} + \mathbf{e} \tag{2}$$

where $\mathbf{e}$ is the measurement noise vector of appropriate size, and $\mathbf{B}$ is the mathematical model that relates $\mathbf{x}$ to $\mathbf{z}$. We will call this second set of measurements “extra measurements” and $\mathbf{y}$ as the “primary measurements”.

2.1. The Augmented Problem

If only the primary measurements are available, one solves the problem defined by Eq. 1 for $\mathbf{x}$. We will refer to this approach as “classical reconstruction”.

To incorporate both types of measurements, we will need to redefine the problem by combining equations 1 and 2 into an augmented form:

$$\mathbf{v} = \mathbf{D}\,\mathbf{x} + \tilde{\mathbf{n}} \tag{3}$$

where

$$\mathbf{v} = \begin{bmatrix} \mathbf{y} \\ \mathbf{z} \end{bmatrix}, \tilde{\mathbf{n}} = \begin{bmatrix} \mathbf{n} \\ \mathbf{e} \end{bmatrix} \text{ and } \mathbf{D} = \begin{bmatrix} \mathbf{A} \\ \mathbf{B} \end{bmatrix} \tag{4}$$

and solve this for $\mathbf{x}$. We will refer to this approach as “augmented reconstruction”.

Note that there is a third possibility, in which only the extra measurements are available, but not the primary measurements. In this case, one solves Eq. 2. This is equivalent to the classical reconstruction with extra data replacing the primary measurements.

All of the equations that use one or both types of measurements have a simple linear relation to the source distribution, and the solution to one equation could be estimated by changing the variables in the others. Therefore, we will present the following mathematical framework for only the classical reconstruction, for space limitations.

3. BAYESIAN ESTIMATION

We use Bayesian maximum *a posteriori* (MAP) estimation to reconstruct the source distribution [8]. We assume that the source distribution, $\mathbf{x}$, is normal with mean $\bar{\mathbf{x}}$ and covariance $\mathbf{C}_x$, the noise in the primary measurements, $\mathbf{n} \sim \mathrm{N}(\mathbf{0},\ \mathbf{C}_n)$, with $\mathbf{C}_n = \sigma_n^2\ \mathbf{I}$, and the noise in the extra measurements, $\mathbf{e} \sim \mathrm{N}(\mathbf{0},\ \mathbf{C}_e)$. $\mathbf{e}$, with $\mathbf{C}_e = \sigma_e^2\ \mathbf{I}$. Both noise terms are uncorrelated with $\mathbf{x}$, and with each other. Then, the solution for the classical reconstruction problem is:

$$\hat{\mathbf{x}} = (\mathbf{A}^T\mathbf{C}_n^{-1}\mathbf{A} + \mathbf{C}_x^{-1})^{-1}(\mathbf{A}^T\mathbf{C}_n^{-1}\mathbf{y} + \mathbf{C}_x^{-1}\bar{\mathbf{x}}). \tag{5}$$

3.1. Estimation Error

The Bayesian MAP reconstruction, $\hat{\mathbf{x}}$, is unbiased under the Gaussianity assumptions. Therefore, the estimation error has zero mean and covariance matrix equal to:

$$\mathbf{C}_\epsilon = (\mathbf{A}^T\mathbf{C}_n^{-1}\mathbf{A} + \mathbf{C}_x^{-1})^{-1}. \tag{6}$$

for the classical reconstruction.

A well-known property of error covariance matrix is that its diagonal elements give the error variance for the estimate in pixel Using this variance and the Bayesian MAP solution, one can obtain confidence intervals for an estimate. For example, with 95% probability, the true solution in lead number j lies within the range:

$$\hat{\mathbf{x}}_i - 2\sqrt{\mathbf{C}_\epsilon(i,i)} \leq \mathbf{x}_i \leq \hat{\mathbf{x}}_i + 2\sqrt{\mathbf{C}_\epsilon(i,i)} \tag{7}$$

where x_i and $\hat{x}_i$ are the i^{th} elements of $\mathbf{x}$ and $\hat{\mathbf{x}}$ respectively, and $[\mathbf{C}_\epsilon]_{ii}$ is the i^{th} diagonal element of $\mathbf{C}_\epsilon$.

The error covariance matrix could be used as a performance analysis tool in Bayesian estimation. Its advantage over traditional error measures, such as relative error or qualitative comparison, is that it only depends on mathematical model, and the probability distributions used for Bayesian estimation: the data pdf and the prior density. It does not depend on the specific experiment from which the measured image is obtained nor knowledge of true value of the solution. Since we do not need to compare the results to original values, it is an attractive candidate as an evaluation tool even in a realistic setting where one does not have access to the true solution. In addition, using the inequality in Eq. 7, one can put more trust in the estimate at a pixel if the error variance of the estimate at that pixel has smaller values than the others. This kind of use of error statistics have been applied to inverse EEG/MEG problem [3], but under simplistic assumptions that assumes $\mathbf{x}$ to be *i.i.d.*, and is novel to inverse ECG problem.

3.2. Using Evidence for Prior Selection

Another Bayesian metric, the "evidence" (*i.e.*, the marginal probability distribution function of the measurement vector), could be used to select the prior model for the source distribution. An algorithm was proposed in [3] to select the noise and source distribution variances in inverse EEG problem by maximizing evidence when the source distribution is also *i.i.d.* and the number of unknowns is only two. When the source distribution has a full covariance matrix, one can compare various prior models, and choose the one that maximizes evidence. Our preliminary studies with a limited number of candidate priors suggested that this is a valid criterion for model selection [9].

4. RESULTS

To demonstrate the use of methods studied in this paper, as an example, we used inverse electrocardiography problem, in which one seeks to reconstruct the source distribution of the heart, given the potential measurements on the body surface and an appropriate model relating the sources and the measurements. We obtained reconstructions for classical and augmented reconstruction schemes, using Bayesian MAP estimation and Tikhonov regularization with the energy constraint. We can summarize these approaches as:

- **TIKH:** Tikhonov regularization with energy constraint, using only the primary measurements.
- **TIKH-ED:** Tikhonov regularization with energy constraint, using both the primary and the extra measurements.
- **MAP:** Bayesian MAP estimate, using the primary measurements, and the prior statistics.
- **MAP-ED:** Bayesian MAP estimate, using both the primary and the extra measurements, as well as the prior statistics.
- **EPI-EST:** Bayesian MAP estimate, using the extra measurements and the prior statistics, but without using primary measurements or solving an inverse problem.

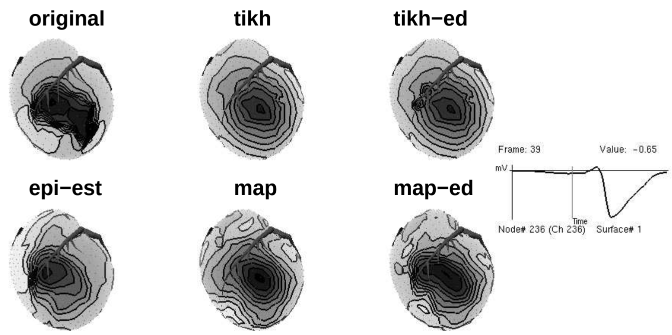

Fig. 1. All methods compared. Original and estimated epicardial potentials.

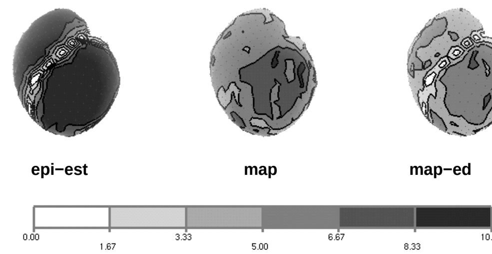

Fig. 2. Two times the error standard deviation maps in millivolts for solutions in Fig. 1.

The source distribution in this problem is the potential distribution map (isopotential map) on the heart surface, which is obtained by contouring the areas on the 3D surface that have similar potential values. The primary measurements are the corresponding potential values on the body surface, and the extra measurements are collected on or near the heart surface (*eg.*, via venous catheters inserted into coronary veins). These measurements are spatially sparse, and only cover a small number of pixels, however, they are direct measurements and do not suffer from attenuation and spatial smoothing. A more detailed presentation of this study can be found in [4].

We simulated sparse extra measurements by selecting sparse leads from a 490-electrode sock applied to an isolated canine heart and added normally distributed zero mean *i.i.d.* noise at 30dB SNR. We simulated torso potentials using a boundary element solution to Laplace's equation for a human shaped torso tank in which the heart was suspended. We then added noise at 25dB SNR to the simulated torso surface potentials. In this work $N = 490$, $M = 771$ and we set $K = 42$.

We obtained *a priori* information from a training set which consists of heart isopotential maps from previous experiments on different canine hearts.

In Fig. 1, we show isopotential contours for the original source distribution and various reconstructions that were evenly and identically spaced between the maximum and minimum of the original map. Dark regions correspond to the more negative potentials and light regions to the more positive. The edges in the isopotential maps, *i.e.,* the rapid transitions from the negative–potential areas to the positive–potential areas, composed of tightly placed contours, are known as "wavefronts". Localization of the wavefront may provide useful information on the functioning of the heart, hence it is essential to reconstruct the wavefront accurately, preserving the edge. The coronary arteries were also included for reference. The top, left-hand panel contains the original measured potentials, while labels on the other panels identify the method used to compute them.

With Tikhonov regularization there is slight improvement in the wavefront reconstruction around the measurement sites (near the coronary artery in the maps) when extra measurements are used, but it is not an impressive improvement. In general, Tikhonov regularization with or without extra measurements produce spatially smooth results with poor reproduction of the waveshape. **MAP** and **MAP-ED** recover the potentials more successfully than Tikhonov regularization. When we compare these two estimates, we observe a wavefront propagation pattern that looks more like a circular propagation pattern rather than the elliptical shape of the original in **MAP**, whereas the **MAP-ED** reconstruction has better fidelity to the original. **EPI-EST** reconstructs the tight wavefront with a good fidelity to the original near the measurement sites (along the coronaries), even better than **MAP**, and comparable to **MAP-ED**. However, as we look away from the measurement sites, the wavefront becomes spread out and smoothed, even more so than **MAP**, **TIKH** and **TIKH-ED**.

To compare the confidence intervals, we plot 2 times the error standard deviation values in Figure 2. The higher these values, the wider the confidence intervals, meaning we have less confidence in the results. The range is fixed for all of the error maps. In general, the error standard deviation values decrease with the addition of sparse extra measurements, with very small error values near measurement sites. The highest error values in **MAP** reconstruction correspond to the region of the heart where the wavefront reconstruction loses its elliptical shape in Fig. 1. **EPI-EST** has small error values around the measurement sites, but much higher values as we move away from these sites, which can help explain its good performance near measurement sites and its failing elsewhere.

5. CONCLUSIONS

In this paper, we presented the mathematical framework to study the effects of incorporating extra measurements and prior statistics into the ill-posed inverse bioelectric problem, with the goal of increasing reliability of the reconstructed bioelectric source distributions. We used Bayesian MAP estimation for the reconstructions, and proposed to use the Bayesian error metrics to evaluate the results, and compare the effects of combining different types of measurements, and the use of "evidence" for prior model selection.

The results showed that Bayesian MAP estimation with the appropriate prior statistics finds better reconstructions than the Tikhonov regularization method. In the Bayesian estimation, combining both types of measurements, even though they are not independent, yields better reconstructions than using any one of the measurements alone. The simulation studies we carried out in [9] already showed that the theoretical error maps using a "good" prior matches well with the ones obtained from the simulations. The results in this study show that Bayesian error covariance is a promising tool for the evaluation and comparison of different reconstructions and designing parameters of experiments such as the number and location of the measurement electrodes. Future work will include the study of how to obtain "good" prior statistics, and determine the number and location of extra measurements. Also analytical and experimental work will be carried out to quantify the sensitivity of the reconstructions and the error metric to the model parameters.

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