Direct and inverse methods for cardiac mapping using multielectrode catheter measurements

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1 Introduction

Detection of cardiac activation and reentry is critical in the diagnosis and treatment of arrhythmia, a heart disorder which affects some 4 million people in the US. Present approaches typically map the sequence of activation by using multiple catheters, or in particularly severe cases, by applying electrode arrays directly to the heart[3]. Catheter based approaches usually measure signals from inside the heart chambers and thus detect only (sub)endocardial excitation and recovery. As a result, a substantial portion of ventricular tachycardias, those that have important epicardial components, cannot be fully characterized.

Recent progress in the fabrication of multielectrode venous catheters permits simultaneous measurement from several catheters, each of which can have up to 16 individual electrodes, providing direct access to even distal segments of epicardial cardiac veins. While coverage of the epicardium is limited to the regions near these veins, we have shown that it is possible to estimate complete epicardial activation patterns from catheter based measurements, provided appropriate training data are available[2]. In this paper we report on further testing of this direct estimation method.

Beyond direct measurement and estimation, another possible approach to estimate epicardial activity is to solve the associated inverse problem in terms of epicardial potentials, which requires knowledge of the torso geometry and a numerical solution to Laplace's equation[5]. The challenges of this problem are formidable because of its ill-posed nature and the very high sensitivity of the solution to even small errors in boundary conditions or geometrical and electrical models. As a consequence, despite some notable recent results, solutions to this problem have not yet achieved clinical utility. The information available from catheter measurements made in the cardiac veins could be useful to improve the accuracy and robustness of such solutions.

Thus, the overall goal of this research is to develop approaches that use the sparsely sampled information from these catheters both directly and as part of inverse solutions in order to develop more accurate epicardial mapping techniques without the need for open chest surgery and direct access to the heart. Here we describe recent results in catheter lead selection for the estimation approach and also a novel means of using catheter signals to improve the accuracy of epicardial inverse solutions.

2 Methods

Experimental preparation For the estimation studies, we created a database of 153 epicardial activation maps as described previously[2]. Briefly, each map captures the activation sequence from a single beat of a dog heart recorded simultaneously from 490 epicardial sites in six separate experiments. The beats were paced from different locations during a variety of interventions that included localized heating and cooling, injection of procaineamide, coronary infusion of ethanol, and a five-day old infarction.

In previous experiments we have shown the equivalence of signals recorded from venous catheters and nearby epicardial sites[2]. By selecting a subset of epicardial sites located close to the coronary veins, we defined 42 candidate sites for consideration as catheter electrodes. These surrogate catheter sites form the basis of the analysis of lead selection in the estimation algorithm described below.

Estimation algorithm In the estimation algorithm, we reordered the covariance matrix made from all maps in the activation map database according to on the N_k "known" electrode sites that we assumed were the surrogate catheter sites. The covariance matrix then consisted of two auto-covariance diagonal blocks, C_{kk}, of size $N_k \times N_k$ and C_{uu} of size $N_u \times N_u$, where $N_k + N_u = 490$ and two off-diagonal cross-covariance blocks, C_{ku} and C_{uk}. The best least-squares estimator is then the matrix $T = C_{ku}^T \, C_{kk}^{-1}$ of size $N_u \times N_k$. To generate an estimated activation map required only a matrix multiplication of TA_m, where A_m are the activation times measured from the surrogate catheter sites. We evaluated two strategies for selecting electrode subsets for the estimator. The first was selecting approximately equidistantly spaced subsets of the original 42 sites. In the second, we used a lead selection strategy proposed by Lux *et al.* that is based on successively finding the site that contributes the most signal energy

to the estimated maps[4]. In both cases, we developed leadsets of 21, 14, 10, and 5 leads.

Training and testing paradigms To evaluate the performance of the estimator with the regularly spaced and selected leadsets, we used a "leave-one-out" protocol, in which we removed one map from the database, computed the estimator, then tested it on the left out map. By repeating this operation for all members of the database, we could compute summary statistics for the error metrics correlation coefficient, root-mean-squared error, and relative error, defined in the usual manner[2]. As the goal of this study was to evaluate regularly spaced and selected leadsets, we compared estimated maps generated from the same number of leads.

Inverse solution approaches In addition to evaluating estimation approaches based on knowledge of sparsely sampled subsets of epicardial potentials, we have also developed several approaches to use this information to solve an electrocardiographic inverse problem defined as:

$$\mathbf{y}(i) = \mathbf{A} \cdot \mathbf{x}(i) + \mathbf{n}(i), i = 1, 2, \ldots, T \qquad (1)$$

where $\mathbf{y}(i)$ is an $M \times 1$ vector of torso potentials at time instant i, $\mathbf{x}(i)$ is the associated $N \times 1$ vector of epicardial potentials, $\mathbf{A}$ is the $M \times N$ matrix representing the forward solution, and $\mathbf{n}(i)$ is measurement noise. In all these approaches, we assume that we have noisy measurements of the potentials at some subset of N_k epicardial sites, which we group together so that $\mathbf{x}$ is the concatenation of N_k measured values $\mathbf{x_m}$ and $N_u = 490 - N_k$ unmeasured values $\mathbf{x_u}$.
The simplest approach is to subtract the contribution of the known epicardial potentials from the torso potentials, and solve the new equation $\tilde{\mathbf{y}} = \mathbf{y} - \mathbf{A_m} \cdot \mathbf{x_m} = \mathbf{A_u} \cdot \mathbf{x_u} + \mathbf{n}$ for the unmeasured potentials only. This reduced problem is still ill-posed and thus we solved it for $\mathbf{x_u}$ using zero-order Tikhonov regularization[5].
A second approach is based on a Bayesian Maximum *a posteriori* (MAP) estimation that maximizes the posterior distribution of $\mathbf{x}$. To obtain tractable models we follow precedent [1, 5] and assume that $\mathbf{n}$ is Gaussian, *i.i.d.*, and independent of $\mathbf{x}$, thus $\mathbf{y}\backslash\mathbf{x} \sim \mathrm{N}(\mathbf{Ax}, \sigma_n^2\ \mathbf{I}_{M\times M})$. Epicardial potentials, $\mathbf{x}$, are modeled as $\mathbf{x} \sim \mathrm{N}(\mathbf{x_o}, \Sigma_{xx})$. Note that we use Σ for the covariance matrices to emphasize that these are matrices for potentials while the C's of the previous part were for activation times. The goal is to use the measured (surrogate) catheter measurements to help define the prior density for $\mathbf{x}$. We describe here two approaches: a deterministic model, in which $\mathbf{x_o}$ is a time-varying mean equal to the time-varying noise-free potentials and Σ_{xx} is the covariance of epicardial measurement noise; and a stochastic model, which assumes constant (zero) mean and a known signal covariance[1, 6] Thus the best case for the deterministic approach is to measure *all* the epicardial potentials (with noise) while for the stochastic approach it is to have the covariance of the signal at all epicardial sites. More realistic approaches would be to use the measured epicardial potentials to estimate either the rest of the epicardial signals or their covariance. One can also use a *mixed model*, which combines a deterministic model for the measured leads and a stochastic model for the unmeasured leads. In this method, the cross covariance terms between the measured potentials and the unmeasured ones are zero and we only need to define Σ_{uu} using the partial epicardial measurements.

3 Results

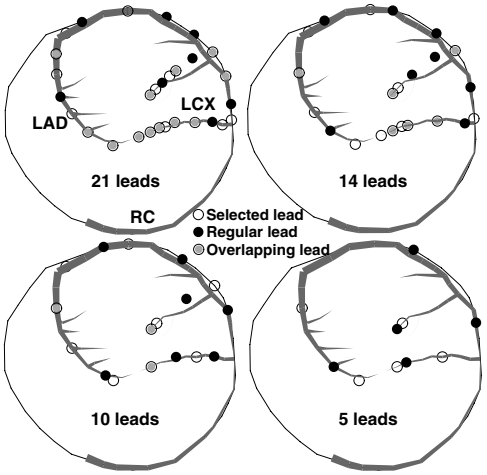

Figure 1: Regularly spaced and selected leadsets. Each panel contains a polar projection of the 490-lead sock with the coronary arteries superimposed for reference. Open circles indicate the optimally selected leads, closed circles the regularly spaced leads, and the concentric circles the leads that belong to both sets.

In Table 1 we show the summary statistics for estimations based on both the regularly spaced and selected leadsets described in Figure 1.
Figure 2 contains a sample of original (upper left hand map) and estimated activation maps for both regularly spaced and selected leadsets.
Figure 3 shows the results from inverse solutions computed using a range of methods based on simulated catheter measurements at 42 out of 490 epicardial leads after adding white Gaussian noise at 30 dB SNR. We first computed torso potentials using our forward model and then solved the inverse problem using the following methods: Tikhonov zero-order applied to the original problem (Panel B) and the reduced problem (Panel C); the stochastic approach assuming known covariance (Panel D); a very simple mixed model in which we assumed unmeasured leads were *i.i.d.*, with power equal to that of measured ones (Panel E); and a hybrid approach that first used estimation to generate the unknown potentials and then the deterministic model to compute the inverse solution (Panel F).

Table 1: Comparison of estimation accuracy for selected and regularly spaced leadsets of 21, 14, 10, and 5 leads. Upper panel: correlation coefficients; middle panel: root mean squared error; lower panel: the difference between the estimated and actual earliest site of activation.

CC (mean ± std)				
Leads	21	14	10	5
Sel.	.953±.05	.949±.05	.944±.04	.912±.07
Reg.	.947±.06	.943±.05	.938±.05	.885±.10
RMSE msec (mean ± std)				
Leads	21	14	10	5
Sel.	6.46±2.2	6.7±2.1	7.2±2.2	9.26±3.0
Reg.	7.01±2.6	7.37±2.6	7.74±2.5	10.96±3.6
LDist mm (mean± std)				
Leads	21	14	10	5
Sel.	7.63±5.9	8.24±5.5	8.92±5.8	12.72±7.6
Reg.	7.81±6.4	8.71±6.3	9.81±6.5	13.24±7.8

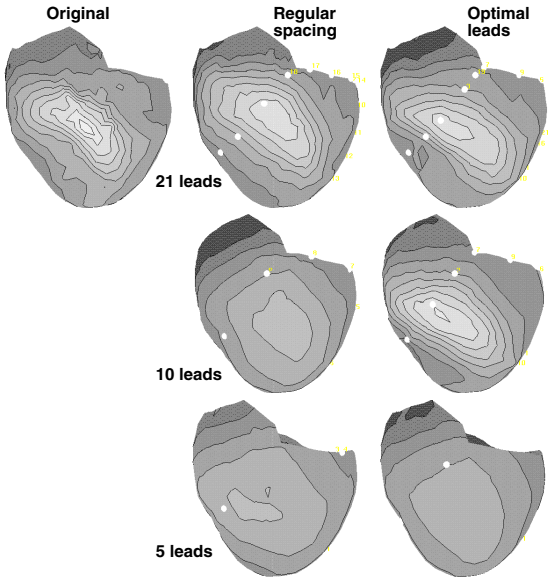

Figure 2: Example of estimated activation maps. Each full column contains estimated activation maps in frontal view for the indicated number of leads and leadset. Lighter shades indicate early activation times and the gray shading and spacing between contours are identical across all maps in the figure.

4 Discussion

The results of the estimation using regularly spaced and selected leads showed consistently higher accuracy for the selected leadsets. Figure 2 illustrates one example in which the selected leads capture the details of the region of early activation. There were a small number of cases in which regularly spaced leads performed better than the selected sets. This occurred in beats stimulated from the right ventricle, a region which received only sparse coverage in the selected leadsets. Future research will include evaluation with our new, larger database that includes more right ventricular beats.
The results of the inverse solutions indicate the value of adequate *a posteriori* knowledge from measurements with the deterministic model based on estimated potentials showing the best results. Such an approach is quite feasible to carry out in practice and so suggests good potential for further development. At this point, we provide these results as a proof of concept of approaches we will continue to develop and refine.

References

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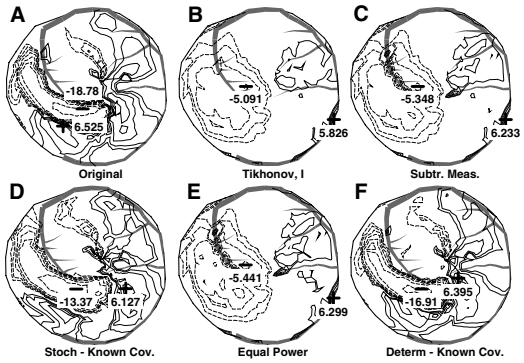

Figure 3: Original epicardial maps in Panel A and those computed using a range of inverse solution approaches. See text for details.