A Convex Relaxation Framework for Initialization of Activation-Based Inverse Electrocardiography

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***Abstract*—In inverse electrocardiography (ECG), the problem of finding activation times on the heart noninvasively from body surface potentials is typically formulated as a nonlinear least squares optimization problem. Current solutions rely on iterative algorithms which are sensitive to the presence of local minima. As a result, improved initialization approaches for this problem have been of considerable interest. In this work, we establish a mathematical optimization framework for the inverse problem, formally show that it is non-convex, and construct a convex relaxation whose solution we use to initialize an iterative algorithm for the original problem. We use simulated experiments based on real canine heart data to test and evaluate this method.**

I. Introduction

The inverse problem of electrocardiography (ECG) is to observe electric potentials on the body surface and estimate source parameters on or in the heart, given a geometric and conductivity model of the torso volume. Activation-based inverse ECG models the functional sources of the heart at any location on the heart surface (synthesized by closing the ventricular endocardium to its epicardium, for example) as having two sequential states: off, then on [1]. One can model the on/off waveform behavior of each source during the QRS complex of a heart beat as a phase-shifted step function, a nonlinear parameterization that reduces the temporal behavior of each source to a single unknown variable: the activation time [2]. Because of the nonlinear waveform parameterization, the inverse problem is typically formulated as a nonlinear least squares (NLLS) minimization problem that is not convex and whose objective function tends to have many suboptimal local minima. This has led to several attempts to incorporate the observed data and prior physiological knowledge into initialization methods, with the belief that local minima found near these initializations are likely to be close to being optimal.

The Fastest Route Algorithm (FRA) is a relatively recently introduced initialization method that employs a simplified wavefront propagation model based on finding the shortest path on a graph. In this method, each edge that connects two nodes of the graph that represents the heart surface is weighted by an assumed propagation velocity [3], [4]. Each node on the surface is considered as a candidate for the site of first activation. An initial earliest node is selected by choosing the resulting wavefront, as determined by the estimated propagation pattern which would follow from a signal triggering activation at that node, whose predicted body surface potentials (BSPs) have the highest correlation with the data. Wavefronts arising from later breakthroughs are then also considered and combined node-wise by retaining the activation time of the first wavefront to arrive [5], [6]. The emphasis of this method is on choosing an initialization with physiologically-plausible propagation behavior that is consistent with the measured BSPs.

Another initialization method, the Critical Point Algorithm (CPA) [7]–[9], has also been widely used to identify independent breakthroughs. CPA does not enforce a propagation model but rather assumes that, because of the geometry of cardiac propagation wavefronts as incident on the heart surface, each activated source that breaks through to that surface can be observed as a sudden increase in the effective rank of the data matrix. When this occurs, activated sources are identified using an approach similar to the MUSIC algorithm [10]. Both FRA and CPA put emphasis on localizing breakthroughs, particularly the initial one [11].

In this work, our approach is to initialize the original NLLS problem using the globally optimal solution to a closely related convex optimization problem. Other work using a constrained convex optimization problem formulation for inverse ECG includes a method reported by Messnarz, *et al.* for finding transmembrane potentials (TMPs) as sources on the heart [12]. Their approach replaces the nonlinear activation time parameterization of TMPs with softer constraints on the optimization variables of a convex quadratic program. This work was done in the context of the "potential-based" formulation of the inverse problem, that is, with the unknowns being free transmembrane potential values at each point on the heart surface at each time instant. The constraints were imposed to "push" the result to have reasonable temporal behavior during activation. Thus, the relationship between the convex optimization problem and an embedded activation-based NLLS problem was not explicitly explored.

The paper by Messnarz, *et al.* was preceded by the work of Brooks, *et al.* which simultaneously imposed spatial and temporal convex quadratic constraints on the potential-based

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inverse ECG problem [13]. This work involved formulating the problem as an unconstrained quadratic program subject to choice of two regularization parameters (determined *a posteriori* using an extension of the L-curve called the L-surface). One major contribution of that paper was to explore the trade-off between fitting the data and obeying the constraints in the potential-based problem setting, but its purpose was not to find improved solutions of the activation-based problem and thus never considered the problem setting found in this paper. Similarly work by the same group using a convex optimization approach, formulated using the nomenclature "admissable solution method", was again set in the context of potential-based solutions, and also combined temporal and spatial constraints [14].

In this paper, we establish a mathematical framework for the original NLLS optimization problem and reformulate it as an equivalent non-convex constrained optimization problem. Using this framework, we isolate the "non-convexity" of the problem to a single constraint on the domain of the optimization variables. We formulate a convex relaxation to the original problem by removing the isolated non-convex constraint. The solution to the convex relaxation is globally optimal but, in general, not feasible for the original non-convex problem. One must take additional steps to find a feasible solution from the solution to the convex relaxation. We propose here one approach that finds the nearest feasible neighbor to the convex relaxation solution and uses it to initialize the NLLS problem[1].

In the rest of this paper, we first, in our background section, define the original optimization problem and analyze its convexity. In the methods section we define the convex relaxation we have developed, explain its relationship to the original NLLS problem, and propose a method of finding the nearest feasible neighbor which we subsequently use to initialize the NLLS problem. We report on numerical experiments in which we apply our method to body surface potentials simulated from known activation times calculated from measured canine data and add noise with an average signal-to-noise ratio (SNR) of 30 dB. Finally, we discuss some alternatives to the nearest feasible neighbor approach and consider the effect of model mismatch on the problem.

II. Background

In this section, we establish a framework for the activation-based problem as an optimization problem. We use this framework to show how the original NLLS problem can be equivalently expressed as a constrained optimization problem. We analyze the new formulation of the problem and show that it is non-convex.

For the remainder of the paper we assume that the data is regularly sampled in time and we only consider those samples that correspond to the QRS complex of a single heartbeat. At any given time, the linear relationship between a vector of body surface potentials, $y \in \mathbb{R}^M$, and a vector of on/off sources on the heart, $x \in \mathbb{R}^N$, is $y = Ax$, where A is the forward matrix that results from solving the forward problem on spatially discretized heart and body surface domains. Furthermore, we assume that the waveforms for the sources are unit step functions whose true amplitudes are known (a vector v) and have been multiplicatively absorbed into the linear forward model ($A \leftarrow A\,\mathrm{diag}(v)$) for notational simplicity.

A. Constrained Optimization Problem

In order to reformulate the NLLS problem as a constrained optimization problem, we define an alternative set of constraints to describe the nonlinearly parameterized waveforms. A discrete time unit step function, $u(t)$, is defined piecewise as:

$$u(t) = \begin{cases} 0 & , \ t < 0 \\ 1 & , \ t \geq 0 \end{cases} .$$

Thus the original nonlinear parameterization is that every source, x_n, has the waveform

$$x_n(t) = u(t - \tau_n)$$

where τ_n is the activation time. Using this parameterization, the original NLLS problem is

$$\text{minimize} \quad \textstyle\sum_t \|y(t) - Ax(t)\|_2^2 + \lambda \|Lx(t)\|_2^2$$

where L is a Tikhonov regularization matrix, λ is the regularization parameter, and the optimization variables are the activation times. The Gauss-Newton algorithm and similar nonlinear least squares solvers require that the objective function is differentiable, so a smoothed step function (with a specified width for the smoothed step transition) is typically used and the subsequent approximate version of the original NLLS problem is solved instead [2], [16].

If we let QRS correspond to the sample times $t = 1, \dots, T$ then we can define a source matrix X that contains all of the temporal samples of each spatial source such that $X_{n,t} = x_n(t)$. Key characteristics of this matrix are that its values are either 0 or 1, are nondecreasing as the column index increases, and that they always increase from 0 to 1 between column indices 1 and T.

Let D be a first-order temporal differencing matrix (i.e. D is $T \times T$ with 1 on the diagonal and -1 on the subdiagonal). If we define the sets $\mathcal{R}$ and $\mathcal{E}$ as

$$\mathcal{R} = \{X \in \mathbb{R}^{(N \times T)} \mid 0 \leq X \leq 1, \ XD^{\mathrm{T}} \geq 0,$$
$$XD^{\mathrm{T}} 1_{(T \times 1)} = 1_{(N \times 1)}\}$$
$$\mathcal{E} = \{X \in \mathbb{R}^{(N \times T)} \mid \ \mathrm{tr}(X^{\mathrm{T}} X) = 1^{\mathrm{T}}_{(N \times 1)} X 1_{(T \times 1)}\}$$

(where $1_{(i \times j)}$ denotes a $i \times j$ matrix of ones) then $X \in \mathcal{R} \cap \mathcal{E}$. Thus we can express the original NLLS problem as a constrained optimization problem

$$\begin{array}{ll} \text{minimize} & \|Y - AX\|_{\mathrm{F}}^2 + \lambda \|LX\|_{\mathrm{F}}^2 \\ \text{subject to} & X \in \mathcal{R} \cap \mathcal{E} \end{array}$$

where the optimization variable is the matrix X and $\|\cdot\|_{\mathrm{F}}$ denotes the Frobenius norm.

[1] An initial report on this method was presented at the 2010 Int. Cong. on Electro., abstract printed in [15].

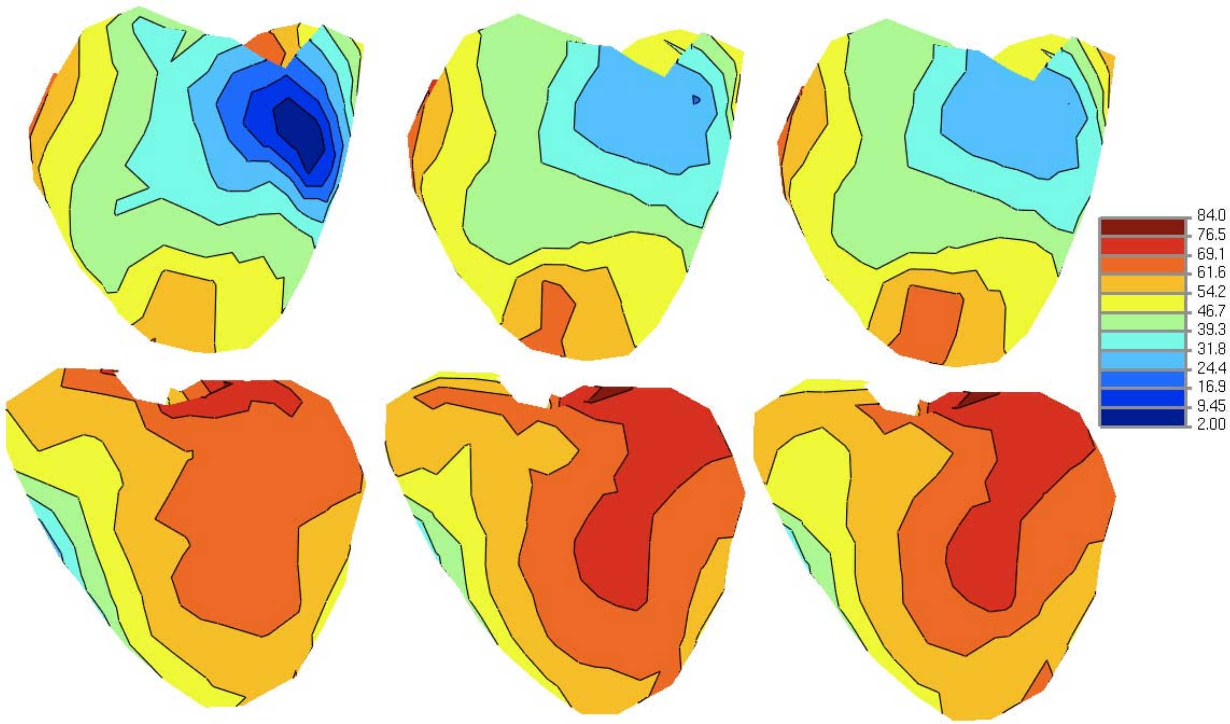


Fig. 1: Isochronal maps, from the epicardially-paced heart beat in Experiment 1, showing *(left)* True activation times, *(middle)* Nearest neighbor initialization activation times, and *(right)* Local minima found with initialization. The top and bottom rows show opposite perspectives of the same isochronal maps. Colormap shows activation times in samples from the start of QRS.

B. Non-Convex Optimization Problem

Here we show, in the context of this formulation, that the constrained optimization problem in the previous section is non-convex. A convex optimization problem is one that can be expressed as the minimization of a convex function whose domain is a convex set. The objective function in our problem

$$f(X) = \|Y - AX\|_{\mathrm{F}}^2 + \lambda\|LX\|_{\mathrm{F}}^2$$

is a linear least squares function with a Tikhonov regularization term and it is convex.

The intersection of the constraints of the optimization problem define the domain of the objective function. In our problem, the set $\mathcal{R}$ is convex because it is defined as the intersection of linear equality and inequality constraints which are convex. However, the set $\mathcal{E}$ is defined by a quadratic equality constraint and it is not convex.

The intersection of a convex set and a non-convex set is also non-convex and therefore, because $\mathcal{E}$ is non-convex, the constraint set for the optimization problem, $\mathcal{R} \cap \mathcal{E}$, is non-convex [17]. This means the domain of the objective function is a non-convex set and thus this constrained optimization problem is non-convex.

III. Methods

For our methods, we formulate a convex relaxation of the original optimization problem by relaxing the domain of the problem to a convex set. From that solution, we return to the domain of the original problem and use it to initialize the original problem.

A. Convex Relaxation

A convex relaxation of an optimization problem is one which replaces or removes non-convex constraints or terms in the objective function with convex ones [17]. In the previous section, we isolated the non-convex part of the problem to a single equality constraint. Our convex relaxation of this problem removes the non-convex constraint and keeps the rest. That is, rather than minimize the function $f(X)$ over the set $\mathcal{R} \cap \mathcal{E}$, we minimize it over $\mathcal{R}$. This means our convex relaxation is defined as

$$\begin{array}{ll} \text{minimize} & f(X) \\ \text{subject to} & X \in \mathcal{R} \end{array}$$

and can be solved globally by any number of numerical optimization methods regardless of initialization.

In this work, we use the Matlab package `CVX` to model the problem [18], [19]. `CVX` interprets the problem, recasts it in a standard form, and then solves it with SDPT3 [20], [21]. The `CVX` specification is

```
B = [A;sqrt(lambda)*L];
U = [Y;zeros(size(L,1),T)];
cvx_begin
    variable X(N,T)
    minimize( norm(U-B*X,'fro') )
```

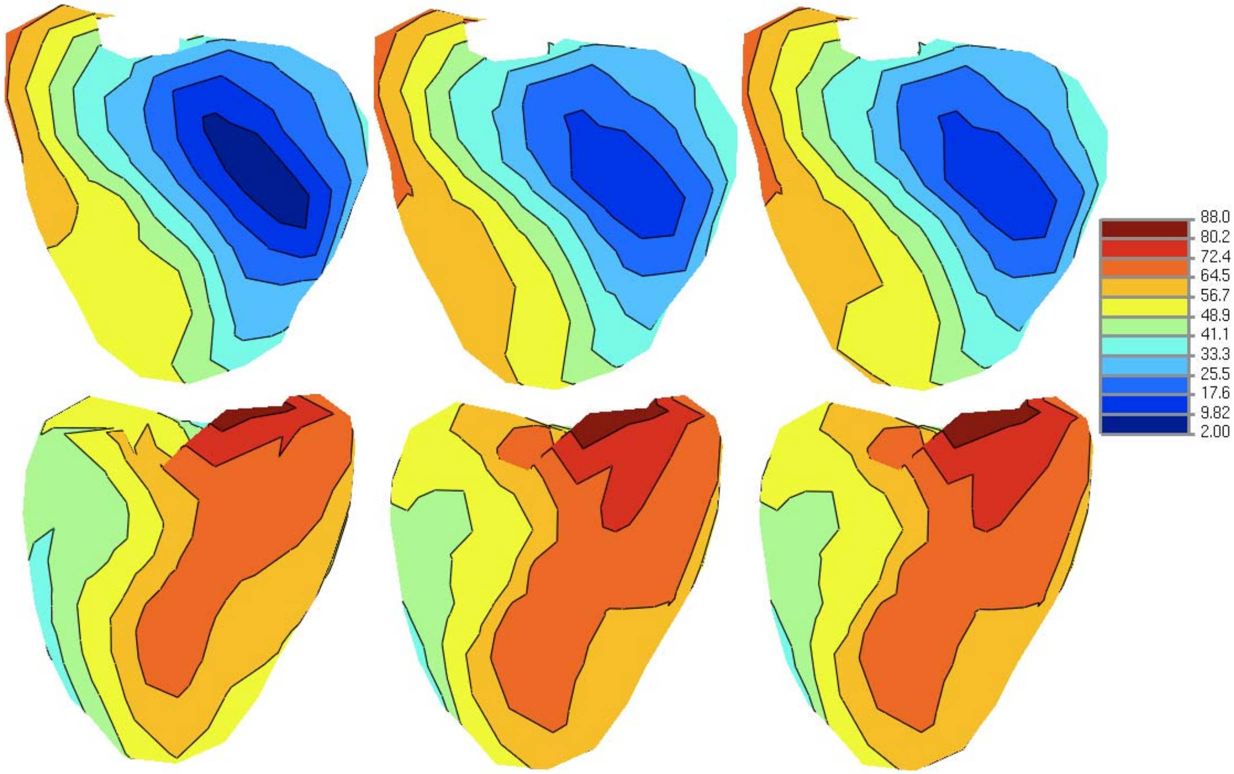


Fig. 2: Isochronal maps from the epicardially-paced heart beat in Experiment 2. Format is the same as Fig. 1

```
    subject to
        X >= 0
        X <= 1
        D*X' >= 0
        sum(D*X')==1
cvx_end
```

where we have expressed the Tikhonov objective function in terms of a single Frobenius norm and explicitly stated the constraints that define the set $\mathcal{R}$.

Theoretically, if the solution to the convex relaxation satisfies $X \in \mathcal{E}$, it is the global solution to the non-convex problem as well. In general, the convex relaxation does not solve the original problem because of infeasibility. In this case, the objective value $f(X)$ for the convex relaxation is simply a lower bound on the objective value of the original constrained problem (which follows from $\mathcal{R} \cap \mathcal{E} \subset \mathcal{R}$ and convex f). That is, if X is infeasible, the objective value for any feasible point in the non-convex set is guaranteed to be greater than $f(X)$.

B. Nearest Neighbor Initialization

As the goal is to solve the original problem, we focus on a way to take advantage of the convex relaxation solution and lower bound. Specifically, if the convex relaxation solution can be made feasible for the original problem by some operations, then it could be useful as an initialization. Even when the convex relaxation solution is infeasible for the original problem, we can quantify its infeasibility by measuring the degree to which the non-convex constraint is violated. There are several ways one could correct this violated constraint, such as adding a heuristic merit function to the objective function. In this paper, we will focus on the simplest approach we have discovered to date: to find the nearest neighbor to the convex relaxation solution in the original feasible set, $\mathcal{R} \cap \mathcal{E}$.

Finding the nearest feasible neighbor means to solve the optimization problem

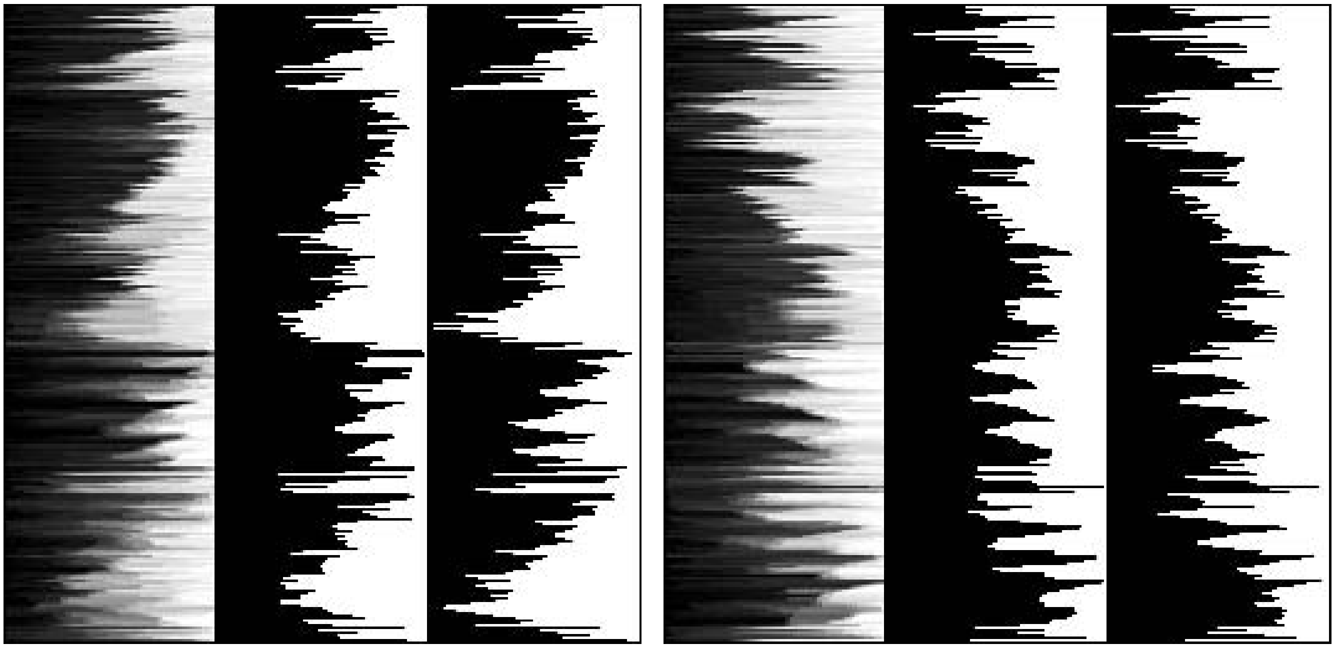
$$\begin{array}{ll} \text{minimize} & \|X_c - X\|_{\mathrm{F}}^2 \\ \text{subject to} & X \in \mathcal{R} \cap \mathcal{E} \end{array}$$

where X_c denotes the solution to the convex relaxation. This problem is row-wise separable, which means that we can solve for each row of X independently. For each row of X, we consider each of the T possible step functions shifted to sample times and choose the one that minimizes the sum of squared differences from the corresponding row of X_c. We choose X as our initialization for the original NLLS problem and solve it for a local minimizer.

IV. Experiments

To test the convex relaxation and nearest neighbor initialization methods we developed, we designed experiments which simulate body surface potentials from known activation times.

Activation times were estimated from data measured on the epicardium of a canine heart under experimental conditions at the Cardiovascular Research and Training Institute (CVRTI) at the University of Utah (see [22], [23] for more detailed description of the experiments and data acquistion). We used data



(a) Convex Relaxation (b) Nearest Neighbor (c) True Sources (d) Convex Relaxation (e) Nearest Neighbor (f) True Sources

Fig. 3: Visualization of source matrices for Experiments 1 *(a-c)* & 2 *(d-f)* with grayscale colormap (black=0, white=1) oriented such that time increases from left to right horizontally in each matrix. We show the *(a,d)* Convex relaxation solutions, *(b,e)* Nearest neighbor initialization source matrices, and *(c,f)* True source matrices for the corresponding experiment.

in which the beat was initiated from an epicardial pacing site and estimated the epicardial activation times. These activation times were mapped to the epicardium of the ECGSIM "normal male" heart geometry (see Figures 1 & 2, [24]), and then propagated to the endocardium [11], [25]. We also used the corresponding torso geometry and ECGSIM boundary element method solution to the forward problem.

Using the original nonlinear parameterization of the sources, we calculated the true source matrix, X, from the estimated activation times and multiplied it by the given forward matrix, A, to obtain our body surface potentials. We added IID normally-distributed pseudorandom noise to the body surface potentials with an average signal-to-noise ratio (SNR) of 30 dB to obtain the noisy observations, Y, which we supplied to our inverse procedure.

This experimental procedure was applied to several data sets, two of which we present in this paper. The known (or "true") activation times for these data sets are shown in the left column of Figures 1 & 2. These particular examples were chosen from all of the experiments because the data sets are from beats that were paced on the epicardium, starting from different sides of the heart, and are representative of typical activation patterns resulting from epicardial pacing in these experiments. We visualized the source matrices for the convex relaxation solution, nearest neighbor initialization, and true activation times for both experiments in Figure 3. The visualizations map the source matrix values in $[0, 1]$ to a grayscale colormap such that zero is black and one is white. Each row of the matrices corresponds to the same spatial source and each column corresponds to the same sample time during QRS. Using this technique, we see that there are similarities between the convex relaxation solutions and the true source matrices that the nearest neighbor initialization method preserves.

From left to right, the columns of Figure 1 show the true, nearest neighbor initialization, and optimization algorithm output activation times displayed as isochronal maps for Experiment 1. Likewise, Figure 2 shows the analogous results for Experiment 2. In both cases, the optimization algorithm does not change the initializations to a visually significant degree. The output of the non-linear iterative algorithm is a local minima of the objective function near the initialization in the solution space. Under these simulated experimental conditions, this is favorable because the nearest neighbor initializations are already quite close to the true answer.

V. Discussion

In this paper, we described a new method for initializing the nonlinear least squares (NLLS) problem posed to solve the activation-based inverse electrocardiography (ECG) problem. To accomplish this, we first expressed the NLLS problem as a constrained optimization problem and analyzed its convexity. Determining formally that the problem is not convex and isolating the non-convex constraint that causes this, we formulated a convex relaxation by removing the responsible constraint while retaining everything else.

To initialize the original NLLS problem, we chose one of many possible procedures to obtain a feasible point from the convex relaxation solution. Specifically, we found the nearest neighbor of the convex relaxation solution in the feasible set. Another option would be to add a heuristic to the objective function that pushes solutions towards the feasible set. Yet another alternative, called a homotopy method, would be to solve a sequence of optimization problems (each of whose solutions initialize the next) during which a slowly-changing variational parameter transforms the convex relaxation into the original problem.

While the nearest neighbor method we suggested in this paper is simple, our experiments show that it works very well, at least under the simulated conditions reported on here. The relatively small changes between the nearest neighbor initializations and the local minima in Figures 1 & 2 indicate that the initializations lie close to local minima. In particular, in the simulated results shown here, we found that the intuition to look for solutions to the NLLS problem that are close to the convex relaxation solution served us well.

In effect, the results presented in this paper were obtained by making the assumption that the model that generated the observations is known. These assumptions include waveform amplitude and shape, as well as heart and body surface geometries. It is unclear how model error, in this sense, will affect the problem and further work must be done to analyze its consequences. However, based on our experience to date, we have observed that another model parameter, the transition width for smoothed step functions (for the approximated NLLS problem supplied to Gauss-Newton-type solvers), can have a considerable effect on the outcome of the optimization procedure. Furthermore, for our method, preliminary results indicate that with clinical data (measured on human subjects with known abnormalities or under known clinical manipulations) there may be significant errors introduced by model mismatch as well. The need to describe these preliminary results in sufficient detail makes it impossible to include more on them here, but we plan to address this further in our presentation at the conference. We will also present comparisons to results with FRA initializations, also omitted here for reasons of space.

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References

[1] J. Cuppen and A. Van Oosterom, "Model Studies with the Inversely Calculated lsochrones of Ventricular Depolarization," *Biomedical Engineering, IEEE Transactions on*, no. 10, pp. 652–659, 1984.

[2] G. Huiskamp and A. Van Oosterom, "The depolarization sequence of the human heart surface computed from measured body surface potentials," *IEEE Transactions on Biomedical Engineering*, vol. 35, no. 12, pp. 1047–1058, 1988.

[3] P. van Dam and A. van Oosterom, "Volume conductor effects involved in the genesis of the P wave," *Europace*, vol. 7, no. s 2, pp. 30–38, 2005.

[4] P. van Dam, T. Oostendorp, and A. van Oosterom, "Simulating ECG Changes during Acute Myocardial Ischemia," *Computers in Cardiology, 2007*, pp. 325–328, 2007.

[5] ——, "Application of the fastest route algorithm in the interactive simulation of the effect of local ischemia on the ECG," *Medical and Biological Engineering and Computing*, vol. 47, no. 1, pp. 11–20, 2009.

[6] P. van Dam, T. Oostendorp, A. Linnenbank, and A. van Oosterom, "Non-invasive imaging of cardiac activation and recovery," *Annals of Biomedical Engineering*, pp. 1–18, 2009.

[7] G. Huiskamp and F. Greensite, "A new method for myocardial activation imaging," *IEEE Transactions on Biomedical Engineering*, vol. 44, no. 6, pp. 433–446, 1997.

[8] A. Pullan, L. Cheng, M. Nash, C. Bradley, and D. Paterson, "Noninvasive electrical imaging of the heart: theory and model development," *Annals of Biomedical Engineering*, vol. 29, no. 10, pp. 817–836, 2001.

[9] A. Pullan, L. Cheng, and M. Buist, *Mathematically Modelling the Electrical Activity of the Heart: From Cell to Body surface and back again*. World Scientific Pub Co Inc, 2005.

[10] P. Stoica and R. Moses, *Introduction to spectral analysis*. Prentice Hall Upper Saddle River, New Jersey, 1997, vol. 57.

[11] B. Erem, P. van Dam, A. Keely, J. Stinstra, T. Oostendorp, and D. Brooks, "Methods for initialization of activation based inverse electrocardiography using graphs derived from heart surface geometry," in *Computers in Cardiology, 2009*. IEEE, pp. 189–192.

[12] B. Messnarz, B. Tilg, R. Modre, G. Fischer, and F. Hanser, "A new spatiotemporal regularization approach for reconstruction of cardiac transmembrane potential patterns," *Biomedical Engineering, IEEE Transactions on*, vol. 51, no. 2, pp. 273–281, 2004.

[13] D. Brooks, G. Ahmad, R. MacLeod, and G. Maratos, "Inverse electrocardiography by simultaneous imposition of multiple constraints," *Biomedical Engineering, IEEE Transactions on*, vol. 46, no. 1, pp. 3–18, 1999.

[14] G. Ahmad, D. Brooks, and R. MacLeod, "An admissible solution approach to inverse electrocardiography," *Annals of biomedical engineering*, vol. 26, no. 2, pp. 278–292, 1998.

[15] B. Erem, A. Ghodrati, G. Tadmor, R. MacLeod, and D. Brooks, "Combining initialization and solution inverse methods for inverse electrocardiography," *Journal of electrocardiology*, vol. 44, no. 2, p. 21, March 2011.

[16] R. Modre, B. Tilg, G. Fischer, and P. Wach, "Noninvasive myocardial activation time imaging: a novel inverse algorithm applied to clinical ECG mapping data," *Biomedical Engineering, IEEE Transactions on*, vol. 49, no. 10, pp. 1153–1161, 2002.

[17] S. Boyd and L. Vandenberghe, *Convex optimization*. Cambridge Univ Pr, 2004.

[18] M. Grant and S. Boyd, "Graph implementations for nonsmooth convex programs," in *Recent Advances in Learning and Control*, ser. Lecture Notes in Control and Information Sciences, V. Blondel, S. Boyd, and H. Kimura, Eds. Springer-Verlag Limited, 2008, pp. 95–110.

[19] ——, "CVX: Matlab software for disciplined convex programming, version 1.21," http://cvxr.com/cvx, Feb. 2011.

[20] K. Toh, M. Todd, and R. Tütüncü, "SDPT3—a Matlab software package for semidefinite programming," *Optimization Methods and Software*, vol. 11, no. 12, pp. 545–581, 1999.

[21] R. Tütüncü, K. Toh, and M. Todd, "Solving semidefinite-quadratic-linear programs using SDPT3," *Mathematical Programming*, vol. 95, no. 2, pp. 189–217, 2003.

[22] R. MacLeod, R. Lux, and B. Taccardi, "A possible mechanism for electrocardiographically silent changes in cardiac repolarization*," *Journal of electrocardiology*, vol. 30, pp. 114–121, 1998.

[23] R. MacLeod, Q. Ni, B. Punske, P. Ershler, B. Yilmaz, and B. Taccardi, "Effects of heart position on the body-surface electrocardiogram," *Journal of Electrocardiology*, vol. 33, pp. 229–237, 2000.

[24] A. Van Oosterom and T. Oostendorp, "ECGSIM: an interactive tool for studying the genesis of QRST waveforms," pp. 165–168, 2004.

[25] A. Keely, "Infrastructure and comparison of inverse solutions to the problem of electrocardiography," Master's thesis, Northeastern University, December 2007.