Identifying Myocardial Ischemia by Inversely Computing Transmembrane Potentials from Body-Surface Potential Maps

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***Abstract*—We attempted to solve the inverse electrocardiographic problem of computing the transmembrane potentials (TMPs) throughout the myocardium from a body-surface potential map, and then used the recovered potentials to estimate the size and location of myocardial ischemia. We modeled the bioelectric process by combining a static bidomain heart model with a torso conduction model. Although the task of computing myocardial TMPs at an arbitrary time instance is still an open problem, we showed that it is possible to obtain TMPs with moderate accuracy during the ST segment by assuming all cardiac cells are at the plateau phase. Moreover, the inverse solutions yielded a good estimate of ischemic regions, which is of more clinical interest than merely reporting the voltage values. We formulated the inverse problem as a minimization problem constrained by a partial differential equation that models the forward problem. This framework greatly reduces the computational costs compared with the traditional approach of building the lead-field matrix. It also enables one to flexibly set different discretization resolutions for the source variables and other state variables, a desirable feature for solving ill-posed inverse problems. We conducted finite element simulations of a phantom experiment over a 2D torso model with synthetic ischemic data. Preliminary results indicated that our approach is feasible and suitably accurate for the common case of transmural myocardial ischemia.**

***Index Terms*—Inverse Problem, Electrocardiography, Finite Element Method, Myocardial Ischemia**

I. Introduction

Myocardial ischemia, a precursor of myocardial infarction, occurs when cardiac myocytes are damaged due to lack of oxygen or nutrients, normally caused by occlusion of coronary arteries. It is one of the most common diseases and a leading cause of death in the western world. Myocardial ischemia is clinically diagnosed in part by the elevation/depression of the ST segment in electrocardiographic (ECG) signals, because the ST-shift is caused by the injury currents resulting from the different transmembrane potentials between healthy and ischemic tissues. However, analyzing ECG morphologies has limited ability to localize ischemic regions, and a computerized method achieving that function would effectively assist physicians in diagnosis and treatment. This paper presents a mathematical approach for identifying ischemic regions by solving an inverse source problem: to compute the transmembrane potentials (TMPs) throughout the myocardium from the voltages measured at the body surface.

The goal of inverse ECG problems is to non-invasively estimate cardiac electrical activities from their induced voltages measured at the body surface. While inverse ECG problems traditionally seek cardiac sources such as epicardial potentials [1], [2] or activation sequences [3], [4], studies of myocardial ischemia typically consider the transmembrane potential as the source model[5]–[9].

However, research has been limited on reconstructing the TMPs within the heart from the body-surface potentials. It still remains an open problem to accurately calculate the transmembrane potentials at an arbitrary time instance, because this inverse problem is severely ill-posed and the solution is not unique. Methods for localizing myocardial ischemia have been proposed such as the model-based optimization [10] or the level set method [11], but these methods avoid direct calculation of TMPs by parameterizing the location and shape of ischemic regions. Another study [12] localized myocardial ischemia by calculating the integral of TMPs during the ST-segment and reported very optimistic recoveries, as the integration supposedly reduced the effect of measurement noise. Finally, the aforementioned methods, before performing the inverse calculation, form a so-called lead-field matrix that maps the TMPs to the body-surface potentials. This process has high computational cost because the associated bidomain problem needs to be solved multiple times.

Our study is based on the hypothesis that despite the ill-posed nature of the problem, one may obtain modestly accurate TMPs at one time instant during the ST interval. Although the reconstructed voltage values are not sufficiently accurate for precise quantification of the potentials, their qualitative "patterns" may enable a satisfying recovery of the size and position of ischemic regions. We modeled the ECG problem by combining a mono-domain torso model with a static bidomain heart model, which represents the cardiac source by the distribution of TMPs. We formulated the inverse problem as a minimization problem constrained by some partial differential equations (PDE) that models the forward problem. The framework of constrained minimization was introduced to the inverse TMP problem by Nielson et al.[11], and we generalized it and included more constraints. This approach differs from the traditional approach of forming a lead-field matrix and "inverting" it by direct Tikhonov regularization, and has two advantages: 1) less computational

cost, and 2) it allows a flexible setting of the discretization resolution for the TMPs and other state variables. The latter is desirable as the ill-posed inverse problem typically requires different resolutions for the sought-for unknowns and other state variables [13], [14].

II. Method

A. The Mathematical Model

Our bioelectric model consists of a static bidomain heart model combined with a mono-domain torso model, as shown in Fig 1. The whole mathematical model is given by the following set of equations:

$$\nabla \cdot (\sigma_i + \sigma_e)\nabla u_e(\boldsymbol{x}) = -\nabla \cdot \sigma_i \nabla v(\boldsymbol{x}),\ \boldsymbol{x} \in H \quad (1)$$

$$\nabla \cdot (\sigma_t \nabla u(\boldsymbol{x})) = 0,\ \boldsymbol{x} \in \Omega \quad (2)$$

$$\vec{n}_T \cdot \sigma_t \nabla u(\boldsymbol{x}) = 0,\ \boldsymbol{x} \in \Gamma_T \quad (3)$$

$$u_e(\boldsymbol{x}) = u(\boldsymbol{x}),\ \boldsymbol{x} \in \Gamma_H \quad (4)$$

$$-\vec{n}_H \cdot \sigma_e \nabla u(\boldsymbol{x}) = \vec{n}_T \cdot \sigma_t \nabla u,\ \boldsymbol{x} \in \Gamma_H \quad (5)$$

$$\vec{n}_H \cdot \sigma_i \nabla (v + u_e) = 0,\ \text{on } \Gamma_H. \quad (6)$$

Eq (1) is the static bidomain equation. As we consider only the plateau phase during which the transmembrane potentials remain largely stable, the time-varying term in the standard bidomain equation is removed, leading to Eq (1). H is the heart volume, σ_i and σ_e are the intra/extra-cellular conductivity, u_e is the extracellular potential and v is the transmembrane potential. Eq (2) describes the passive torso volume conductor Ω, where u is the potential field within the torso and σ_t denotes the tissue conductivity. Eq (3) implies zero electrical currents leave the torso surface, Γ_T. Eq (4) - (6) state the boundary conditions at Γ_H, the interface between the heart and the torso. Eq (4) implies the extracellular potential is continuous. Eq (5) states that the electrical currents flowing out of the heart is equal to the currents flowing into the torso. Eq (6) means that the cardiac intracellular space is insulated from the torso. ($v + u_e$ gives the intracellular potential.) Details of this model can be found in Chapter 5 of [15].

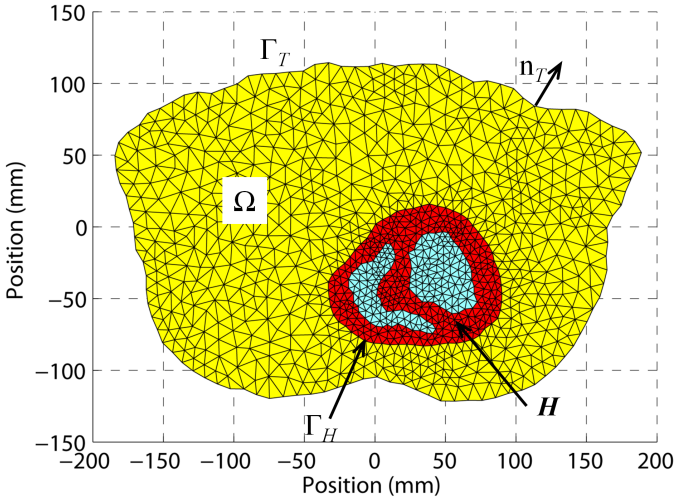

Fig. 1. The torso mesh. The red part is the myocardium. The cyan region denotes the two ventricle cavities, which are treated as part of the torso volume Ω in our model equations.

By combining the heart and torso models, we may express the above equations in a simplified form of a Poisson equation:

$$\nabla \cdot \sigma \nabla u(\boldsymbol{x}) = \begin{cases} 0, & \boldsymbol{x} \in \Omega, \\ -\nabla \cdot \sigma_i \nabla v(\boldsymbol{x}), & x \in H, \end{cases} \quad (7)$$

$$\vec{n_T} \cdot \sigma \nabla u(\boldsymbol{x}) = 0,\quad \boldsymbol{x} \in \Gamma_T, \quad (8)$$

$$u(\boldsymbol{x}) = \begin{cases} \text{torso potential}, & x \in \Omega, \\ \text{extracellular potential}, & x \in H, \end{cases} \quad (9)$$

$$\sigma(\boldsymbol{x}) = \begin{cases} \sigma_i + \sigma_e, & x \in H, \\ \sigma_t, & x \in \Omega. \end{cases} \quad (10)$$

Eq (7) dictates the relation between the transmembrane potential field $v(\boldsymbol{x})$ and its resulting extracellular potential field $u(\boldsymbol{x})$. The forward problem estimates the field u given an characterization of v, whereas the inverse problem aims to recover v given $u(\boldsymbol{x})$ that resides on the body surface. In this study, we solved Eq (7) by the finite element method, which converts the equation into a matrix system as follows:

$$Au = Sv \quad (11)$$

where A and S are the stiffness matrix corresponding to the operators on both sides of Eq (7).

B. Ischemia Modeling

We adopted a synthetic ischemia model proposed in [16] and used for inverse simulation in [17], in which healthy and ischemic heart tissues are characterized by the transmembrane potential at the plateau phase. The setting is given below:

$$v(x) = \begin{cases} 0\ mV, & \text{in healthy tissue;} \\ -30\ mV, & \text{in ischemic tissue.} \end{cases} \quad (12)$$

where plateau potentials between healthy and ischemic cells differ by an assumed 30 mV, an approximation suggested by previous studies and, more importantly, a value that is not critical to the simulations because of the threshold operation performed on the solution (see below). When implementing Eq (12) by the finite element method, we assumed a linear transition of $v(x)$ in the border zone: when a node belongs to the ischemic tissue and its adjacent node belongs to the healthy tissue, v is a linear function within the element connecting the two nodes.

With this model, we simulated the effect of myocardial ischemia of different locations and sizes. Our inverse calculation did not incorporate any *a priori* information of the TMP field. When estimating the ischemic regions based on the inverse solution, we exploited the assumption that the TMP field at the plateau phase is binary: any region where the TMP is below a threshold value is regarded as an ischemic region.

C. Solve the Inverse Problem

The traditional way of solving our inverse ECG problem is to numerical discretize the Poisson equation (7) and derive a lead-field matrix $\mathbf{K}$ that relates the torso surface potential u_T and the TMP v: $u_T = \mathbf{K}v$. Because $\mathbf{K}$ is ill-conditioned,

regularization such as the Tikhonov method is applied to acquire v:

$$v = \underset{v}{argmin} \{\|\mathbf{K}v - u_T\|_2 + \lambda\|\mathbf{W}v\|_2\}. \quad (13)$$

Although this approach is feasible for the inverse problems that recover epicardial potentials or activation sequences, its computational cost is too high to make it feasible for the inverse problem we consider. Suppose the discrete Poisson equation (11) has a size of m and v has a size of n, deriving the lead-field matrix requires one to solve a m by m linear system for n times. For a bidomain model in three dimension, m and n can easily reach hundreds of thousands.

We solved the inverse problem by formulating it as a constrained minimization problem, given as follows:

$$v = \underset{v}{argmin}\|W(v - v_{prior})\|_2 \quad (14)$$

$$\text{subject to } Au = Sv \quad (15)$$

$$\text{and } \|Qu - u_T\|_2 \leq \epsilon\|u_T\|_2 \quad (16)$$

where W is a matrix describing which property of the inverse solution is to be constrained. The matrix Q maps the entire potential field u to the measurement locations at the body surface. Eq (16) states that the misfit between the predicted data and the measured data (u_T) should be within the noise level ϵ, which is known in experiments. Eq (15) is the discrete version of the forward problem Eq (7).

This constrained minimization problem is well-studied by the optimization community. It is transformed into a quadratic program or a second-order cone program, and then solved by a primal-dual algorithm or a log-barrier algorithm [18]. Mature optimization solvers are available for this task. We used the CVX, a package for specifying and solving convex programs [19].

It is worth mentioning that the constrained minimization formulation is essentially equivalent to the Tikhonov regularization given by Eq (13), but without needing to tune the parameter λ. Instead ones need to search a trust region of radius ϵ when solving the minimization, *e.g.*, by interior-point methods.

D. Simulation Setup

We conducted finite element simulation of a phantom experiment based on a 2D thorax domain. As shown in Fig 1, the thorax domain consists of 1329 triangle elements in the torso volume, 547 elements in the myocardium, and 299 elements in the ventricular cavities, with a total of 1141 nodes. Both the extracellular and transmembrane potential fields were defined over mesh nodes. As the goal of the current study was to validate the feasibility of the optimization method, we attempted to minimize the effect of the conductivities by using simple phantom values. The conductivities are given as $\sigma_i = \sigma_e = [0.5, 0.5]$ and $\sigma_t = [1.0, 1.0]$, along the longitudinal and transverse directions, respectively.

We first specified an ischemic region in the myocardium, and set the synthetic transmembrane potential data according to the model of Eq (12). We then performed forward simulation to obtain the torso-surface potentials, which, after being contaminated with noise, served as the input for the inverse calculation. Ischemic regions were estimated from the calculated TMP field by the following criterion: if the TMP at a node was below a threshold value, the node was an ischemic site and all elements adjacent to this node were regarded as ischemic regions. The threshold value for a given TMP field v was determined by

$$threshold = mean(v) - 0.3(mean(v) - min(v)) \quad (17)$$

based on the hypothesis that the TMP at an ischemic site should be notably below the average TMP voltage because ischemic regions were assumed to account for a minor part of the myocardium.

III. Results

Fig 2 shows a case of transmural ischemia at the anterior right ventricle and its resulting extracellular potential field (the forward solution). Recall that the transmembrane potentials at the plateau phase were -30mV for ischemic region and 0mV for health region.

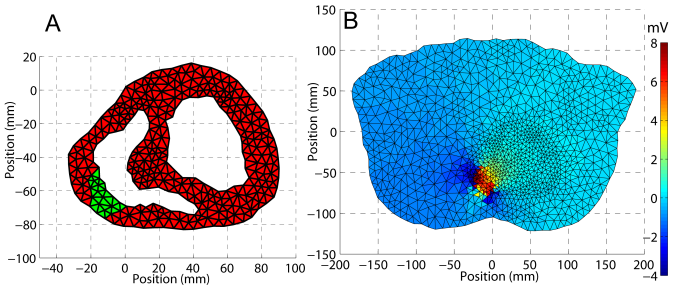

Fig. 2. Left: the "true" ischemic region denoted by the green color. Right: the resulting extracellular potential field.

We solved the inverse problem by applying the zero-order (magnitude), first-order (gradient), and second-order (Laplacian) constraints on the pursued transmembrane potentials, respectively. This was achieved by choosing different operator W in Eq (14). Because our optimization framework is mathematically equivalent to the Tikhonov method, we hereafter use the term "the *k*th-order Tikhonov method" to describe which quantity is being minimized. Readers are reminded that the methods were implemented by the aforementioned optimization framework.

The zero-order Tikhonov method yielded a nearly all-zero solution and thus are not presented in this paper. In the first-order Tikhonov (FOT), W was the variational-form gradient operator we previously developed [20], for it is difficult to formulate a discrete gradient operator over irregular meshes. In the second-order Tikhonov (SOT), W was a discrete Laplacian operator obtained by second-order Taylor expansion at each node, as proposed in [21].

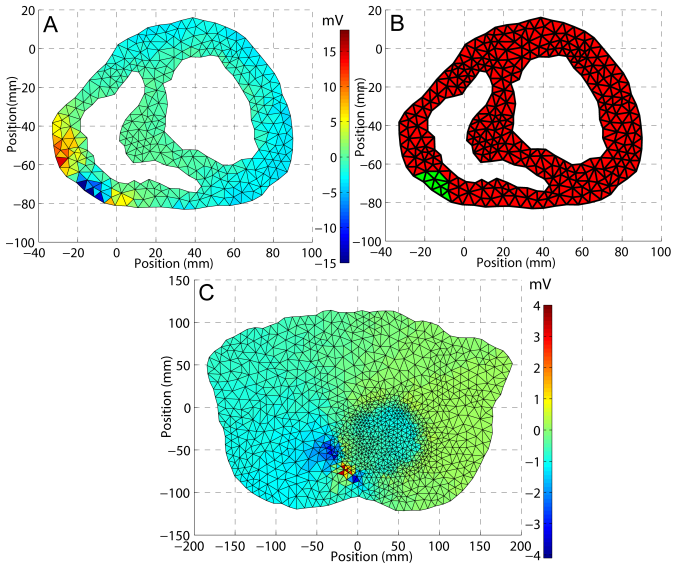

Fig. 3. Inverse solutions by the FOT given 30dB input noise. A: the computed TMP field. B: the inferred ischemic region. C: the reconstructed extracellular potential field.

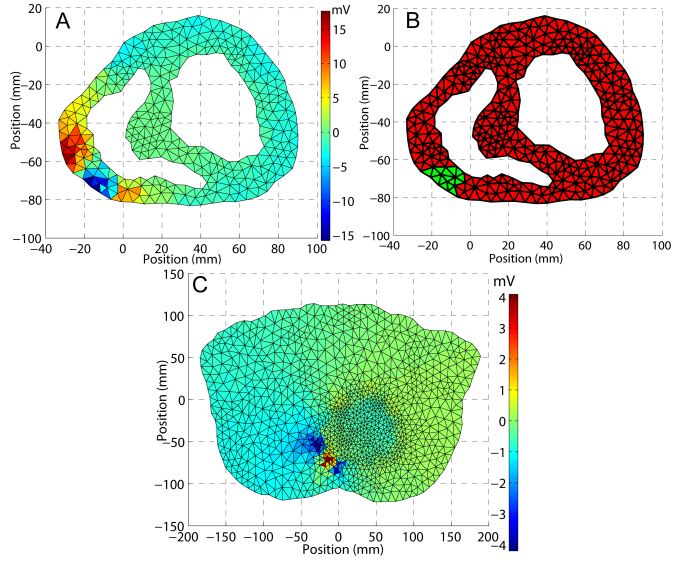

Fig. 4. Inverse solutions by the SOT given 30dB input noise. A: the computed TMP field. B: the inferred ischemic region. C: the reconstructed extracellular potential field.

The inverse calculation was made with the input torso potential being contaminated by a white noise of 30dB SNR ratio. The results are shown in Fig 3 for the FOT method and in Fig 4 for the SOT method. The results achieved by both methods were similar and consistent. As anticipated, the L2-norm-based Tikhonov regularization yielded a smoothed inverse solution of transmembrane potentials. However, with proper color rescaling one may see that the recovered fields preserved the polarity of the original field, thereby enabling a satisfactory estimate of the ischemic region after a simple thresholding.

IV. Discussion

The forward simulation in Fig 2 shows that transmural ischemia results in an elevation of extracellular potentials at the ischemic region and two regions of depression over opposite sides of the ischemic region. This elevation/depression pattern is a characteristic of transmural ischemia according to previous studies [5], [6]. The consistency of our results with the literature demonstrates the efficacy of our method of integrating the bidomain heart with the torso for ischemia simulations.

The first-order and second-order Tikhonov methods produced results of similar quality. Both methods successfully located the position of ischemia, and the SOT was slightly better in estimating the shape of the ischemic region. The calculated TMPs (by both methods) were not in the range of -30-0 mV as given by our source model. The reason is that we provided no *a priori* knowledge of the myocardial transmembrane potentials, without which, there is insufficient information for accurate absolute values. The goal of ischemia detection is simply to identify the region affected rather than the absolute values of TMPs.

We also observed that elevated values of TMP in some healthy regions near the ischemic zone, even though these regions are expected to have the same amplitude as the rest of the heart. This artifact is due to the limitation of the ordinary Tikhonov regularization, which applies a constraint globally to the entire heart without considering local features. Additional constraints may be included in the inverse optimization, such as a condition that the normal regions should have uniform amplitude. This is a possible direction for future research.

The constrained optimization framework for inverse calculation has several advantages. First, this framework allows flexible integration of multiple constraints. One may apply not only constraints on the transmembrane potentials but also constraints on other state variables such as the extracellular potentials or conductivities. The reason is that all the variables are intrinsically related by the forward model, which is incorporated in the framework as a constraint.

A second advantage is that this framework allows one to flexibly discretize different variables with different resolutions. Our previous studies revealed that discretization choices heavily impact the inverse ECG solutions in practical situations [13], [14]. In the ischemia-estimation study, one may desire to limit the resolution for the transmembrane potential field in order to constrain both the numerical ill-conditioning and computation cost. Conversely, a fine mesh for calculating the bidomain model may be appropriate for obtaining accurate extracellular potentials. The constrained minimization framework enables such specific adjustments so as to make the computation tractable while maintaining accuracy.

Another technical issue worth mentioning is that the inverse solution is sensitive to the numerical accuracy of the operator W that specifies the constraint. The myocardium geometry is very irregular, so one needs to ensure the numerical values for the operator is accurate over the geometry, especially at the

boundary. If the constraining operator is inaccurate or excludes the boundary, the inverse solution may be poorly regularized at the boundary. In this study, we constructed the Laplacian and gradient operators based on the entire heart geometry (including the cavities), and then extracted the submatrix that corresponds to the myocardium.

V. Conclusion and Future Work

This paper reports our initial investigation of estimating myocardial ischemia by inversely solving the transmembrane potentials within a heart from a body-surface potential map. We integrated the bidomain heart model with the monodomain torso model, and solved the inverse problem within a constrained minimization framework. Our motivation was that although accurately reconstructing the transmembrane potentials is highly difficult, if not unlikely, it may be possible to reconstruct the "patterns" of the TMP field which enables us to estimate the ischemic regions in the heart. Simulation results based on a 2D torso anatomy with synthetic ischemic data indicated that our approach is feasible.

Future work include extending this approach to three-dimensional simulations and exploring advanced constraints that yield more accurate inverse solutions. Total variation method and L1-norm minimization are some methods worth investigation. When it comes to realistic anatomical models in three dimension, the problem size and computation cost will become a major concern, and it is important to explore discretization strategies that achieve a good balance between model accuracy, ill-conditioning and computation cost.

Our ultimate goal is to validate the simulated results with the experimental data from the the clinical ischemia research conducted at the Cardiovascular Research and Training Institute at the University of Utah.

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