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Inverse electrocardiographic source localization of ischemia: An optimization framework and finite element solution

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ABSTRACT

With the goal of non-invasively localizing cardiac ischemic disease using body-surface potential recordings, we attempted to reconstruct the transmembrane potential (TMP) throughout the myocardium with the bidomain heart model. The task is an inverse source problem governed by partial differential equations (PDE). Our main contribution is solving the inverse problem within a PDE-constrained optimization framework that enables various physically-based constraints in both equality and inequality forms. We formulated the optimality conditions rigorously in the continuum before deriving finite element discretization, thereby making the optimization independent of discretization choice. Such a formulation was derived for the L_2-norm Tikhonov regularization and the total variation minimization. The subsequent numerical optimization was fulfilled by a primal–dual interior-point method tailored to our problem's specific structure. Our simulations used realistic, fiber-included heart models consisting of up to 18,000 nodes, much finer than any inverse models previously reported. With synthetic ischemia data we localized ischemic regions with roughly a 10% false-negative rate or a 20% false-positive rate under conditions up to 5% input noise. With ischemia data measured from animal experiments, we reconstructed TMPs with roughly 0.9 correlation with the ground truth. While precisely estimating the TMP in general cases remains an open problem, our study shows the feasibility of reconstructing TMP during the ST interval as a means of ischemia localization.

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1. Introduction

Electrocardiography (ECG) aims to non-invasively capture the electrophysiological activity of the heart by measuring its resulting potential field at the body surface. Because of recent advances in computational modeling, computing power and imaging technology, ECG is evolving from a basic clinical tool into a new era of personalized healthcare, in which computer models integrate not only unprecedented complexity and realism but also biophysical information specific to individual subjects [27]. Subject-specific computer models, typically in anatomical or physical aspects, are poised to promote mechanistic and functional studies at various biological levels ranging from cells up to organs, opening promising opportunities for clinical diagnosis, intervention planning and therapy delivery. Essential to this emerging paradigm, and the overarching goal of

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this study, is the development of computational methods that efficiently handle enough model complexity and realism to be useful for clinical needs.

The foundation of ECG is an inverse source problem governed by partial differential equations (PDEs) which describe the bioelectric source/conduction model of the heart and body. The most biophysically accurate yet tractable heart model is the bidomain approach [25], in which the cardiac source is represented by the transmembrane potential (TMP), embedded within interleaved intracellular and extracellular domains. Research on recovering this source model from body-surface ECG has been limited compared with the studies on other cardiac source models, such as epicardial potentials [2] or activation time [8]. Inverse ECG problems are generally ill-posed, and recovering TMP is more difficult and computationally demanding than recovering other source models [23].

This study aimed to inversely calculate the TMP throughout the myocardium from the body-surface potentials with the specific goal of localizing myocardial ischemia. A leading cause of cardiac death [18], myocardial ischemia typically results from occlusion of coronary arteries. The disease occurs when the blood flow shortage causes cardiac myocytes to undergo acidosis and anoxia, resulting in a progressive deterioration of electrical and mechanical activity of the affected heart tissue, ultimately leading to life threatening rhythm abnormalities. Traditional ECG diagnosis needs expert interpretation and has limited ability to localize ischemic regions. The ability to acquire a whole-heart TMP map will greatly enhance clinicians' ability to identify the location and extent of ischemia. While reconstructing the TMP through all time remains an open problem, this is not necessary for ischemia localization, which may be achieved instead by identifying spatial nonuniformity of the TMP at the plateau phase.

Our major contribution lies in presenting a new computational methodology for inverse TMP estimation using measured ischemia data obtained from animal experiments. Inverse ECG problems are conventionally solved in several steps. Based on the physical model, one derives a mathematical transformation that relates the unknown source parameters directly to the measurements, and then minimizes the misfit between the predicted and measured data. The misfit term is typically augmented with regularization terms in order to mitigate the ill-conditioning. This approach, essentially an unconstrained optimization scheme, allows constraints only on the source parameters, and hence is inadequate for complex formulations such as the bidomain model. In contrast, we treated our inverse problem in a PDE-constrained optimization framework that incorporates the whole PDE model as a constraint. Our approach offers ample flexibility not only for adjusting the underlying physical model but also for applying various physically-based constraints simultaneously.

PDE-constrained optimization has been a frontier in scientific computing research over the last decade, and numerous theoretical accomplishments [11] have laid the foundation for its application. Its initial introduction to ECG problems [23] was limited to quadratic objective functions with equality constraints. Here we extended that inaugural work by allowing non-linear objective functions and constraints in both equality and inequality forms.

Solving PDE-constrained optimization numerically is more challenging than solving an ordinary optimization problem or a PDE alone. The task involves forming the optimality conditions and solving them through iterative methods, with each iteration solving the entire PDE system at least once. As such, most existing PDE solvers cannot be directly used when a PDE becomes a constraint in the optimization context. Also, the large size of the discretized PDE constraints poses a challenge for contemporary optimization algorithms.

To tackle these difficulties, one needs not only to efficiently integrate generic optimization algorithms, advanced PDE solvers such as adaptive finite element methods, and large-scale scalable linear algebraic solvers such as the Newton–Krylov method [3], but also to create a framework that exploits the mathematical structure specific to the physical model being considered, in our case bioelectric models. Such integration has yet to be fulfilled. Rather, most engineering studies formulate the inverse problem in a discrete, algebraic form based on a predefined mesh, and then use numerical optimization methods. However, such a practice does not guarantee mathematical rigor and may lead to inconsistencies when simulations are performed over different meshes.

This study investigated the formulation, discretization and numerical solution of our PDE-constrained optimization framework realized by the finite element method. We explored two minimization schemes: the Tikhonov regularization and the total variation (TV) regularization. Our contribution features the following new ingredients: (1) formulating optimality conditions in the continuum before discretization, thereby achieving consistency over multiscale simulation; (2) comparing this approach with the discretize-then-optimize approach; (3) deriving robust finite element formulation for both the Tikhonov and the TV regularization; (4) incorporating inequality constraints in optimization, handled by a tailored primal–dual interior-point method that exploits the block-matrix structure so as to optimize numerical efficiency.

This paper is organized as follows. Section 2 describes the mathematical model. Section 3 describes the optimization framework for the inverse problem, its finite element solutions, and the primal–dual interior method. Section 4 presents numerical experiments. Section 5 discusses computational and biophysical issues.

1.1. Background and related work

Inverse ECG problems have been formulated in terms of various heart source models, such as dipoles models, epicardial potentials, the activation wavefront, the monodomain model and the bidomain model (see an overview by Gulrajani [10]). Among these models the bidomain model is the most physically realistic, and its source, the TMP (whose time course is known as the "action potential"), is described by numerous membrane kinetic models that account for electrophysiological activities at the cell level [29]. The bidomain model is the predominant choice for simulating cardiac electrical activity at the