Inverse Problem of Electrocardiography: Estimating the Location of Cardiac Ischemia in a 3D Realistic Geometry

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Abstract. The inverse problem of electrocardiography (IPE) has been formulated in different ways in order to non invasively obtain valuable informations about the heart condition. Most of the formulations solve the IPE neglecting the dynamic behavior of the electrical wave propagation in the heart. In this work we take into account this dynamic behavior by constraining the cost function with the monodomain model. We use an iterative algorithm combined with a level set formulation and the use of a simple phenomenological model. This method has been previously presented to localize ischemic regions in a 2D cardiac tissue. In this work, we analyze the performance of this method in different 3D geometries. The inverse procedure exploits the spatiotemporal correlations contained in the observed data, which is formulated as a parametric adjust of a mathematical model that minimizes the misfit between the simulated and the observed data. Numerical results over 3D geometries show that the algorithm is capable of identifying the position and the size of the ischemic regions. For the experiments with a realistic anatomical geometry, we reconstruct the ischemic region with roughly a 47 % of false-positive rate and a 13 % false-negative rate under 10 % of input noise. The correlation coefficient between the reconstructed ischemic region and the ground truth exceeds the value of 0.70).

1 Introduction

Cardiac arrhythmias are disturbances in the normal rhythm of the heart produced by an abnormal electrical activity. They are one of the major causes of death worldwide [19]. Cardiac arrhythmias can be analyzed by means of non-invasive procedures aiming to characterize the cardiac electric sources (membrane potential, epicardial or endocardical potentials, activation times) and/or the cardiac substrate (ischemia regions, post-infarct scars) from voltages recorded by electrodes systems which are not in direct contact with the cardiac tissue [2,17]. From a mathematical point of view, the problem of recovering the

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heart electrical activity from remotes voltages can be formulated as an inverse problem, known as the inverse problem of electrocardiography (IPE) [8]. The IPE is a hard technological challenge since in its general formulation is an ill-posed problem so a number of regularization approaches have been developed over the years to obtain stable and realistic solutions [3,7,9].

In the present study we analyze the IPE in terms of localizing cardiac ischemic regions from remote voltage measurements. Cardiac ischemia is a pathology produced by the lack of blood supplied to the heart muscle that generates electrophysiologically-abnormal substrate which may lead to life threatening arrhythmias, and ultimately to a heart attack [10]. In the clinical practice, determining the size and location of cardiac ischemic regions has shown limited accuracy, specially in severe damaged hearts [20]. Ischemia alters the propagation properties of the electrical impulse through the cardiac muscle and this results in alterations in the associated voltage measurement recordings. These alteration patterns are temporally stable, making it feasible to inversely reconstruct ischemic regions from voltage measurements recordings [22].

Previous works have analyzed the localization of cardiac ischemia from remote voltage measurements [1,5,11,12,22]. In [5,11] the size and position of myocardial infarction is estimated by minimizing the difference between real voltage measurements and model-simulated ones. In [12,15,18] ischemic regions are assessed by reconstructing the epicardial potentials at a single time-instant during the plateau phase of the cardiac membrane potential by using a level-set formulation. Wang *et al.* [22] formulated the IPE as a constraint minimization problem, in which the size and position of ischemic regions were estimated by inversely computing the membrane potential at a single time instant during the plateau phase. While showing promising results towards clinical validation [15,22], in these studies time instants are treated independently from the others, thus ignoring the spatiotemporal correlation information contained in the voltage measurements. On the other hand, Álvarez *et al.* [1] presented an algorithm being able to reconstruct disconnected cardiac ischemic regions with a limited number of recording sites by exploiting the spatiotemporal correlation contained in the measured data.

Here, we extend the work presented in [1] to 3D geometries. We analyze the performance of the method in a model of spheres and then we study its use on 3D realistic anatomical model. Our results show that the algorithm is capable of identifying the position and, in most of the cases, approximates the size of the ischemic regions.

2 Forward Calculation

2.1 Action Potential Model

Cellular electrical activity was simulated using a modified version of the Two-Current model (TC), proposed by Mitchell and Schaeffer [14]. The TC consists of just two ordinary differential equations for two variables: the transmembrane potential $v(t)$, and the inactivation gate variable $h(t)$. The voltage, which is dimensionless and varies between zero and one, is defined as follows

$$\frac{dv}{dt} = J_{TC} = J_{stim}(t) + J_{in}(v,h) + J_{out}(v)\,, \tag{1}$$

where J_{stim} represents the initial stimulus, J_{in} and J_{out} denotes the sum of all inward and outward currents, respectively, which are defined as

$$J_{in}(v,h) = \frac{h(1-v)(v-v_{rest})^2}{\tau_{in}}, \tag{2}$$

$$J_{out}(v,h) = -\frac{v-v_{rest}}{\tau_{out}}. \tag{3}$$

where v_{rest} is the resting potential. This parameter was not considered in the original formulation. It was incorporated in [1] to simulate the increase of the resting potential during ischemia.

The gating variable $h(t)$ is dimensionless and varies between zero and one. This variable regulates inward current flows and obeys the following equation

$$\frac{dh}{dt} = \begin{cases} (1-h)/\tau_{open}, & v < v_{crit} \\ -h/\tau_{close}, & v \geq v_{crit} \end{cases} \tag{4}$$

where v_{crit} is the change-over voltage. This model contains four time constants (τ_{in}, τ_{out}, τ_{open} and τ_{close}) which correspond to the four phases of the cardiac action potential: initiation, plateau, decay and recovery (see [1] for details).

The effects of ischemia are simulated by modifying the values of τ_{in} and v_{rest} [4]. For ischemic cells, we set the parameter τ_{in} and v_{rest} equal to 0.8 ms and 0.1, respectively. For healthy cells τ_{in} and v_{rest} are set to 0.2 ms and 0, respectively.

2.2 Cardiac Tissue Model

Let $\Omega_H \in \mathcal{R}^3$ be the cardiac tissue, and $v = v(\boldsymbol{r_H}, t)$ the membrane potential with $\boldsymbol{r_H} \in \Omega_H$. The propagation of v is described according to the monodomain formalism,

$$\frac{\partial v}{\partial t} = \nabla D \cdot (\nabla v) + J_{TC} \tag{5}$$

where J_{TC} is the ion current term current provided by TC model, and D is the intracellular conductivity tensor (assumed constant $D = 1.4\mathcal{I}\,(\mathrm{mm}^2/\mathrm{ms})$). Equation (5) is solved by imposing the initial conditions $v = v_{rest}$ at $t = 0$, and no-flux boundary conditions.

To simulate the effects of ischemia at the tissue level, we consider a regional model of ischemia where the parameters $\tau_{in}(\boldsymbol{r_H})$, $v_{rest}(\boldsymbol{r_H})$ vary linearly between healthy and ischemic values [1,21].

2.3 Model of Remote Recordings

According to the Volumen Conductor Theory [13,16], the resulting potential distribution at position $\boldsymbol{r_T} \in \Omega_T$ outside the cardiac tissue Ω_H, is calculated as

$$\varphi(\boldsymbol{r_T}, t) = \frac{1}{4\pi\sigma_0} \int_{\Omega_H} \frac{\nabla D \cdot (\nabla v(\boldsymbol{r_H}, t))}{R(\boldsymbol{r_H}, \boldsymbol{r_T})}\, d\Omega_H \tag{6}$$

where $R(\boldsymbol{r_H}, \boldsymbol{r_T}) = ||\boldsymbol{r_T} - \boldsymbol{r_H}||$ represents the distance from the source location point $\boldsymbol{r_H}$ to the observation point $\boldsymbol{r_T}$, σ_0 is the medium conductivity (assumed homogeneous and set to $1\mathrm{Sm}^{-1}$), and $v(\boldsymbol{r_H}, t)$ is solution of (5). Equations (1)–(6) comprise a complete description of the forward problem.

3 Inverse Procedure

Let Ω_H be a synthetic cardiac tissue which contains an ischemic region, and $\varphi_R^i(t)$ be a set of associated remote measurements. Note that $\varphi_R^i(t) = \varphi(\boldsymbol{r_T^i}, t)$ with $t \in [0, T]$ and $i = 1, 2, \ldots, N$, being T the total recording time, and N the number of recording points. Hereinafter, we assume that the regional ischemia constitute our true ischemic configuration, and $\varphi_R^i(t)$ is our observed data.

The aim of the inverse procedure is to estimate the shape and the location of the ischemic areas by adjusting the spatial distribution of τ_{in} and v_{rest}. This is achieved by minimizing the misfit between the observed data $\varphi_R^i(t)$, and the data associated to a guess configuration: $\varphi_S^i(t; \tau_{in}, v_{rest}) = \varphi(\boldsymbol{r_T^i}, t; \tau_{in}, v_{rest})$. We use an iterative scheme in which the following cost functional

$$\mathcal{J}(\tau_{in}, v_{rest}) = \frac{1}{2} \int_0^T \sum_{i=1}^{N} \left|\left| \varphi_R^i(t) - \varphi_S^i(t; \tau_{in}, v_{rest}) \right|\right|^2 \, dt \tag{7}$$

is reduced at each step of the reconstruction process. We use an adjoint formulation to find a direction in the parameter space (τ_{in}, v_{rest}) such that the cost functional decreases. The ischemic region is defined by a level set function [1].

Since both parameters, τ_{in} and v_{rest}, define the same region, we only consider the variation of τ_{in} for the gradient computation. Following [1], the gradient of the function $\mathcal{J}$ over the parameter τ_{in} is given by

$$grad_{\tau_{in}} \mathcal{J} = \int_0^T w \frac{h\,(v - v_{rest})^2\,(v-1)}{\tau_{in}^2} \, dt \tag{8}$$

where adjoint state $w = w(\boldsymbol{r_H}, \boldsymbol{t})$ is the solution of the following problem

$$\begin{cases} \dfrac{\partial w}{\partial t} + \nabla D \cdot \nabla w - \dfrac{\partial J_{TC}}{\partial v} w = -\dfrac{1}{4\pi\sigma_0} \displaystyle\sum_{i=1}^{N} \mathcal{M}_i \;\; \nabla^2 \left(\frac{1}{R_i} \right) \quad \text{in} \quad \Omega_H \\ \dfrac{\partial w}{\partial \boldsymbol{n}} = \dfrac{1}{4\pi\sigma_0} \displaystyle\sum_{i=1}^{N} \mathcal{M}_i \; \frac{\partial}{\partial \boldsymbol{n}} \left(\frac{1}{R_i} \right) \quad \text{on} \quad \partial\Omega_H \\ w = 0 \quad \text{at} \quad t = T, \end{cases} \tag{9}$$

here $\mathcal{M}_i = ||\, \varphi_R^i(t) - \varphi_S^i(t, \tau_{in}, v_{rest})||$, $R_i = ||\boldsymbol{r_T^i} - \boldsymbol{r_H}||$ and

$$\frac{\partial J_{TC}}{\partial v} = \frac{h}{\tau_{in}}(v - v_{rest})(2 - 3v + v_{rest}) - \frac{1}{\tau_{out}}. \tag{10}$$

4 Results

We conduct three experiments in order to analyze the scope of the proposed algorithm on 3D geometries: (1) we initialize the method with different initial guesses using a two concentric spheres geometry; (2) we analyze the approach with different noise levels using the spherical geometry; (3) we study the performance of the algorithm in a real anatomical geometry. For all the experiments, the reconstruction algorithm is applied to a single cardiac cycle of length $T = 240$ ms in the steady state. The inverse procedure stops when the functional cost becomes stationary. We evaluate the inverse solutions using three metrics: (1) the correlation coefficient (CC) between the real and the reconstructed τ_{in} configuration; (2) the sensitive error (SN), which is defined as the rate of true ischemia that is not detected by the algorithm (false negative); and (3) the specificity error (SP) , which is defined as the rate of the misjudged ischemic region out the reconstructed ischemic region (false negative) [22].

4.1 Model of Spherical Surface

We consider the cardiac tissue Ω_H as spherical surface of radius 50.0 mm, which was discretized by a triangular finite element mesh of 4470 nodes generated with Gmsh [6]. For the remote measurement electrodes Ω_T, we set an arrangement of 232 points located on the surface of a concentric sphere of radius 65.0 mm.

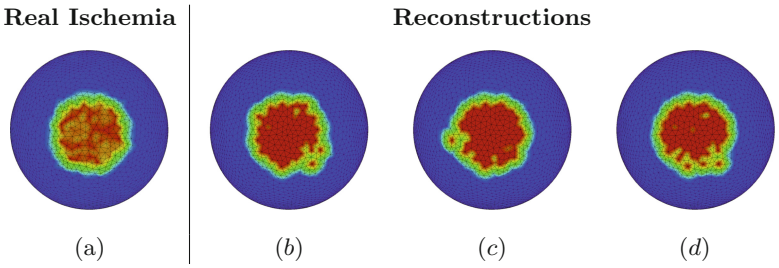

Fig. 1. Reconstruction of a ischemic area considering different initial guesses in a spherical geometry with random fluctuation of 10 % to the parameter values. (a) Represents the spatial distribution of the real ischemia: red ischemia, green border zone and blue health tissue. Panels (b), (c) and (d) represent final reconstruction of the ischemic region considering different initial guesses ($\tau_{in}(\boldsymbol{r_H})$ configuration). (b) Case 1, a healthy cardiac tissue. (c) Case 2, initializing with an small ischemic region close to the real one. (d) Case 3, considering an ischemic region elsewhere in the cardiac tissue. (Color figure online)

In this experiment a true circular ischemic region of radius 14 mm was considered, as is shown in Fig. 1 panel (a). We added random fluctuations of 10 % to the model parameters values. The aim of this experiment is to verify if the inverse procedure is able to reconstruct a single ischemia independently of the initial guess. We simulated three different cases: Case 1, a healthy cardiac tissue

Table 1. Comparative quality metrics for the model of spheres when considering different initializations of the reconstruction method with 10 % of noise. Case 1, a healthy cardiac tissue is assumed, i.e., there is not an ischemic region. Case 2, initialize the method with a ischemic region close to the real ischemic area. Case 3, considering an ischemic guess elsewhere in the cardiac tissue.

Experiment	CC	SN×10	SP×10
Case 1	0.92	0.16	0.62
Case 2	0.93	0.22	0.56
Case 3	0.91	0.14	0.53

Table 2. Comparative quality metrics for the model of sphere when a healthy cardiac tissue is assumed as initial condition and adding different noise levels: 15 %, 20 % and 25 %.

Noise	CC	SN×10	SP×10
15 %	0.89	0.18	0.54
20 %	0.85	0.29	0.75
25 %	0.73	0.33	1.04

is assumed, i.e., there is not an ischemic region, Case 2, initialize the method with a ischemic region close to the real ischemic area and Case 3, considering an ischemic guess elsewhere in the cardiac tissue. Figure 1 panel (*b*), (*c*) and (*d*) show reconstructed $\tau_{in}(\boldsymbol{r_H})$ profile for each case, respectively. A qualitative comparison between the obtained reconstruction and the real ischemic region shows that position and size of the ischemia was reconstructed successfully for all cases. For all cases (see Table 1), CC exceeds a value of 0.89 which is consistent with the reconstructions observed in Fig. 1. Similarly, we obtain a SN and a SP ratios less than 0.3×10 and 0.7×10 for all cases, respectively.

Following with the model of a spherical surface, we study the behavior of the method at different noise levels. We consider a circular ischemia and we added random fluctuations of: 15 %, 20 % and 25 % to the parameters values. Results are shown in Table 2.

4.2 Realistic Anatomical Model

We use a 3D mesh of torso and heart surfaces obtained from a CT scan of a 43 years old woman (Fig. 2 panel (a)). We use the medical imaging software Osirix to segment the heart and the torso from the CT scan DICOM files. We then construct the meshes using the CardioViz3D software. The heart and torso domains are discretized using triangular meshes of nodes 5842 and 2873, respectively.

In this experiment a circular ischemic region of radius 13 mm on the cardiac surface was considered, as is shown in Fig. 2 panel (*b*). We consider random fluctuations of 10 % to the model parameters values. The remote measurement

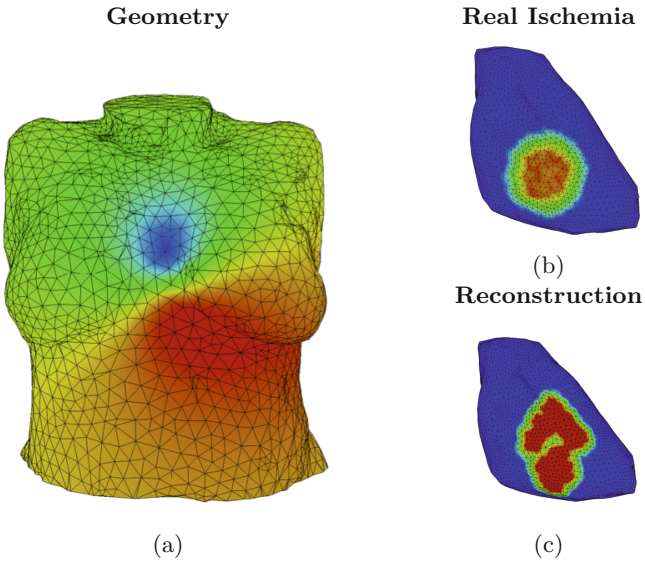

Fig. 2. Reconstruction of an ischemic region in a real anatomical geometry with 10 % of noise. (a) A snapshot of the torso potential at time 170 ms. (b): Representations of the true ischemic region $\tau_{in}(\boldsymbol{r_H})$ configuration). (c): The reconstructed ischemia region.

are located at the torso surface. In contrast to the methodology used in [1], in this experiment we do not assume an ischemic initial guess. We start the iterative method assuming healthy conditions for the entire tissue. At each iteration, the functional cost gradient is computed and both parameters, $\tau_{in}(\boldsymbol{r_H})$ and $v_{rest}(\boldsymbol{r_H})$, are updated. After 32 iterations, stop criteria is accomplished obtaining the final reconstruction. For this scenario, we obtain a correlation coefficient up to CC= 0.72 between the reconstructed ischemic region and the ground truth, for all cases. Additionally, we compute the false-negative and false-positive error ratio obtaining a value of $SN = 1.39 \times 10$ and $SN = 4.75 \times 10$.

5 Conclusions

A number of methodologies have been proposed to address the problem of localizing ischemic regions using voltage measurements recorded at the body surface. Most of these methods consider inverse procedures at a single time instant, thus ignoring the spatio-temporal information contained in the recorded body signals. Alternatively, the model proposed in [1] provides a regularization method that exploits the spatio-temporal correlations of cardiac signals.

Here, we extend the methodology proposed in [1] to different 3D geometries. First, we analyze its performance in a geometric model of concentric spheres. We found that the inverse procedure does not depend on the initial guess. Then, we test the algorithm using noisy data by adding different noise levels, showing

in all cases high performance. Finally, we analyze the methodology on a realistic geometry, considering that data was corrupted by a 10 % of noise level. Also in this case, the ischemic region is located satisfactorily.

In a future work, we aim to incorporate more realistic settings using an electrophysiology detailed model, with a physiological representation of the ischemia model. We will also investigate the performance of this method in localizing ischemia from real clinical measurements. This assumes that the electrophysiological model that would be used to constrain the minimization problem is sufficiently accurate.

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