On the Use of the Bidomain Equations for Computing the Transmembrane Potential Throughout the Heart Wall: An Inverse Problem

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Abstract

In this paper we will explain how one may use the bidomain model to solve the inverse ECG problem in which the transmembrane potential throughout the myocardium is used as the unknown source. The accurate and efficient numerical solution of this problem can, for example, provide valuable insight into the electrophysiological nature of arrhythmias, the location and extent of ischemia and infarction, and can lead to new medical imaging devices.

This inverse problem is ill-posed, i.e. it is unstable and, even under ideal conditions, it can be shown that the transmembrane potential cannot be uniquely identified from body surface potential maps (BSPMs) - additional information is needed. The purpose of this paper is to show how the bidomain equations can be combined with apriori information and suitable numerical techniques to partially enforce uniqueness as well as stability in this inverse problem.

1. Introduction

The bidomain equations are widely accepted as an accurate model for the electrical activity in the myocardium [1]. They were introduced during the seventies by Tung, Geselowitz, Miller and Schmitt et al., and have been studied by several scientists, see e.g. [2, 3] for further details. In terms of mathematical symbols, this model may be expressed on the form

$$v_t + I(v,q) = \nabla\cdot(M_i\nabla v) + \nabla\cdot(M_i\nabla u) \text{ in } H, \quad (1)$$

$$\nabla\cdot(M_i\nabla v) + \nabla\cdot((M_i+M_e)\nabla u) = 0 \text{ in } H, \quad (2)$$

where H is the domain occupied by the heart, and v and u represent the transmembrane and extra-cellular potentials, respectively. The tensors M_i and M_e are the intra- and extra-cellular conductivities, and the function I incorporates the ionic currents into the model. More precisely, I is a function of both the transmembrane potential v and the ionic concentrations q.

In addition to (1)-(2), an equation governing the potential distribution outside the heart, i.e. in the torso T, is needed:

$$\nabla\cdot(M_o\nabla u) = 0 \text{ in } T, \quad (3)$$

along with suitable interface and boundary conditions at the heart and body surfaces, respectively.

The objective of this text is to show how one may combine equations (2) and (3), biological knowledge about the voltage distribution in the heart, BSPMs, and mathematical techniques to approximately compute the transmembrane potential v in the myocardium. We will present a series of examples that indicate rather strongly that such methods may possess the ability to approximately recover v, during specific time intervals of the heart cycle, throughout the myocardium. These experiments will not be limited to ideal situations, but also include noisy BSPMs and cases in which the position and volume of the heart are uncertain.

During the last three decades several researchers have studied inverse problems arising in connection with ECG recordings. In particular, the challenges of computing the epicardial potential and the myocardial surface activation wavefront have received a lot of attention. These problems are ill-posed in the sense that their numerical solutions are highly unstable with respect to the involved input data, see [4] and references therein. This is, of course, also the case for the inverse problem in which one tries to recover the transmembrane potential throughout the heart from BSPMs. However, by invoking apriori knowledge and suitable regularization techniques, it turns out that it might be possible to approximately solve this problem.

2. Methods

According to lab measurements

$$v \approx -90\text{mV} \text{ in } H, \quad (4)$$

in a healthy heart during the resting phase of the heart cycle, see e.g. [5]. If an individual suffers from some sort of

heart disease, for example a myocardial ischemia, (4) may not hold. We will exploit this fact and combine it with the so-called output least squares technique for inverse problems to recover v. That is, provided that d denotes a BSPM recorded during the resting phase of the heart cycle, we propose to compute v by solving the following problem:

$$\min_v J_\alpha(v), \tag{5}$$

where

$$J_\alpha(v) = \|u(v) - d\|^2_{L^2(\partial B)} + \alpha \int_H |\nabla v|^2 \, dx, \tag{6}$$

subject to the constraints

$$\nabla \cdot (M_i \nabla v) + \nabla \cdot ((M_i + M_e)\nabla u) = 0 \text{ in } H, \tag{7}$$

$$\nabla \cdot (M_o \nabla u) = 0 \text{ in } T, \tag{8}$$

$$M_o \nabla u \cdot \vec{n} = 0 \text{ on } \partial B, \tag{9}$$

$$\text{interface conditions on the heart surface } \partial H. \tag{10}$$

(Details about the conditions along ∂H can, e.g., be found in [3]). Here, $\vec{n}$ denotes the outwards directed normal vector of unit length along the body surface ∂B, and the notation $u = u(v)$ is used to emphasize that the solution u of (7)-(8) depends on v. Furthermore, α is a small regularization parameter and, due to (4), the second term in (6) has been added to enforce v to have small gradients throughout H.

In all the experiments presented below, we solved (5)-(10) with the Landweber scheme:

$$v^{n+1} = v^n - \beta \nabla J_\alpha(v^n), \tag{11}$$

where v^n denotes the nth approximation of the solution v of (5)-(10) and $\beta > 0$ is a small parameter. A healthy heart was used as initial guess in the iteration (11), i.e. $v^0 = -90\text{mV}$ - see (4). Furthermore, in the inverse solution process we neglected the fact that the conductivities can change in the case of disease.

Note that the apriori information (4) is used extensively in the scheme presented above. This means that we can only expect this method to work properly for the resting phase of the heart cycle. The challenge of computing the transmembrane potential distribution in the heart during other time intervals is, as far as we know, still an open problem.

3. Results

In a healthy heart (4) holds. Thus, if the estimated resting transmembrane potential does not approximately satisfy (4), then this would indicate some kind of malfunction. We have tested this procedure in the case of regional ischemia.

The scheme has not been validated for real world data. So far we have only tested it with synthetic BSPMs produced by solving the forward problem. More specifically, the body surface potential d, present in (6), and the "true" transmembrane potential v_{true} in the heart wall were produced by the following procedure:

- An ischemia was inserted into the heart model.
- A forward simulation was performed. In 2D we solved the time dependent bidomain equations and in 3D the stationary model (7)-(10).
- The body surface potential d and the "true" transmembrane potential v_{true} in the heart during rest were recorded.
- All information, except d, about the bidomain simulation was put aside.

Thereafter we used d and the scheme presented above to investigate whether or not we could approximately recover the "true" resting transmembrane potential v_{true}.

Figures 1 and 2 contain the results obtained in 2D, with various degrees of noise in the observation data d, for transmural anterior and posterior ischemia, respectively. In both cases, the technique provides rather accurate information about the "true" potential distribution. Note that the results for the anterior ischemia are slightly better than those computed for the posterior test problem.

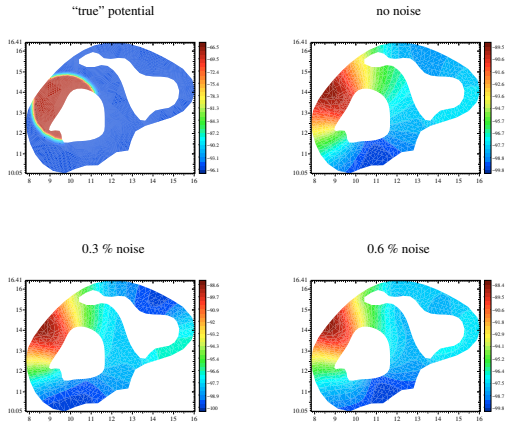

Figure 1. The "true" transmembrane potential v_{true} and estimates of it computed with noise free and noisy observation data (recorded at the body surface). Results obtained in the case of transmural anterior ischemia.

The results generated for a 3D heart in torso model, with uncertainties in the heart volume, are depicted in Figure 3 and quantified in Table 1. Here, the numbers $-27, -14, +16$ and $+33\,\%$ mean that the volume of the heart used in the solution procedure of the inverse problem has been changed by $-27, -14, +16$ and $+33\,\%$ compared with the true volume (used in the forward simulation to produce the body surface data d), respectively. These experiments indicate that the proposed scheme is rather robust with respect to changes in the size of the myocardium.

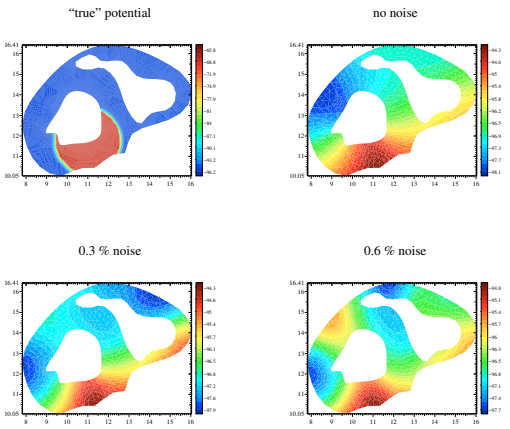

Figure 2. The "true" transmembrane potential v_{true} and estimates of it computed with noise free and noisy observation data (recorded at the body surface). Results obtained in the case of transmural posterior ischemia.

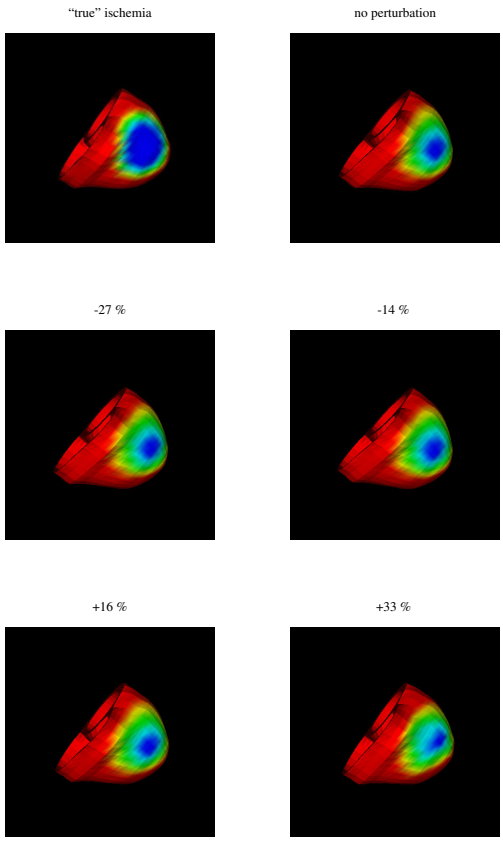

Figure 3. Results obtained in 3D for a heart in torso model. The numbers above the individual figures quantify the volume perturbations of the heart model used in the inverse solution procedure. (The size of the heart is scaled with respect to the size of the panels).

Table 1. Results obtained in 3D with perturbations of the heart volume. Note that, except for the result obtained with a heart that is 33 % too large, the ratio $V_{\mathrm{isch}}/V_{\mathrm{heart}}$ between the volume of the ischemia and the volume of the heart is almost constant. (More precisely, V_{heart} is the volume of the heart minus the volume of the atriums).

Perturbation	-27%	-14%	0%	+16%	+33%
V_{heart} (cm^3)	124.3	146.1	170.4	197.3	226.9
$V_{\mathrm{isch}}/V_{\mathrm{heart}}$	0.22	0.21	0.23	0.19	0.13

Effects of uncertainties in the position of the myocardium are shown in Figure 4 and Table 2. Here, the notation $(0, 0, -1)$ means that the heart used in the recovery process is positioned 1cm too low, and so on. Furthermore, we write COM for center of mass, i.e. the second row in Table 2 contains the errors in the center of mass of the estimated ischemia. For these rather moderate perturbations, our scheme performed well. (Due to the extensive volumes occupied by the lungs in our geometrical model, it was difficult to run simulations with larger uncertainties in the position of the heart).

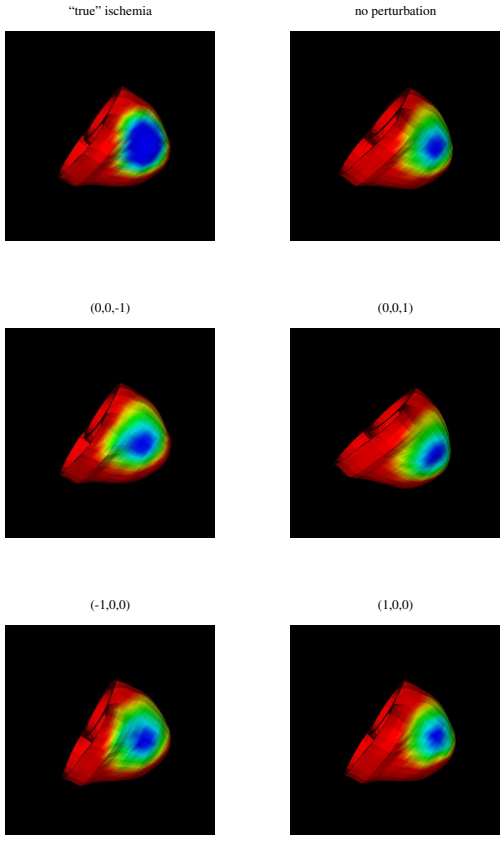

Figure 4. Results obtained with uncertainties in the position of the heart.

In the examples presented above, the synthetic reference

Table 2. This table contains the errors in the center of mass of the estimated ischemia for various perturbations of the position of the heart.

Perturbation	(0,0,-1)	(0,0,1)	(0,0,0)	(-1,0,0)	(1,0,0)
Error COM	0.54 cm	0.79 cm	0.34 cm	0.71 cm	0.44 cm

data d and v_{true} were generated by either performing time dependent bidomain simulations or solving the stationary model (7)-(10) with conductivities M_i and M_e that change in the ischemic regions, see [6, 7] and [8]. Ideally, we should of course have used real world data, measured in a lab. However, such recordings are currently not available to us.

Let us examine the influence of the model used to produce d and v_{true} in the present investigation. (This topic is linked to the concept of so-called "inverse crimes" in the literature addressing inverse problems). Table 3 capitalizes on this subject. More specifically, this table contains the L^2 errors in the inversely estimated transmembrane potentials obtained by using different synthetic observation data. Along with the results generated by applying bidomain reference data, it contains the errors associated with BSPMs produced by the stationary model (7)-(10). Both results with conductivities being dependent and independent of the ischemia are presented. In the latter case, severe "inverse crimes" are committed - the models used to produce the observation data and to solve the inverse problem are identical.

We conclude that using reference data produced by the stationary model, with conductivities depending on the disease, and time dependent bidomain simulations yield approximately the same result. However, severe "inverse crimes" must be avoided, they can easily lead to too optimistic conclusions.

Table 3. The relative L^2 errors of the inverse solutions, in the case of anterior ischemia, obtained with different reference data. These numbers should be considered in view of the fact that the L^2 difference between the "true" potential and the initial guess ($v^0 = -90$mV) used in (11) is 0.126.

Model used to produce reference data	relative error
Bidomain model	0.111
Stationary model, ischemia dependent conductivities	0.112
Stationary model	0.103

4. Discussion and conclusions

We have investigated the possibilities for using computers, mathematics and BSPMs to compute the transmembrane potential in the myocardium during the resting phase of the heart cycle. Our methodology is defined in terms of an inverse problem for the bidomain equations.

In the case of regional ischemia, our scheme recovered the transmembrane potential throughout the heart wall rather accurately. Moreover, the method seems to be rather robust with respect to noisy observation data and uncertainties in the heart volum and position. Thus, even though the problem under consideration is highly unstable, our experiments (with synthetic data) indicate that it might be solvable, provided that proper mathematical techniques are used and that suitable apriori information about the voltage distribution in the myocardium is taken into consideration.

Acknowledgements

It is a pleasure to thank Dr. Tveito and Dr. Grøttum for interesting discussions about electrocardiography.

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