Bidomain Simulations of Subendocardial Ischemia: The Forward and Inverse Problems

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Abstract

We provide an analysis of the bidomain theory in relation to anterior subendocardial ischemia. Using the static bidomain model, this analysis explains why simulations often do not produce ST depression when the ischemia is introduced into an anisotropic model. More precisely, if the ischemic border zone is represented as a smooth surface, then almost right angles between the normal vector of the border and the tangential plane of the fibers will lead to cancelling effects. The simulated transmembrane current flux, entering the ischemic region, will thus be underestimated, and the expected ST depression in chest leads may not occur.

We propose to solve this problem by either representing the ischemic border zone as a zigzag surface or by specifying the transmembrane current flux along the border zone, instead of the shift in the transmembrane potential. We employ the latter approach and show that this method always yields ST depression in chest leads positioned above the lesion. A number of simulation studies will be presented, including clinical cases. Both the forward and the inverse problems of electrocardiography are addressed. We consider the inverse ECG problem in which ischemic heart disease is assumed to be the source of changes in the body surface potential maps (BSPMs).

1. Introduction

ST depression in chest leads can indicate anterior subendocardial ischemia. Simulation studies [1–7] have shown that it is difficult to replicate this phenomenon with the static bidomain model:

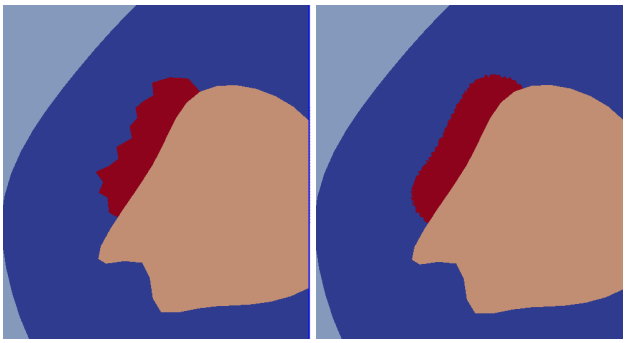
$$\nabla \cdot ((\sigma_i + \sigma_e)\nabla\phi) = -\nabla \cdot (\sigma_i \nabla v) \qquad \text{in } H. \qquad (1)$$

In this model, v is the ST-shift in the transmembrane potential (TMP), ϕ is the ST-shift in the extracellular potential (EP), σ_i and σ_e are the intracellular and extracellular conductivity tensors, respectively, and H is the domain of the heart. According to lab data, normalized with respect to measurements acquired at rest,

$$v(x) \approx \begin{cases} 0 \text{ mV} & x \in H \setminus D, \\ -50 \text{ mV} & x \in D, \end{cases} \qquad (2)$$

where D is the ischemic region.

The tissues outside the myocardium are modeled as an isotropic medium. Hence, the electrical potential in this volume is assumed to satisfy a homogeneous potential equation. Further information about this topic, including a description of the heart-torso interface conditions, can be found in [8].

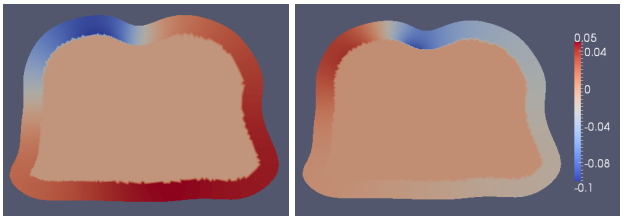


(a) Ischemic region with zigzag border (b) Ischemic region with smooth border

Figure 1. A close-up view of a heart-in-torso geometry. The torso, heart, ischemic area and the left ventricle are visualised in light blue, dark blue, red and beige, respectively.

Figure 1 shows two almost identical anterior subendocardial ischemic regions, but the area in the left panel has a zigzag border, which is different from the smooth interface displayed in the right panel. From a medical perspective, one would expect that these two lesions would pro-

duce very similar ST-shifts at the body surface. However, if the model (1)-(2) is employed, this is not the case, see Figure 2.



(a) ST-shift using a zigzag border (b) ST-shift using a smooth border

Figure 2. Simulated ST-shifts at the body surface using the standard model (1)-(2). Both results are obtained with an anterior subendocardial ischemic region. The result in (a) is produced by a zigzag border and in (b) with a smooth interface. In these figures, ST depression is visualised in blue and ST elevation is visualised in red.

The purpose of this paper is to explore this phenomena and to propose modifications yielding a model that consistently produces the expected ST depressions.

2. Forward problem; methods and results

In order to analyze the simulations presented in Figure 2, we study the transmembrane current

$$\mathbf{J} \cdot \mathbf{n} = (\sigma_i \nabla v) \cdot \mathbf{n}$$

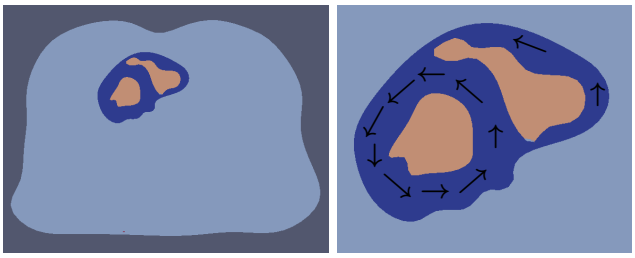
entering the ischemic volume due to the TMP-shift (2). Here, $\mathbf{n}$ denotes the outward directed normal vector, of unit length, of the ischemic border. Figure 4 shows this flux for the two lesions depicted in Figure 1. We observe that, if the border is smooth, then the transmembrane flux at the border segment directly below the epicardium is almost zero, whereas a zigzag curve gives rise to a significant influx. Consequently, zigzag and smooth borders yield ST depression and elevation, in leads positioned directly above the ishemic area, respectively, see Figure 2. Note that we used the fiber field depicted in Figure 3(b) in these simulations.

A mathematical line of considerations [9], reveals that

$$\begin{aligned} \mathbf{J} \cdot \mathbf{n} &= (\sigma_i \nabla v) \cdot \mathbf{n} \\ &\approx \kappa_l [\mathbf{n} \cdot \mathbf{r_l}]^2 \\ &\quad + \kappa_t [\mathbf{n} \cdot \mathbf{r_t}]^2 \\ &\quad + \kappa_n [\mathbf{n} \cdot \mathbf{r_n}]^2, \end{aligned} \tag{3}$$

where $\mathbf{r_l}(\mathbf{x}), \mathbf{r_t}(\mathbf{x}), \mathbf{r_n}(\mathbf{x})$ is a set of perpendicular unit vectors:

- $\mathbf{r_l}(\mathbf{x})$ is directed along the fibers.
- $\mathbf{r_t}(\mathbf{x})$ is perpendicular to the fibers, but in the sheet plane.



(a) 2D geometry (b) Fiber orientation

Figure 3. The heart-in-torso geometry is visualised in (a), and a close-up view of the fiber orientation is shown in (b).

- $\mathbf{r_n}(\mathbf{x})$ is normal to the sheet plane.

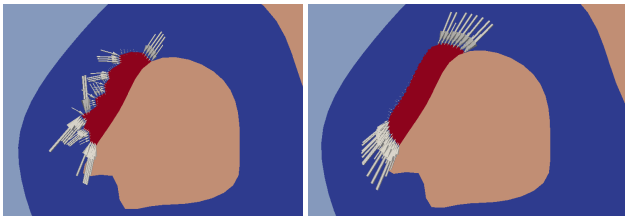
The conductivities associated with these three directions are denoted

$$\kappa_l,\ \kappa_t,\ \kappa_n,$$

and

$$\frac{\kappa_t}{\kappa_l} \approx \frac{\kappa_n}{\kappa_l} \approx \frac{1}{10}.$$

Hence, the two last terms in (3) will typically be much smaller than the first term. Also, if $\mathbf{n}$ and $\mathbf{r_l}$ are almost orthogonal, then the flux $\mathbf{J} \cdot \mathbf{n}$ will be small. This explains why we get a close-to-zero flux at the border segment beneath the epicardium in Figure 4(b). Using a zigzag border representation prevents such right angles, and the (desired) ST depression will occur in electrodes positioned above the lesion, see Figure 2(a) and 4(a).



(a) Zigzag border (b) Smooth border

Figure 4. Visualization of fluxes using the standard model (1)-(2). Both results were obtained with an anterior subendocardial ischemic region. The result in (a) was produced with a zigzag border and in (b) with a smooth interface. In these figures, the direction and the magnitude of the inflow are visualized in terms of white arrows.

Due to the complexity of the system supplying blood to the heart, the ischemic border zone will, most likely, tend to be fractal, rather than smooth. Therefore, the area in which the normal vector $\mathbf{n}$, of the ischemic border zone, is approximately perpendicular to the fiber direction $\mathbf{r_l}$ will be neglectable. The canceling effect, discussed above, seems to be an artifact of the model and will not occur in real life.

There are at least two straightforward changes of the model that can rectify this:

- One can represent the ischemic border zone in terms of a high frequent zigzag border. This is conceptually simple, but inconvenient because it requires a fine computational mesh.
- One can directly specify the border current $\mathbf{J}$, instead of providing the TMP-shift with the formula (2).

We chose the latter approach, which yields the state equation

$$\nabla \cdot ((\sigma_i + \sigma_e)\nabla\phi) = -\nabla \cdot \mathbf{J} \qquad \text{in } \mathbf{H}. \tag{4}$$

More specifically,

$$\mathbf{J} \approx c \cdot \mathbf{n} \text{ at the border,} \tag{5}$$

$$\mathbf{J} \approx \mathbf{0} \text{ elsewhere,} \tag{6}$$

where c is a given negative constant. Using a current flux of constant magnitude along the entire boundary of the ischemic region, i.e. employing the model (4)-(6), yields a ST depression at the body surface very similar to the results shown in the left panel of Figure 2.

3. Inverse problem; methods and results

BSPMs and MRI data were recorded, during exercise testing, at Oslo University Hospital. The BSPMs consist of data recorded from 64 electrodes positioned at the chest and back of the patients, using a uniform distribution of the electrodes. From the MRI data we constructed suitable computational meshes [10], and the FENICS software tool was used to implement solvers for the eqs. presented above. Thereafter, we solved the inverse ECG problem in which ischemic heart disease is assumed to be the source of changes in the BSPMs, see [8].

Inverse solutions were computed with both the standard model (1)-(2) and the modified eqs. (4)-(6). The results obtained for a patient with an apical-anterior lesion are shown in Figure 5 and Figure 6. Comparing these figures with the SPECT image displayed in Figure 7, shows that the standard approach fails to identify the correct region in this case, whereas the modified model provides sound results. Similar simulations were also undertaken for a patient suffering from a basal-posterior lesion, but in this case both models managed to identify the correct segments.

4. Discussion

Our results indicate that consideration of the border zone boundary is critically important for the use of inverse solutions to predict the location of subendocardial ischemia. Using traditional simulation methods, due to the anisotropy of the cardiac tissue, even small changes to the border zone geometry can dramatically alter ST-shifts at

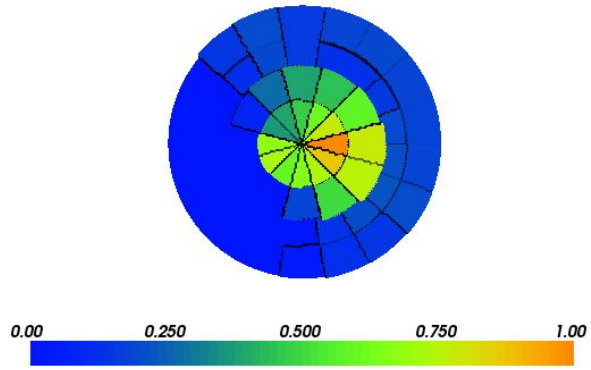


Figure 5. Inverse solution computed with the modified model (4)-(6). The heart is devided into 60 segments. Each segment is assigned a value between 0 and 1, where 0 indicates normal perfusion and 1 means 100% perfusion defect.

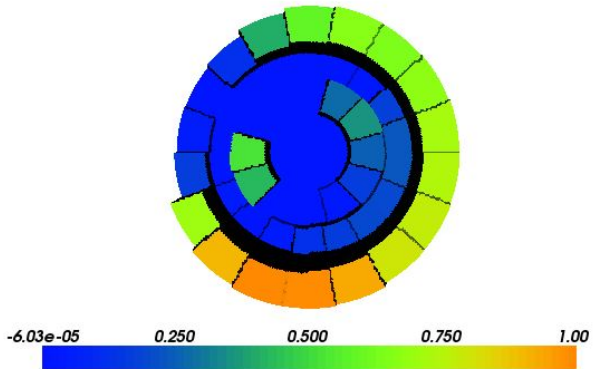


Figure 6. Inverse solution computed with the standard model (1)-(2). The heart is devided into 60 segments. Each segment is assigned a value between 0 and 1, where 0 indicates normal perfusion and 1 means 100% perfusion defect.

Figure 7. Scintigraphy (SPECT) recorded at Oslo University Hospital. The ischemic regions are visualized in terms of hashed areas (reversible perfusion defects), and the colored region indicates normal perfusion.

the epicardium and the body surface. Hence, inverse solutions using this traditional approach are highly sensitive to the assumptions of border zone geometry, and if these assumptions are not correct, this sensitivity will add substantial error to the solution. In order to alleviate this specific problem, we use a method to calculate border zone currents which depend on the size and rough shape of the ischemic zone more than the specific geometric depiction of the border zone boundary. This method is able to reproduce the area of ischemia from a clincial case much more accurately than using traditional simulation of the border zone currents.

However, although we show a clinical case where the use of this methodology predicts the location of ischemia, we have used a situation where the actual ST depression is above the ischemic region. It is well established, though, that ST depression does not always locate directly over the ischemic region, with clinical studies showing a significant number of patients presenting ST depression in areas remote from the ischemia [11]. Detailed experimental results have also demonstrated this, with nearly identical occulasion procedures in sheep createing ST depression both over the region of ischemia as well as on its periphery [6]. Therefore, there has been considerable debate over the generation of ST depression from subendocardial ischemia, with numerous analysis and models proposed to solve this problem [1–7].

Transient subendocardial ischemia is likely a complex phenomena. It is unlikey that it appears as one monolithic region, and interaction of this changing region with the anisotropic nature of the myocardium will likely give rise to complex ST-shifts on the epicardium of the heart and hence onto the body surface. However, in this work we show that proper handling of the currents that develop in ischemia is critical to modeling the rise of ST depression, and as we find more about how transient ischemia develops spatially and temporally, using these methods will improve the ability to locate ST depression in the myocardium using inverse methods.

Acknowledgements

We would like to thank Kristina Hermann Haugaa, Andreas Abildgaard and Jan Gunnar Fjeld at Oslo University Hospital and Per Grøttum at Faculty of Medicine, University of Oslo for providing us with the clinical data that was used in this study.

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