Mathematical Biosciences 266 (2015) 15–22

Contents lists available at ScienceDirect

Mathematical Biosciences

journal homepage: www.elsevier.com/locate/mbs

Determining six cardiac conductivities from realistically large datasets

Barbara M. Johnston*, Peter R. Johnston

School of Natural Sciences and Queensland Micro and Nanotechnology Centre, Griffith University, Nathan, Queensland 4111, Australia

ARTICLE INFO

Article history:
Received 14 October 2014
Revised 20 May 2015
Accepted 22 May 2015
Available online 3 June 2015

Keywords:
Bidomain model
Cardiac conductivities
Electrode array
Inverse methods
Simulation
Electrophysiology

ABSTRACT

Simulation studies of cardiac electrophysiological behaviour that use the bidomain model require accurate values for the bidomain extracellular and intracellular conductivities to produce useful results. This work considers an inversion algorithm, which has previously been shown, using simulated data, to be capable of retrieving six bidomain conductivities and the fibre rotation angle from measurements of electric potential made in the heart. The aim here is to see whether it is possible to improve the accuracy of the retrieved parameters. The scenario of retrieving only conductivities and not fibre rotation is examined but this does not lead to a worthwhile improvement in retrieval accuracy. It is also found that it is possible to retrieve the bidomain conductivities using not two but just one pass of the algorithm, made on a 'widely-spaced' electrode set. This appears to work because the algorithm is still very sensitive to the extracellular conductivities. However, the single-pass method is not recommended because the intracellular conductivities that are retrieved are not as accurate as those that are retrieved in the usual two-pass method, particularly for higher values of added noise. The second part of this work considers retrieving the six conductivities and fibre rotation from realistically large sets of potential measurements and identifies the best data analysis method. It is found that, even with added noise of up to 40%, the extracellular conductivities can still be retrieved extremely accurately (relative errors of around 2% on average) and so can the intracellular longitudinal conductivities and fibre rotation (errors less than 8% on average). The remaining intracellular conductivities have errors that are generally less than twice the added noise, particularly for the higher noise values.

© 2015 Elsevier Inc. All rights reserved.

1. Introduction

Increases in computational power over the past ten years or so have led to major advances in the ability of researchers to realistically simulate cardiac electrophysiological behaviour and even to work towards the use of heart models that can guide clinical decisions. Along with these advances, has come the realisation of the importance of accurate values for the parameters in these models. For example, this is the case for the conductivity values used in the bidomain model that is commonly used to model cardiac tissue [1,2]. In addition, not only is it essential to find conductivity values that represent normal tissue, it is also necessary to understand how these are affected in diseased and damaged tissue [1,3].

Despite the bidomain model being used for modelling electrophysiological phenomena for nearly fifty years [1], only three sets of experimentally determined bidomain conductivities exist [4–6]. Unfortunately, these values are inconsistent [7] and can lead to very different results in simulation studies [8]. Moreover, these studies assume that the conductivities in the directions transverse to the cardiac fibres (that is within the sheet of fibres and between the sheets of fibres) are equal [2]. This assumption is inconsistent with the results of imaging studies of ventricular architecture [2] and has also been shown to be invalid by experimental studies that have demonstrated that there are three distinct propagation directions in cardiac ventricular tissue [9,10]. The only two available datasets that do not make this assumption [11,12] have not been fully experimentally determined and also produce inconsistent results in simulations [13].

There are two areas of major challenge associated with determining accurate conductivity values. One is associated with the practicalities of actually making the measurements and the other is related to the computational difficulties that occur because the problem of retrieving the conductivity values from measurements of potential is mathematically ill-posed.

Recent work in the first of these areas relates to the design and fabrication of micro-electrodes that can be used to make measurements that will lead to values for cardiac conductivities. For example, Hooks and Trew [10] have constructed a plunge electrode array, which was used to measure monodomain conductivities. This work was extended [14] to a 325 electrode array that was used to demonstrate the electrically orthotropic nature of cardiac ventricular tissue. Other groups [15,16] are working on an approach that uses

* Corresponding author. Tel.: 61 7 3735 4405, Fax: 61 7 3735 7656.
E-mail address: Barbara.Johnston@griffith.edu.au (B.M. Johnston).

http://dx.doi.org/10.1016/j.mbs.2015.05.008
0025-5564/© 2015 Elsevier Inc. All rights reserved.

MEMS fabricated blocks in conjunction with multi-site interstitial stimulation.

Some recent work in the second area includes mapping the electrical activation of the tissue and then using a least squares and singular value decomposition method to obtain the conductivities [17], while another approach [18] looks at breaking the problem into a subset of computationally tractable sub-problems. One recent promising approach that could be used to overcome the difficulties associated with the inverse problem of estimating parameters from non-invasive measurements is the Reduced-order Unscented Kalman Filter method [19], which has been used successfully, using simulated measurements, to identify material parameters in a non-linear mechanical model of the left ventricle.

Proof of concept has recently been shown *in silico* by the present authors [20,21] for a technique that can determine the six bidomain conductivity values (two domains with three propagation directions in each) that are required to fully describe cardiac tissue conductivity [9,22]. This is achieved by applying a sub-threshold stimulating current during the non-excitory phase of the cardiac cycle (ST segment) and making measurements, using a multi-electrode array, *in vivo* in cardiac ventricular tissue in an animal model. These measurements are then used in conjunction with a novel mathematical inversion method to retrieve the conductivities. An additional parameter, the fibre rotation angle, is also retrieved with this method. This is the angle through which the sheets of cardiac fibres rotate relative to one another between the inner and outer heart surfaces. A recent implementation of the inversion routine on GPUs [23] has resulted in a speedup that has allowed a more realistic investigation into the accuracy of these retrievals to be undertaken.

The purpose of this work is first to examine aspects of the inversion method to see if it is possible to improve the accuracy of the retrieved conductivities, in particular the intracellular conductivities, which to date have not been retrieved nearly as accurately as the extracellular conductivities. The second and major aspect of this work is to consider a realistic simulation where large numbers of potential measurements would be recorded on the measuring array and to examine the accuracy of the inversion technique.

This paper presents the model and solution technique in Section 2 and the inversion algorithm is discussed in Section 3. Various aspects of the inversion algorithm, such as the effect of retrieving the fibre rotation in addition to the conductivities, and the effect of using a single pass of the algorithm rather than two passes, are examined in the first part of Section 4. The second part considers sets of one hundred measurements of potential that are used to mimic a realistic experimental scenario and from these one hundred sets of parameters are determined for a range of noise levels associated with two starting sets of six conductivity values [11,12]. Various data analysis techniques are considered for dealing with the non-physiological values that are sometimes found, while results for the 'best' technique are presented along with conclusions in the final section.

2. Model and solution method

2.1. Model geometry

Cardiac tissue consists of parallel strands of cells, arranged in sheets that rotate relative to one another along a line between the epicardium (outer heart surface) and the endocardium (inner heart surface). It is well-known that current is able to flow more easily in the longitudinal (l) direction along the fibres, than transverse (t) to the fibres within the sheet or between, that is normal (n) to, the sheets of fibres.

The model considered here is a block of cardiac ventricular tissue with dimensions 2 cm × 2 cm × 1 cm in (x, y, z) space, lying between the x–y plane at $z = 0$, which represents the epicardium, and the x–y plane at $z = 1$, which represents the endocardium. From $z = 1$, extending to infinity in the positive z direction there is assumed to be a volume of blood that is in contact with the endocardium. The ventricular tissue is approximated using the bidomain model [1,24–26]. This regards the tissue as consisting of extracellular (e) and intracellular (i) interpenetrating domains, over which the cardiac properties are averaged, thus leading to six bidomain cardiac conductivity values g_{el}, g_{et}, g_{en}, g_{il}, g_{it}, g_{in} being required in the model.

2.2. Governing equations and boundary conditions

The potentials in cardiac tissue are given by the bidomain governing equations [25]

$$\nabla \cdot \mathbf{M}_i \nabla \phi_i = \frac{\beta}{R}(\phi_i - \phi_e) \quad \text{and} \quad \nabla \cdot \mathbf{M}_e \nabla \phi_e = -\frac{\beta}{R}(\phi_i - \phi_e) - I_s \tag{1}$$

where i = intracellular, e = extracellular, I_s is a sub-threshold external current source per unit volume applied in the extracellular space, ϕ_j $(j = i, e)$ is the potential, β is the surface to volume ratio of the cells and R is the specific membrane resistance. The tensors $\mathbf{M}_j$ $(j = i, e)$ take into account the anisotropic nature of the tissue, which comes not only from the varying conductivity values, but also from the fibre rotation within the cardiac tissue [27]. Hence, for a rectangular block of tissue, the $\mathbf{M}_j$ are of the form

$$\mathbf{M}_j(x, y, z) = \begin{pmatrix} (g_{jl} - g_{jt})c^2 + g_{jt} & (g_{jl} - g_{jt})cs & 0 \\ (g_{jl} - g_{jt})cs & (g_{jl} - g_{jt})s^2 + g_{jt} & 0 \\ 0 & 0 & g_{jn} \end{pmatrix} \tag{2}$$

where $j = i, e$, $c = \cos \alpha z$ and $s = \sin \alpha z$ and α is the fibre rotation angle.

The potential distribution in the blood, ϕ_b, is governed by Laplace's equation

$$\nabla^2 \phi_b = 0. \tag{3}$$

The boundary conditions used to solve the model follow from the assumptions that the epicardium is insulated, there is continuity of potential and current at the interface between the tissue and the blood, and the intracellular space is insulated by the extracellular space,

$$\frac{\partial \phi_e}{\partial z} = \frac{\partial \phi_i}{\partial z} = 0 \quad \text{at} \quad z = 0 \tag{4}$$

and

$$\phi_e = \phi_b, \quad g_b \frac{\partial \phi_b}{\partial z} = g_{en} \frac{\partial \phi_e}{\partial z}, \quad \frac{\partial \phi_i}{\partial z} = 0 \quad \text{at} \quad z = 1 \tag{5}$$

where g_b is the conductivity of blood and ϕ_b is the potential in the blood. Also, $\phi_b \to 0$ as $z \to \infty$, since it is assumed that the blood mass is infinite in the positive z direction. Assuming that the boundaries of the domain are insulated, gives the final boundary conditions at the x and y boundaries

$$\mathbf{M}_e \nabla \phi_e \cdot \mathbf{n} = 0, \ \mathbf{M}_i \nabla \phi_i \cdot \mathbf{n} = 0 \quad \text{and} \quad \nabla \phi_b \cdot \mathbf{n} = 0, \tag{6}$$

where $\mathbf{n}$ is the outward pointing normal from the boundary.

The model, Eqs. (1)–(3), subject to boundary conditions (4)–(6), is solved by expanding each of the potentials ϕ_e and ϕ_i as a Fourier series, where for $j = i, e$

$$\begin{aligned} \phi_j(x, y, z) = \sum_{r=0}^{\infty} \sum_{s=0}^{\infty} & C_{rs}^j(z) \cos(s\pi y) \cos(r\pi x) \\ & + D_{rs}^j(z) \sin(s\pi y) \cos(r\pi x) + E_{rs}^j(z) \cos(s\pi y) \sin(r\pi x) \\ & + F_{rs}^j(z) \sin(s\pi y) \sin(r\pi x) \end{aligned} \tag{7}$$

Download English Version:

https://daneshyari.com/en/article/4500001

Download Persian Version:

https://daneshyari.com/article/4500001

Daneshyari.com