A Bidomain Model for Neural Tissue

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Abstract. Bidomain models have most commonly used to simulate cardiac tissue. They have only infrequently been used to model neural tissue as they are often computationally intensive and other modeling techniques such as the core conductor model are more appropriate for studying phenomena such as propagation in neural systems. A bidomain model of an aplysia abdominal ganglion was created using COMSOL Multiphysics and used to estimate the impedance and magnetic flux density perturbations caused by external application of current to the complex. Using this model it was found that magnetic flux density changes due to changes in membrane conductivity were below the noise threshold of a 17 T system, but that it may be possible to detect changes with additional averaging or longer current injection.

Keywords: Bidomain, Membrane, aplysia, MREIT, CDI, FEM

1. Introduction

The bidomain model [Henriquez 1993] is an approximation to the quasi-static electrical behavior of axonal and dendritic tissue. It is so named because the model consists of two domains - intracellular (Ωᵢ) and extracellular or interstitial (Ωₑ) spaces - occupying the same region of space. The domains are coupled via a passive or active membrane model that determines the flow of current from one space to another. The membrane can be thought of as occupying the same volume as the intra- and extracellular spaces. Further, the bidomain may be placed into an external 'bath' that couples to the extracellular space and can also share current with the bidomain structure. Both spaces may be anisotropic and share a principal anisotropic axis. In general (and in real tissue) the degree of anisotropy, defined as the ratio of conductivity along the principal axis to across it, is different in extracellular and intracellular spaces. We are interested in modeling behavior of active tissue in order to determine the feasibility of a method based on magnetic resonance electrical impedance tomography (MREIT) to detect perturbations in MRI phase images due to membrane conductivity changes. We believed the bidomain model would be suitable for estimating these changes, as an alternative to estimations based on detailed modeling of neural complexes (e.g. [Cassarà 2008]).

2. Material and Methods

Our model was based on a simple representation of the aplysia abdominal ganglion (AG). A central body and four radial unmyelinated neural bundles were modeled, as shown in Fig. 1. Model parameter values were taken from the literature. In the following two sections are described the bidomain framework and specific parameters applying to the AG model subject to a bath current injection.

2.1. The Bidomain Equations

The equations describing the bidomain are as follows. The intra and extracellular spaces share current density according to

\[ \nabla \cdot \mathbf{J}_i = \nabla \cdot \mathbf{J}_e = \dot{i}_m \]  \hspace{1cm} (1)

where \( \dot{i}_m \) is the current passing through the membrane in A/m³.
In the model $i_m$ was defined as being due to passive conduction through the membrane only and that

$$i_m = \beta G_m$$

where $\beta$ and $G_m$ are the surface to volume ratio of the tissue in m$^{-1}$ and the membrane surface conductance in $\Omega$m$^{-2}$ respectively. In general the membrane current is defined by a time dependent membrane model, but our initial model only includes a passive membrane.

$J_i$ and $J_e$ are defined as

$$J_i = -D_i \nabla \phi_i \quad \text{and} \quad J_e = -D_e \nabla \phi_e$$

where

$$D_{i,e} = \begin{bmatrix}
  k_{xx} & k_{xy} & k_{xz} \\
  k_{xy} & k_{yy} & k_{yz} \\
  k_{xz} & k_{yz} & k_{zz}
\end{bmatrix}$$

is a tensor with six distinct entries that describes properties of the intra or extracellular tissue with respect to the principal model directions. If the tissue is effectively two dimensional then there are only three independent parameters in each space and we have that

$$k_{xx} = g_L \cos^2 \alpha + g_T \sin^2 \alpha$$

$$k_{xy} = (g_L - g_T) \cos \alpha \sin \alpha$$

$$k_{yy} = g_T \cos^2 \alpha + g_L \sin^2 \alpha$$

where $g_L$ and $g_T$ are conductivities along and across tissue axes, respectively, and $\alpha$ is the angle between the tissue axis and the x-axis of the measurement coordinate system.

If the bidomain tissue is in contact with an isotropic conducting medium, for example blood (in the case of the heart) or plasma-like fluid in the case of neural tissue, the bath equation is described by Laplace's equation in the bath potential $\phi_e$.

**Boundary Conditions**

At the extracellular space-bath boundary we have that

$$\phi_o = \phi_e$$

Further, at the intracellular-extracellular boundary we have that

$$\frac{\partial \phi_i}{\partial n} = 0$$

**Figure 1.** (a) Light microscope image of aplysia abdominal ganglion (b) Simple model of ganglion, showing bath and current application ports.
2.2. Finite element model formulation

The AG was approximated as a spheroidal structure with dimension 1.2 mm with five radiating neural bundles. The spheroid was denoted the body and the neural bundles the arms. Intra- and extracellular conductivities, the fraction of intracellular space of tissue, and membrane conductivity were assigned with reference to standard works. The parameters used are shown in Table 1 below. No anisotropy was assigned to the central ganglion structure, but anisotropic tensors for the five neural bundles in each space were assigned according to (5). The domains in the finite element model are shown in cross-section in Fig 1(b). The model mesh had 1,168,197 degrees of freedom. The overall dimensions of the cell were about 9 mm x 9 mm x 8 mm.

2.3. Model Equation Definitions, Source and Boundary Conditions and Solution strategy

Comsol (Comsol AB, Burlington MA) software was used to create a three-component coupled finite element model. To solve for flux densities we used a static version of a general electromagnetic solution that solved for Voltage (V), A and $\psi$. Components of flux density $B$ were then calculated from $A$. Voltage values and magnetic potentials in each space were denoted as $V_o$, $A_o$, $\psi_o$; $V_e$, $A_e$, $\psi_e$; and $V_i$, $A_i$, $\psi_i$, respectively.

<table>
<thead>
<tr>
<th>Table 1. Bidomain Parameters</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\sigma_i$</td>
<td>0.638</td>
</tr>
<tr>
<td>$\sigma_e$</td>
<td>1.538</td>
</tr>
<tr>
<td>$\sigma_0$</td>
<td>1</td>
</tr>
<tr>
<td>$\sigma_p$</td>
<td>1</td>
</tr>
<tr>
<td>$f$</td>
<td>0.7</td>
</tr>
<tr>
<td>$\beta$</td>
<td>20000</td>
</tr>
<tr>
<td>$G_{m, \text{rest}}$</td>
<td>6.7</td>
</tr>
<tr>
<td>$G_{m, \text{active}}$</td>
<td>320</td>
</tr>
</tbody>
</table>

A magnetostatic partial differential equation was defined all three domains and then modified such that charge could flow between intra- and extracellular domains by specifying additional source terms. Thus, in the extracellular space the equation solved included the source density term

$$Q_e = \beta G_m (V_i - V_e)$$  \hspace{1cm} (8)

and in the intracellular space the corresponding source was

$$Q_i = -Q_e = \beta G_m (V_e - V_i)$$  \hspace{1cm} (9)

There were no sources inside the bath, therefore we specified $Q_o = 0$ for this domain.

**Boundary Conditions**

It was specified at all bath-extracellular space boundaries, as in (6), that

$$V_o = V_e.$$  \hspace{1cm} (10)

As specified in (7), at all intracellular domain boundaries there was no current flow, that is

$$\mathbf{J} \cdot \mathbf{n} = 0$$  \hspace{1cm} (11)

In the bath, fixed voltages of $\pm 1$ V were applied to two opposite ports. All other bath external boundaries were electrically and magnetically insulated. Solutions were obtained using the Conjugate Gradient method using an algebraic or geometric multigrid preconditioner. A relative tolerance of $1 \times 10^{-10}$ was chosen to ensure good accuracy over all subdomains. Solutions for the electrostatic only case were very fast, typically requiring around one minute on a Linux Workstation with 450 MHz processor and 16 GB RAM. Magnetostatic solutions, which had three times as many degrees of freedom for the same mesh, were much slower and took around six hours to reach a solution to the same tolerance.

2.4. Voxel Calculations

Expected $B_z$ values were assessed by averaging calculated results over a voxel structure overlaid on the model. Several resolutions were used, (64 x 64 x 8), (32 x 32 x 8), (16 x 16 x 8) and (128 x 128
Within each voxel, flux density values were calculated by estimating the parameter of interest on an 11 x 11 x 11 grid and then integrating $B_z$ values over a tetrahedral mesh defined on the grid. Where a parameter was undefined on a portion of a voxel, such as on a model or subdomain boundary, the meshing procedure excluded these areas. Final average $B_z$ values in each voxel were calculated by dividing the integrated value by the volume of the voxel. Voxel dimensions used were as follows. Three different in plane resolutions were tested with eight slices with thicknesses of 1 mm and $xy$ dimensions of 281, 562 and 1120 $\mu$m respectively. These dimensions were chosen to be reasonable for both detection of neural activity and maximizing signal to noise ratios. Differences on a fourth finer voxel pattern with slice thickness of 500 $\mu$m and in plane resolution of 140 $\mu$m were also calculated.

3. Results

3.1. $B_z$ deviations

With the sample dimensions chosen and applying $\pm$ 1 V to opposite ports, a current of 1.74 mA flowed across the domain. The $B_z$ standard deviations between active and rest membrane cases are shown in Table 2.

<table>
<thead>
<tr>
<th>Resolution</th>
<th>Volume (mm$^3$)</th>
<th>Intracellular (i)</th>
<th>Extracellular (e)</th>
<th>Bath (o)</th>
<th>Expected Noise level</th>
</tr>
</thead>
<tbody>
<tr>
<td>128 x 128 x 16</td>
<td>0.01</td>
<td>5.04 x 10$^{-10}$</td>
<td>1.68 x 10$^{-10}$</td>
<td>9.25 x 10$^{-11}$</td>
<td>4.80 x 10$^{-9}$</td>
</tr>
<tr>
<td>64 x 64 x 8</td>
<td>0.079</td>
<td>3.70 x 10$^{-10}$</td>
<td>1.24 x 10$^{-10}$</td>
<td>8.53 x 10$^{-11}$</td>
<td>1.70 x 10$^{-9}$</td>
</tr>
<tr>
<td>32 x 32 x 8</td>
<td>0.32</td>
<td>2.83 x 10$^{-10}$</td>
<td>9.51 x 10$^{-11}$</td>
<td>7.33 x 10$^{-11}$</td>
<td>8.50 x 10$^{-10}$</td>
</tr>
<tr>
<td>16 x 16 x 8</td>
<td>1.2</td>
<td>1.97 x 10$^{-10}$</td>
<td>6.56 x 10$^{-11}$</td>
<td>5.88 x 10$^{-11}$</td>
<td>4.25 x 10$^{-10}$</td>
</tr>
</tbody>
</table>

3.2. Typical $B_z$ noise levels

From measurements performed in a 17.6 T scanner, signal to noise ratios in single excitation magnitude images were around 65 at a resolution of 58 x 58 x 500 $\mu$m. Using the procedure detailed in Sadleir (2005) these values were translated to $B_z$ noise levels using the test resolutions and a current injection time of 14 ms, and these levels are shown in the rightmost column of Table 2.

4. Discussion

Table 2 clearly shows that average differences occurring within the bath were smaller than the estimated noise from single excitation scans. At this resolution, maximum changes in $B_z$ were of the order of 1 nT. Naturally, it is expected that averaging data over multiple excitations should lead to detection of signals in the bath. However, these figures are of the maximum possible changes that may occur between active and rest states. Three factors will modify these figures. The first modification relates to the proportion of tissue that is active. We used the gill withdrawal reflex as a model of activity [Zečević 1989] and estimated that around one third of the tissue was active during this reflex. The second modification depends on the number of spikes occurring during the time current is applied (typically 16 ms) and the integrated conductivity change over that time. We determined typical spike rates during the gill withdrawal reflex and determined that this modification accounts for a further decrease in the total conductivity change of one third. The third consideration is of the effect of imaging currents on active tissue. High current densities (> 1.2 A/m$^2$ at 1 mm [Reilly 1998]) may cause imaging currents to stimulate activity. While this event may be advantageous in initial testing, in general it will be necessary to reduce current densities to subthreshold levels. To some degree, current density maxima can be controlled by modifying electrode areas, chamber shape and size. With the chamber shown in Figure 1(b), current densities at threshold levels will be applied to tissue at a current of about 200 $\mu$A. Thus, using conventional MREIT, actual changes may be at best about 0.1, and at worst about 0.01, those shown. However, newly developed modifications of MREIT, including ICNE [Park et al. 2007], and current pulse width optimization [Lee et al. 2006] should allow us to reduce noise levels further, bringing this method of detection closer to reality. Based on this work, performed at 3 T, we believe use of these combined strategies should allow us to reduce noise by approximately 85% when translated to high field environments. Therefore, modifications of MREIT pulse sequences and averaging over multiple stimuli should result in detection of neural activity via this route.
5. Conclusions

A novel bidomain model of the *aplysia* AG was created. The results presented here indicate that the noise levels in a 17 T scanner may be too large to be able to detect perturbations in membrane voltage without additional effort. However, careful adjustment of MREIT imaging parameters combined with data averaging should result in this method becoming feasible.

References


Henriquez, C. S. Simulating the electrical behavior of cardiac tissue using the bidomain model. *Critical Reviews in Biomedical Engineering*, 21, 1-77, 1993


