

The Determination of the Bidomain Conductivity Values of Heart Tissue

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Abstract

A method for determining the bidomain conductivity values was developed. The study was due to the different sets of conductivity values reported in the literature, each producing significantly different bidomain simulation results.

The method involves mapping the propagation of the electrical activation of cardiac tissue, initiated by point stimulation, via extracellular electrodes. A time-dependent bidomain model is used to simulate the electrical phenomena. The optimum set of conductivity values is achieved by minimising the difference between the bidomain model output and the measured extracellular potential, by means of inverse techniques in parameter estimation, such as least-squares (LS) and Singular Value Decomposition (SVD). The method takes a different approach to the conventional four-electrode technique, as it does not require the small electrode separation needed to separate the extracellular current from the intracellular.

1. Introduction

The bidomain model [1] is used to simulate the electrical activity of the heart, and can be used to study the effects of cardiac abnormalities. Due to the myocardial fibre arrangement, the electrical conduction in the heart is described as anisotropic; that is, the current propagates more readily along the tissue fibres than across them [2, 3, 4]. The anisotropy is represented mathematically by two conductivity tensors in the bidomain equations, for intracellular and extracellular space. The conductivity values within these tensors are defined in the directions along (longitudinal) and across (transverse) the tissue fibres; giving a total of six conductivity values in three-dimensions.

There are a number of sets of conductivity values available to use in bidomain simulations; and each of these sets are different [5]. The issue is when these sets of conductivity values are used in bidomain simulations, they produce significantly different simulation output, and there is no general agreement as to which set is the most preferred. For example, a study of ST segment shift in subendocardial ischaemia by Johnston and Kilpatrick [6] showed that

the different sets of conductivity values produced significantly different epicardial potential distributions.

With discrepancies in simulation results, the measurement of the bidomain conductivity values requires further investigation. In this study, a method was developed to measure the bidomain conductivity values, which took on a different approach to the four-electrode technique. LS and SVD methods were tested, using synthetic data with added random noise.

2. Method

The method for determining the bidomain conductivity values is based on the potential mapping of the elliptical depolarising wave on the epicardium, initiated from a point current source. When observing the elliptical depolarising wave, its shape reflects the anisotropy of the cardiac tissue, with its major axis aligning with the myocardial fibre direction [7]; the local fibre direction can then be determined by the orientation of the elliptical wave [8], which is useful information for calculating the conductivity values.

Simulations of the propagating depolarising cardiac tissue from point stimulation, for different sets of conductivity values, have showed marked differences in extracellular potential distribution [9]. Features in the elliptical wave such as its morphology, magnitudes, electrograms, the spacings of the isopotential lines, and the potential maxima and minima are different. From these observations it is possible, based on the information observed in the elliptical wave, that there can be a unique set of conductivity values which produce a distinct potential distribution.

To determine the conductivity values which produce potential that is consistent with experimental observations, parameter estimation techniques are used, such as Least-Squares (LS) estimation. The optimum set of conductivity values is achieved when the difference between model and experimental observations comes to a minimum.

2.1. Bidomain simulations

The bidomain model describes the current flow between intracellular and extracellular space. It is a macroscopic model, with the assumption that the electric poten-

tial varies over distances greater than the dimensions of a single cell. The bidomain model is represented by the following partial differential equations [1, 10]:

$$\nabla \cdot (\mathbf{D}_i \nabla \Phi_i) = I_m - I_{si}, \quad (1)$$

$$\nabla \cdot (\mathbf{D}_e \nabla \Phi_e) = -I_m - I_{se}, \quad (2)$$

where Φ_i and Φ_e are the intracellular and extracellular potentials, \mathbf{D}_i and \mathbf{D}_e are the conductivity tensors, I_{si} and I_{se} are externally applied current sources. The transmembrane current density, I_m , is the sum of capacitive and ionic currents, given by the following expression:

$$I_m = \beta \left(C_m \frac{d\Phi_m}{dt} + I_{ion} \right). \quad (3)$$

where Φ_m is the transmembrane potential, which is defined as:

$$\Phi_m = \Phi_i - \Phi_e. \quad (4)$$

The C_m term is the transmembrane capacitance, β is the ratio of membrane surface area to tissue volume, and the I_{ion} term is the sum of transmembrane ionic currents. Membrane models consisting of first-order non-linear ordinary differential equations describes the behaviour of the I_{ion} term.

For this investigation, CardioWave software [11] was used to solve the bidomain equations, with the choice of time-stepping schemes and iterative solvers. The finite element method was performed in SCIRun software [12], to discretise the elliptical operators in the bidomain Equations (1) and (2). Simulation runs were performed in parallel on a SGI Altix 4700 supercomputer.

2.2. Parameter estimation

The difference between model data and experimental data can be defined as the objective function \mathbf{O} , it is a measure of fit, the smaller its value, the greater consistency between model and observations. By linearising the problem, the objective function by LS can be given by the following expression [13]:

$$\mathbf{O} = (\mathbf{r} - \mathbf{J}(\mathbf{p} - \mathbf{p}_0))^t \mathbf{Q}(\mathbf{r} - \mathbf{J}(\mathbf{p} - \mathbf{p}_0)), \quad (5)$$

the residual \mathbf{r} , is given by:

$$\mathbf{r} = \mathbf{c} - \mathbf{c}_0. \quad (6)$$

where \mathbf{c} contains the experimental observations, \mathbf{c}_0 contains the model output, \mathbf{Q} is the weighted matrix, and \mathbf{J} is the Jacobian matrix; \mathbf{p} holds the desired parameters, and \mathbf{p}_0 holds the current estimate of the parameters. Equation (5) is an approximation of the objective function, and it improves as \mathbf{p}_0 is closer to \mathbf{p} . In order to minimise the

objective function, the parameter upgrade vector $(\mathbf{p} - \mathbf{p}_0)$ is calculated by:

$$\mathbf{u} = (\mathbf{J}^t \mathbf{Q} \mathbf{J} + \alpha \mathbf{I})^{-1} \mathbf{J}^t \mathbf{Q} \mathbf{r}. \quad (7)$$

where α is the Marquart parameter, and \mathbf{I} is the identity matrix. The Marquart parameter determines how large a step the parameters are updated between optimisation iterations. SVD may be applied to expression $(\mathbf{J}^t \mathbf{Q} \mathbf{J})$ in Equation (7) when experiencing near singularity. The Jacobian matrix \mathbf{J} is obtained by calculating the derivatives of the forward model output with respect to the estimated parameters. A flow chart of the parameter estimation algorithm is shown in Figure 1. PEST software [13] was used to apply the LS and SVD methods to the bidomain model.

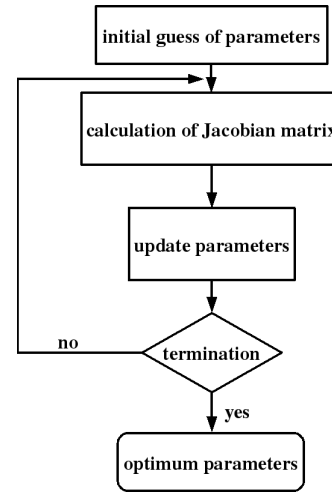


Figure 1. Flow chart: algorithm for parameter estimation.

3. Validation

The parameter estimation method was tested with synthetic data, produced from a 2D bidomain simulation with known conductivity parameter values. Chosen conductivity values are shown in Table 1, second column [3]. Random noise was added into the synthetic data to test how well the original values were calculated back. The noise was generated from a Gaussian distribution, with a zero mean and its standard deviation calculated by the following expression:

$$b = (\sqrt{2}/2) u_{max} p. \quad (8)$$

where u_{max} is the absolute maximum potential in the model output, and p is the percentage of noise contamination.

Cardiac activation for a duration of 10 *ms* from point stimulation was simulated. The tissue domain had dimensions of $1.2 \times 1.9 \text{ cm}^2$, with a grid of 121×191 nodes,

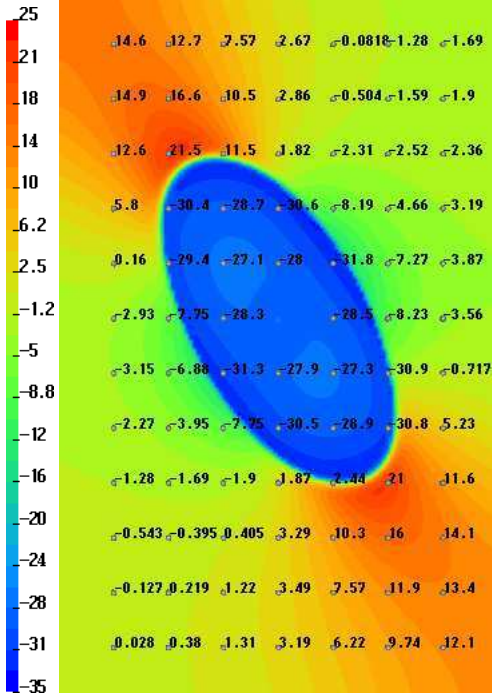


Figure 2. Potential map of bidomain simulation output, at 10 *ms* after stimulation at the centre of the domain. Fibre direction is at 121° from the horizontal. Extracellular potential values (mV) are shown at electrode sites, which were used as synthetic data. Electrode separation is 1.5 *mm*

hence the node spacing was 0.01 *cm*. For the boundary conditions, a group of nodes were assigned to zero to act as the ground, located in the bottom left hand side of the domain. A current density of 1000 $\mu A cm^{-2}$ for a duration of 1 *ms* was set to a group of nodes at the centre of the domain to act as the pacing stimulus. The membrane model used was the Luo-Rudy model. Membrane capacitance C_m and the ratio of membrane surface area to tissue volume β were set to 1 $\mu F cm^{-2}$ and 2000 cm^{-1} respectively. Figure 2 presents the extracellular potential distribution from the bidomain simulation, showing the propagation of the depolarising wave, with faster conduction in the direction along the tissue fibres, which is at 121° from the horizontal. Data used in the parameter estimation was the extracellular potential values at the electrodes sites, such as those in Figure 2. The frequency of the data used was every 1 *ms*, for a duration of 10 *ms*, from the start of activation. Conductivity parameters had values of 1 $mS cm^{-1}$ at the start of the estimation process. Table 1 and 2 shows the estimated parameters from the synthetic data with 5 % and 10 % noise, using LS and SVD methods. Statistical values such as the objective function *O*, the correlation coefficient *r*, number of optimisation it-

Table 1. Estimated conductivities σ from synthetic data with 5 % added noise ($mS cm^{-1}$). Subscripts *i* and *e* denote intracellular and extracellular; and *l* and *t* longitudinal and transverse.

	original values	LS 5 %	SVD 5%
σ_{il}	2.8	2.801 ± 0.178	2.800 ± 0.017
σ_{it}	0.26	0.264 ± 0.003	0.264 ± 0.003
σ_{el}	2.2	2.199 ± 0.017	2.199 ± 0.017
σ_{et}	1.3	1.289 ± 0.014	1.291 ± 0.014
<i>O</i>		1298	1298
<i>r</i>		0.991	0.991
<i>OI</i>		11	12
<i>MC</i>		95	88

OI - optimisation iterations

MC - model calls

Table 2. Estimated conductivities from synthetic data with 10 % added noise ($mS cm^{-1}$).

	LS 10%	SVD 10%
σ_{il}	2.793 ± 0.038	2.795 ± 0.04
σ_{it}	0.257 ± 0.007	0.256 ± 0.01
σ_{el}	2.211 ± 0.038	2.211 ± 0.04
σ_{et}	1.331 ± 0.032	1.331 ± 0.03
<i>O</i>	5874	5874
<i>r</i>	0.959	0.959
<i>OI</i>	12	12
<i>MC</i>	105	84

erations (parameter updates), and the number of forward model calls (for the construction of the Jacobian matrix) made during the estimation process are also presented. Both methods retrieved the values back successfully. As expected the increase in noise level increased the uncertainty. Both methods, LS and SVD, recovered the parameter values with the same accuracy; though, as the noise levels increased, it took SVD less forward model runs than LS, hence less computational time. The greater number of forward model runs for the LS method was due to the calculation of the best value for the Marquart parameter α , in order to lower the objective function. Figure 3 shows a contour plot of the objective function in parameter space. The plot is to observe the behaviour of the objective function in relation to the intracellular conductivities, whilst holding the extracellular conductivities fixed. Similarly, Figure 4 shows the behaviour for the extracellular conductivities. It can be seen that there is only one objective function minimum, where the original values reside, giving the assurance of unique values. The closeness of the contour lines indicates the rapid increase in the objective function, away from the minimum. The crosses joined by the line in Figure 3 and 4 shows an example of the steps between optimisation iterations towards the desired parameter values.

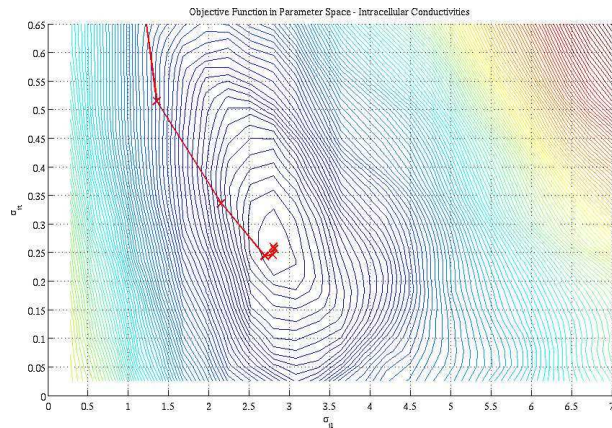


Figure 3. Contour plot of objective function in intracellular parameter space. Minimum at $\sigma_{il} = 2.8$ and $\sigma_{it} = 0.26 \text{ mScm}^{-1}$.

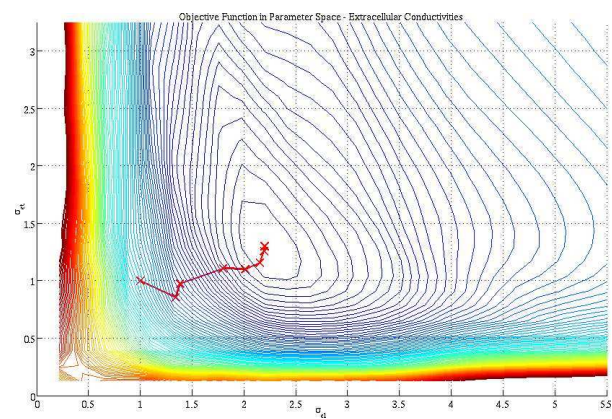


Figure 4. Objective function in extracellular parameter space. Minimum at $\sigma_{el} = 2.2$ and $\sigma_{et} = 1.3 \text{ mScm}^{-1}$.

4. Conclusion

A method for measuring the bidomain conductivity parameters was developed. It takes advantage of parameter estimation techniques, and parallel computing to repeatedly solve for a full bidomain model. Only extracellular potential needs to be measured, with techniques of cardiac mapping already available. Knowledge of the fibre direction can be determined by the orientation of the depolarising ellipse. The method takes on a different approach to the four-electrode technique, as it does not require electrode separation in the micron range, necessary to isolate the extracellular potential from the intracellular. Uniqueness can be judge upon inspecting the objective function in parameter space, statistical measures, its performance with synthetic data, and comparing experimental and simulated potential distributions. Other parameters such as membrane capacitance and local fibre direction can also be determined.

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