How Accurately can Cardiac Conductivity Values be Determined from Heart Potential Measurements?

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Abstract

Although realistic cardiac electrophysiological simulations require accurate model parameters, no fully experimentally determined sets of six cardiac conductivity values exist. The present authors have recently proposed a method to determine the six bidomain conductivity values, for the extra– and intracellular domains in the longitudinal, transverse and normal directions, from measurements of potential made in cardiac tissue in vivo. The method uses a 3D mathematical model, a microelectrode measuring array and a novel inversion technique, which retrieves the conductivities and the fibre rotation angle from the potential measurements.

In this work, a number of different data analysis methods are compared for realistically large sets of these simulated potential measurements and the best method is identified. Using synthetic data it is found that the three extracellular conductivities can be retrieved extremely accurately, with relative errors of less than 5%, even with noise of up to 40% added to the potential measurements. In addition, the intracellular longitudinal conductivity and the fibre rotation can be retrieved with relative errors at worst around the added noise. The intracellular transverse and normal conductivities are often more difficult to retrieve, with relative errors of around four times the added noise.

1. Introduction

Accurate values for the cardiac bidomain conductivities have been sought for many years for use in simulations of cardiac electrophysical phenomena [1]. The only sets of measured values [2–4] that exist were found in excised tissue and have been shown to be inconsistent [5] and to produce different results in simulation studies [6]. These three studies also found values for only four bidomain conductivities, whereas it has been shown [7] that six values are necessary to account for the anisotropy in directions along and across the cardiac fibres, as well as between the sheets of fibres, within the two domains (extra– and intracellular). However, no such sets of six values have yet been determined due to difficulties associated with both making and interpreting the measurements.

Recently, some groups [8, 9] have proposed methods for determining the six conductivities by using multi–site stimulation. In addition, the present authors [10–13] have demonstrated, using synthetic data, that their inversion technique is capable of determining six bidomain conductivities and the fibre rotation angle associated with the rotation of the sheets of cardiac fibres between the epicardium and endocardium. These are found from measurements of electric potential that are made on a multi–electrode micro–array and are determined using a 3D mathematical model [12], as well as a novel inversion technique.

The present study mimics a realistic experimental set–up by producing 100 sets of simulated heart potential measurements for each added noise level. Such work is now possible because the inversion method has recently been implemented on GPUs [14], with a resultant speedup of at least 60 times in the C++ code. A number of methods to perform the data analysis, after the inversion method retrieves each set of parameters, are considered and since it is found that the data analysis method appears to be increasingly important in the case where high amounts of noise are present in the potential measurements. This is due to the fact that the inversion routine occasionally converges to non-physiological conductivity values and it is necessary to find a way to automatically identify and remove these values from the analysis. The best data analysis method is identified and it is then used to study the accuracy of the inversion method for much higher added noise levels than have been considered previously.

2. Methods

2.1. Governing equations and model

The electric potential in a slab of cardiac ventricular tissue and the blood adjacent to the tissue is modelled by the bidomain (i=intracellular, e=extracellular domain) equations [15], as well as Laplace's equation in the blood (b)

$$\nabla \cdot M_i \nabla \phi_i = \frac{\beta}{R}(\phi_i - \phi_e)$$

$$\nabla \cdot M_e \nabla \phi_e = -\frac{\beta}{R}(\phi_i - \phi_e) - I_s$$
$$\nabla^2 \phi_b = 0$$

where ϕ_p, $p = i, e, b$ is the potential, β is the cell surface to volume ratio, R is the membrane resistance and I_s is the sub–threshhold current, which is applied during the ST segment when the heart is assumed iso–electric. Cardiac conductivity is anisotropic due to the different propagation speeds of the current, along the cardiac fibres (longitudinal = l), across the fibres (transverse = t) and between the sheets of fibres (normal = n), which rotate, relative to one another, linearly through an angle α, between the epicardium and the endocardium. This leads to six bidomain conductivity values $g_{pq}, p = i, e,\ q = l, t, n$ and the anisotropy is accounted for by the conductivity tensors $M_p, p = i, e$. Full details of the model, its boundary conditions and solution technique have been published previously [10, 12].

In this study, the model is solved using the six conductivity dataset of Hooks et al. [16], where $g_{el} = g_{il} = 2.63$, $g_{et} = 2.45, g_{en} = 1.087, g_{it} = 0.263$ and $g_{in} = 0.08$ mS/cm, together with model parameters [11] $g_b = 6.7\,\text{mS/cm}$, $\beta = 2000\,\text{cm}^{-1}$, $R = 9100\,\Omega\text{cm}^2$, $I_s = 50\,\text{mA/cm}^3$ and $\alpha = 2\pi/3$.

2.2. Simulations and inversion method

An inversion method is used to find the six conductivities and fibre rotation from measurements of electric potential that are made on the heart during the ST segment using a micro–electrode array [13] (Figure 1). The method uses a two–pass approach, where firstly a subset of 25 electrodes is used to make potential measurements (Figure 1, inner square of cyan electrodes) that are then used in conjunction with the inversion method to find the three extracellular conductivities. The full set of 73 electrodes is then used to make measurements of potential in the second pass, from which the intracellular conductivities and the fibre rotation are found [13]. The inversion method is based on minimising a Tikhonov functional, which is described in full in the following reference [12].

Recently, the inversion routine has been implemented on GPUs [14]. The resultant speed–up has allowed a more realistic set of simulated potential measurements to be used in conjunction with the inversion method, as follows. The model was used to calculate the potentials at each of the measuring electrodes and then noise was added to these potentials before the inversion technique was used to retrieve the conductivities. Here, 100 sets of simulated potential measurements were used in the first pass and from each of these, a parameter set of six conductivity values and fibre rotation was determined. The final set of parameter values was determined by finding the means of each parameter in the 'acceptable' parameter sets (see below).

The inversion routine occasionally converges to a set of parameters that contains a non–physiological conductivity value. Previously [12], this has been dealt with by imposing a selection criteria that rejects a set of parameters if three or more are outside one standard deviation from the mean. This is designated as the 'old' method in this work. An alternative method is also considered here (the 'new' method) where a set of parameters is only accepted if, in the first pass, all three extracellular conductivities are within one standard deviation of the mean.

A similar process is used in the second pass, except that the extracellular conductivities found in the first pass are held constant in the second pass and only the intracellular conductivities and fibre rotation are determined in this case. Again 100 sets of simulated potentials are used and, in a similar fashion to the first pass, in the 'new' method sets of parameters are only deemed acceptable if all four parameters (three intracellular conductivities and fibre rotation) are within one standard deviation of the mean. The 'old' method uses the same criteria as in the first pass, viz. sets of parameters are rejected if three or more are outside of one standard deviation from the mean.

Finally, the accuracy of the inversion method is determined by comparing each of the parameters with its correct value (see Section 2.1) by means of its percentage relative error.

3. Results and discussion

Percentage relative errors $\pm$ one standard deviation (std), averaged over 100 first and 100 second passes, for various noise levels, are given in Tables 1 and 2, respectively. The errors in retrieving the parameters are compared for three different data analysis methods, keep 'all', 'new' and 'old' (Section 2.2).

A comparison of the three analysis methods for the first pass (Table 1) indicates that, based on relative errors, one method is not consistently superior to the others, up to noise levels of 30%, at which point keeping some inaccurate values affects the 'all' category. In the second pass (Table 2), there is little difference in the methods for the lower noise levels, but from 20% noise onwards it is generally the case that the 'new' method is superior to both keeping all the data and also the 'old' method. Given these results, it would seem that the 'new' method is the best overall data analysis method.

The fact that, for higher noise levels, the methods that eliminate some of the sets of parameters are more accurate than the one that does not is perhaps not surprising. However, another aspect to consider is why the 'new' method works more successfully than the 'old' method. This would seem to be because the 'new' method involves keeping the sets of parameters only if all the *relevant* parameters are within 1 std of the mean. This means in the

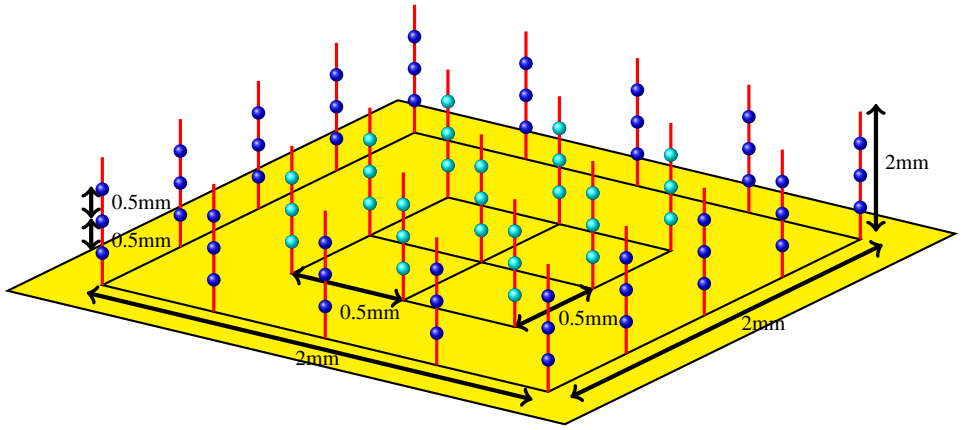

Figure 1. The multi-electrode (three electrodes per needle) array used for making the potential measurements. The 'closely–spaced' electrodes on the needles in the inner square (cyan) are used in the first pass. The second pass uses all the electrodes.

Table 1. Percentage relative errors ± 1 standard deviation (std), for various noise levels, when retrieving the indicated cardiac conductivities, in the first pass, using all the data or the 'new' method (keep set if all three extracellular conductivities are within 1 std of the mean) or the 'old' method (reject if any three parameters are outside 1 std of the mean).

	All data			'New' method			'Old' method		
Noise	g_{el}	g_{et}	g_{en}	g_{el}	g_{et}	g_{en}	g_{el}	g_{et}	g_{en}
5%	0.5±2.0	0.1±2.7	0.3±1.6	0.4±1.0	0.5±1.2	0.5±0.8	0.8±1.6	1.1±1.8	0.0±1.2
10%	1.0±3.3	0.8±4.2	0.8±2.2	0.4±1.6	1.4±2.2	1.3±1.3	0.9±2.7	1.6±2.9	0.6±1.7
15%	2.4±5.4	0.7±5.5	0.2±3.7	2.6±2.8	0.7±2.2	0.1±1.6	2.9±4.3	2.2±4.5	0.8±2.5
20%	1.2±5.9	2.8±7.2	1.8±4.0	2.3±3.2	2.5±4.0	2.1±2.3	2.7±4.9	0.9±6.0	0.5±3.0
25%	0.3±6.2	0.7±9.6	1.4±5.1	0.8±2.9	1.7±4.1	2.4±2.7	1.3±5.2	0.1±5.2	0.9±4.1
30%	1.7±7.7	1.6±9.9	0.2±6.3	0.9±3.3	2.7±4.2	0.5±2.4	1.0±6.2	3.0±5.4	0.0±5.2
35%	13±87	21±224	1.3±9.2	5.1±7.5	0.3±8.3	1.1±3.9	5.6±8.5	0.6±9.0	0.4±7.5
40%	35±230	25±160	3.4±9.1	0.7±9.5	0.3±17	4.1±4.8	3.3±11	2.1±20	1.5±6.5

Table 2. Percentage relative errors ± 1 standard deviation (std), for various noise levels, when retrieving the indicated cardiac conductivities, in the second pass, using all the data or the 'new' method (keep set if all four parameters are within 1 std of the mean) or the 'old' method (reject if any three parameters are outside 1 std of the mean).

	All data			'New' method			'Old' method		
Noise	g_{il}	g_{it}	g_{in}	g_{il}	g_{it}	g_{in}	g_{il}	g_{it}	g_{in}
5%	0.3±4.1	2.9±15	18±15	0.3±2.3	4.9±7.3	19±10	1.0±4.0	3.7±14	20±14
10%	1.8±7.7	14±31	42±31	2.1±3.8	11±16	47±15	0.4±7.2	15±30	41±30
15%	9.1±13	14±56	4.1±36	8.4±8.1	1.5±23	1.2±15	8.4±12	3.5±45	2.9±33
20%	1.1±19	96±130	38±72	1.6±9.7	75±70	47±37	0.5±19	98±130	42±73
25%	26±42	91±170	34±82	13±18	14±58	32±46	26±41	90±170	31±76
30%	11±55	8.3±91	17±63	9.4±18	34±37	26±33	0.8±29	1.9±88	12±63
35%	11±36	25±80	37±94	19±17	17±35	4.4±38	14±24	23±77	35±91
40%	29±120	63±190	122±230	3.2±26	19±49	61±85	28±120	59±190	110±220

first pass, which is only 'sensitive' [13] to the extracellular conductivities, it is sensible to make decisions as to whether to keep or reject sets of parameters based only on the extracellular conductivities and not on all the parameters, as in the 'old' method. Similarly, in the second pass all three intracellular conductivities as well as fibre rotation are relevant and so all of these are part of the selection criteria.

In terms of the accuracy of the conductivities that are found by the inversion method, the 'new' part of Table 1 indicates that the first pass is able to retrieve the extracellular conductivities extremely accurately, with relative errors

that are less than 5% even with added noise as high as 40%. The intracellular conductivities cannot be retrieved as accurately as this (Table 2), although the relative errors for g_{il} are less than the added noise, as are those for the fibre rotation α (not presented). The relative errors for g_{it} and g_{in} are at most around four times the added noise, although in most cases they are considerably less than this.

4. Conclusion

Using a 3D bidomain model of cardiac tissue, a micro–needle measuring array and an inversion technique implemented on GPUs, it has been shown that it is possible to determine six cardiac bidomain conductivity values and fibre rotation from large sets of simulated measurements of heart potentials. It was found that the best data analysis method is one that takes into account only the relevant parameters in each pass of the inversion method. Using this technique it was found that the extracellular conductivities can be retrieved extremely accurately, even with 40% added noise. Future work will include checking these conclusions for the other existing six conductivity dataset [17].

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