

## Finding cardiac conductivity values: An inverse problem approach

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### SUMMARY

Accurate determination of cardiac conductivity values is of paramount importance for detailed simulation of many electrophysiological phenomena. Here we present an approach to determine these values using Tikhonov regularisation applied to potential measurements made on a micro-needle array. Results show that it is possible to accurately retrieve most of the required values with measurement noise as high as 10%.

**Key Words:** *cardiac conductivity, bidomain model, electrophysiology, inverse problem, Tikhonov regularisation*

## 1 INTRODUCTION

Values for the bidomain electrical conductivities play a significant role in the modelling and simulation of many cardiac related phenomena, for example, activation sequences [1], fibrillation [2], ST segment shifts [3] and defibrillation [4]. To date, work on determining accurate cardiac conductivity values has centred on developing mathematical methods, and, to a lesser extent, experimental techniques, for determining these values. Most of these methods are based on the so-called four electrode technique [5], which uses four collinear equi-spaced electrodes, where current is applied to the outer pair, and measurements are made on the inner pair, of electrodes.

Recently, several alternative methods have been presented for determining the conductivity values. One new experimental technique [6] maps cardiac tissue activation and then obtains the cardiac parameters using a least squares and singular value decomposition approach. A new computational approach [7], although only presently applied to a 2D monodomain, suggests simplifying the problem of retrieving conductivities from transmembrane potential measurements made by microelectrode arrays, by using a novel parallel optimisation algorithm. Johnston et al. [8] demonstrated that a two pass approach, using ‘closely’ and ‘widely’ spaced subsets of electrodes (Figure 1(left)) and an inversion technique based on Tikhonov regularisation [9], was able to accurately retrieve four conductivities and fibre rotation from a simulated set of potentials to which noise was added.

Recently, work by Hooks and Trew [10] has confirmed that three unique intracellular electrical conductances can be defined at any point in the ventricular wall and this has added impetus to the search for techniques that will enable six, rather than four, cardiac conductivity values to be determined. As a result, it has been shown recently [11,12] using a three-layered multi-electrode array and a similar mathematical model and inversion technique to that discussed above [8], that it is possible to retrieve all six conductivities as well as fibre rotation. Here we discuss the performance of this method of conductivity value determination in the sense of an inverse problem.

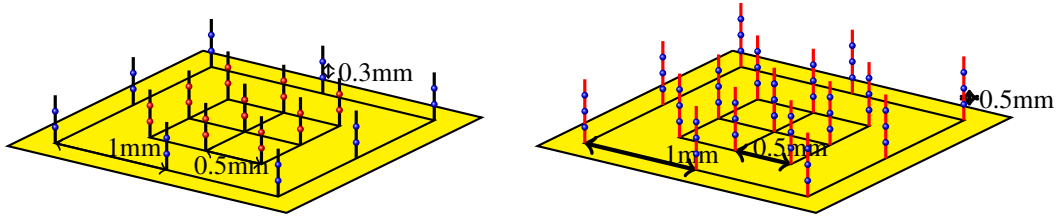


Figure 1: Two-layer (left) and three layer (right) multi-electrode arrays used to retrieve four and six conductivity values (respectively). Subsets of the electrodes are used in a two-pass protocol.

## 2 METHODS

Mathematically, the bidomain equations governing the electric potential in a slab of cardiac tissue and the adjacent blood mass are given by

$$\nabla \cdot \mathbf{M}_i \nabla \phi_i = \frac{\beta}{R}(\phi_i - \phi_e), \quad \nabla \cdot \mathbf{M}_e \nabla \phi_e = -\frac{\beta}{R}(\phi_i - \phi_e) - I_s, \quad \nabla^2 \phi_b = 0. \quad (1)$$

where  $\phi_h$  ( $h = i, e$  or  $b$ ) is the potential, ( $i$ =intracellular,  $e$ =extracellular,  $b$ =blood),  $I_s$  is the applied current,  $\beta$  is the surface to volume ratio for the cells and  $R$  is membrane resistance. The conductivity tensors, which can be written as  $\mathbf{M}_h = \mathbf{A} \mathbf{G}_h \mathbf{A}^T$  ( $h = i$  or  $e$ ) where  $\mathbf{A}$  represents the local direction of the fibres and  $\mathbf{G}_h$  is a diagonal matrix, containing the longitudinal ( $g_{hl}$ ), transverse ( $g_{ht}$ ) and normal tissue conductivities ( $g_{hn}$ ) along the diagonal, reflect the fact that current can flow along the direction of the fibres (longitudinally) more easily than it can across the sheets of fibres (transversely) or between the sheets (normally).

The boundary conditions necessary to solve the above equations are derived from the assumptions that: the epicardium is insulated; there is continuity of potential and current at the interface between the tissue and the blood; the intracellular space is insulated by the extracellular space; the blood mass is assumed infinite in the positive  $z$  direction; and finally, the boundaries of the tissue and blood are insulated.

The model, described by equations (1), shows that the potentials depend on the conductivity parameters in a nonlinear fashion,

$$\mathbf{F}(\mathbf{m}) = \Phi \quad (2)$$

where  $\Phi$  is the vector of measured potentials,  $\mathbf{m} = [g_{il}, g_{it}, g_{in}, g_{el}, g_{et}, g_{en}, \alpha]^T$  ( $\alpha$  is the total fibre rotation through the slab) and  $\mathbf{F}$  represents the forward model. To obtain  $\mathbf{m}$  from equation (2) it is then necessary to minimise the Tikhonov functional

$$\|\mathbf{F}(\mathbf{m}) - \Phi\|_2^2 + \gamma^2 \|\mathbf{m}\|_2^2 \quad (3)$$

since there will be noise in the measurement vector  $\Phi$ . Here  $\gamma$  is the regularisation parameter.

Minimisation of the functionals is performed using the SolvOpt solver [12], which minimises non-linear multivariate functions using a modified Shor's  $r$ -algorithm. The constraints applied for the minimisation are that  $0 \leq \alpha \leq \pi$  and that the conductivities are positive. The termination criteria used [12] is that the relative error in the functional is less than  $10^{-6}$  for two successive iterations.

For the first pass of the algorithm the Tikhonov functional, from equation (3), to be minimised is

$$f_1 = \sum_{i=0}^{24} [\phi_M(i) - \phi_C(i)]^2 + \gamma_1^2 [g_{il}^2 + g_{it}^2 + g_{in}^2 + g_{el}^2 + g_{et}^2 + g_{en}^2] + \gamma_2^2 \alpha^2 \quad (4)$$

Noise	$g_{el}$	$g_{et}$	$g_{en}$	$g_{il}$	$g_{it}$	$g_{in}$	$\alpha$
1%	$0.5 \pm 0.4$	$0.3 \pm 0.4$	$0.3 \pm 0.3$	$2.2 \pm 1.5$	$2.6 \pm 2.3$	$1.9 \pm 1.5$	$3.0 \pm 2.5$
2%	$0.2 \pm 0.5$	$0.4 \pm 0.8$	$0.4 \pm 0.6$	$1.3 \pm 1.6$	$0.1 \pm 3.3$	$3.6 \pm 3.7$	$2.2 \pm 4.6$
5%	$1.1 \pm 0.9$	$2.3 \pm 2.1$	$1.1 \pm 1.6$	$2.1 \pm 3.0$	$15.7 \pm 8.0$	$1.7 \pm 7.3$	$8.2 \pm 7.9$
10%	$2.0 \pm 3.0$	$0.6 \pm 4.1$	$1.5 \pm 3.1$	$3.0 \pm 6.6$	$9.2 \pm 18.6$	$17.6 \pm 14.0$	$1.4 \pm 20.3$
20%	$3.3 \pm 4.1$	$4.5 \pm 5.3$	$2.3 \pm 5.3$	$25.6 \pm 14.5$	$13.7 \pm 28.2$	$22.9 \pm 37.9$	$29.7 \pm 42.5$

Table 1: Average percentage relative errors  $\pm 1$  standard deviation for the MacLachlan *et al.* [12] dataset, for various noise levels, where the  $g_{eh}$  values are retrieved in the first pass and the  $g_{ih}$  and  $\alpha$  values are retrieved in the second pass.

where  $\phi_M$  is the difference in measured potential between electrode  $i$  and the reference electrode and  $\phi_C$  is similar but for the calculated value at each iteration of the solver. Due to the difference in the magnitudes of the conductivity values and  $\alpha$ , two regularisation parameters,  $\gamma_1 = 10^{-2}$  and  $\gamma_2 = 10^{-5}$  are used. Initial values used are  $\alpha = 1$ , with the conductivity values all equal to  $1 \times 10^{-3}$ , except for  $g_{in} = 1 \times 10^{-4}$ .

In the second pass, the mean values for  $g_{el}$ ,  $g_{et}$  and  $g_{en}$  from the first pass are held constant and only values for  $g_{il}$ ,  $g_{it}$ ,  $g_{in}$  and  $\alpha$  are retrieved, using starting values from the first pass. The Tikhonov functional to be minimised is now

$$f_2 = \sum_{i=0}^{72} [\phi_M(i) - \phi_C(i)]^2 + \gamma_1^2 [g_{il}^2 + g_{it}^2 + g_{in}^2] + \gamma_2^2 \alpha^2 \quad (5)$$

### 3 RESULTS

In order to demonstrate the ability of the electrode array and computational algorithm to determine the conductivity values, as well as the total fibre rotation, a forward simulation was performed using the conductivity values mentioned by MacLachlan *et al.* [12]. The “measured” potentials calculated from the forward simulation were then contaminated with varying levels of noise and the two pass Tikhonov regularisation approach was used to recover the original conductivity values. This process was repeated 15 times and the resulting percentage relative errors are given in Table 1. As the described above, the extracellular conductivities were determined from the first pass of the algorithm and the intracellular conductivities and the fibre rotation were determined from the second pass.

From the table it can be seen that the algorithm can obtain the extracellular conductivities more accurately than the intracellular conductivities. Generally, the extracellular conductivities can be recovered to a level of accuracy of about a quarter to a half the size of the added noise. However, the intracellular conductivities can only be recovered to an accuracy of about 2-3 times the added noise.

In the execution of the algorithm it can be seen that the first pass is quite sensitive to the extracellular conductivities, but not to the intracellular conductivities or the fibre rotation. This provides accurate extracellular conductivities for the second pass, which is important because they are held constant there while the algorithm retrieves the intracellular conductivities and fibre rotation. The lack of accuracy in the intracellular starting values for the second pass is not a drawback since the second pass is not particularly sensitive to these starting values. It is worth noting that, although 20% noise appears to be near the limit of the algorithm for retrieving the intracellular conductivities and fibre rotation, it is still able to retrieve the extracellular conductivities quite accurately even for noise levels of 20%.

## 4 CONCLUSIONS

This paper has presented a two pass approach, based on Tikhonov regularisation, to obtain cardiac conductivity values and fibre rotation from measurements of potential made on a multi-electrode array. It has been shown that, even in the presence of high levels of noise, the conductivities can be obtained to a reasonably high level of accuracy. In particular, of the six conductivity values required, it has been shown that three of these can be retrieved to an accuracy of less than half the added noise in the system.

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