The Effect of Simplifying Assumptions in the Bidomain
Model of Cardiac Tissue: Application to ST-Segment
Shifts During Partial Ischaemia

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April 7, 2005

Abstract

In this study various electrical conductivity approximations used in bidomain models of cardiac tissue are considered. Comparisons are based on epicardial surface potential distributions arising from regions of subendocardial ischaemia situated within the cardiac tissue. Approximations studied are a single conductivity bidomain model, an isotropic bidomain model and equal and reciprocal anisotropy ratios both with and without fibre rotation.

It is demonstrated both analytically and numerically that the approximations involving a single conductivity bidomain, an isotropic bidomain or equal anisotropy ratios (ignoring fibre rotation) results in identical epicardial potential distributions for all degrees of subendocardial ischaemia. This result is contrary to experimental observations. It is further shown that by assuming reciprocal anisotropy ratios, epicardial potential distributions vary with the degree of subendocardial ischaemia. However, it is concluded that unequal anisotropy ratios must be used to obtain the true character of experimental observations.

Keywords: Bidomain Model, Simplifying Assumptions, ST Depression, Subendocardial Ischaemia.

1 Introduction

The bidomain model for the representation of cardiac tissue has been a popular method for studying electric currents for many years [1, 2, 3]. The model assumes that the intracellular and extracellular spaces are represented by spatially coexisting domains, with differing conductivities in each domain. It is also well recognised that cardiac tissue consists of layers of fibres of cardiac cells [4, 5, 6]. Within this structure it is assumed that electric current can flow through the fibres as well as through the extracellular space outside the cells. In addition it is assumed that the conductivities in the two orthogonal directions perpendicular to the fibres are the same but different from the conductivity along the fibre direction. Traditionally, this gives rise to four conductivity parameters: longitudinal and transverse, in both the intracellular and extracellular spaces. These conductivity values have been measured experimentally [7, 8, 9] as well as analysed in a non-dimensional fashion [10]. Another aspect of the traditional implementation of the bidomain model is that it allows for the observed fibre rotation from the epicardium to the endocardium [6].

The bidomain model has been used in many modelling situations in cardiac tissue. For example, it is used in the study of electrical propagation along single fibres [11], through bundles of cardiac fibres [11, 12, 13, 14], through thin layers of cardiac cells [15] and even through the whole heart [16], as well as in defibrillation studies [17] and cardiac stimulation studies [18, 19]. It is also included in the forward and inverse problems of electrocardiology [20] and recently in studies of ST segment shift in subendocardial ischaemia [21, 22, 23].

It is often the case that simplifying assumptions regarding the conductivities are made to facilitate the straightforward mathematical solution of the bidomain model equations. The most common assumption is that of equal “directional” anisotropy ratios, where it is assumed that the ratio of intracellular to extracellular conductivities is the same in both the longitudinal

and transverse directions [17]. Other approximations used are: reciprocal anisotropy ratios ignoring the fibre rotation (that is parallel fibres) [24]; equating the longitudinal and transverse conductivities in each domain (giving an isotropic bidomain) [25] and finally, assuming all conductivities are equal [26].

Potential distributions have also been recorded experimentally during the ST segment with partial thickness ischaemia [27, 25]. These distributions are typically complex and show changing patterns with increasing degrees of subendocardial ischaemia, large potential gradients near the ischaemic boundary and mixtures of positive and negative potentials (ST elevation and ST depression). It would be reasonable to expect models attempting to represent this phenomenon to at least qualitatively mimic these experimental observations.

This paper will present a study on the effects of the above simplifying assumptions, with particular reference to the problem of ST segment shift in subendocardial ischaemia. Here, a slab geometry [21] simplification is made to render the mathematics more tractable. All results presented here can be generalised to a cylindrical model of the left ventricle [28], although the algebra involved is somewhat more tedious.

2 Model Description

The bidomain model for cardiac tissue can be written via a partial differential equation for the extracellular potential, ϕ_e , as

$$\nabla \cdot (\mathbf{M}_i + \mathbf{M}_e) \nabla \phi_e = -\nabla \cdot \mathbf{M}_i \nabla \phi_m \quad (1)$$

where $\phi_m = \phi_i - \phi_e$ is the transmembrane potential and ϕ_i the intracellular potential [2, 3, 21].

The conductivity tensors, $\mathbf{M}_e$ and $\mathbf{M}_i$, reflect the anisotropy of the cardiac tissue and will be described below. Finally, the cardiac tissue is in contact with a region of blood, which is source

free, hence the electric potential in the blood, ϕ_b , is governed by Laplace's equation

$$\nabla^2 \phi_b = 0. \quad (2)$$

The tissue is modelled as a three dimensional slab which is infinite in the x and y directions with the epicardium at $z = 0$ and the endocardium at $z = 1$ with the endocardium in contact with an infinite blood mass.

Cardiac tissue is an electrically anisotropic structure, consisting of layers of parallel strands of cells, where it is much easier for current to flow along the fibres than across them. Therefore, four conductivity values are required to fully describe the conductivity in the intracellular and extracellular spaces: $\sigma_l^i, \sigma_t^i, \sigma_l^e, \sigma_t^e$, where the superscripts i and e refer to intracellular and extracellular domains, respectively, and the subscripts l and t refer to longitudinal and transverse directions, respectively. Here, the longitudinal direction is oriented along the direction of the fibres and transverse means across the fibres, perpendicular to the longitudinal direction.

The tensors $\mathbf{M}_e$ and $\mathbf{M}_i$ reflect the anisotropic conductivity, as well as the fibre rotation within the cardiac tissue. Explicitly, the conductivity tensors can be written as

$$\mathbf{M}_n = \begin{pmatrix} (\sigma_l^n - \sigma_t^n)c^2 + \sigma_t^n & (\sigma_l^n - \sigma_t^n)cs & 0 \\ (\sigma_l^n - \sigma_t^n)cs & (\sigma_l^n - \sigma_t^n)s^2 + \sigma_t^n & 0 \\ 0 & 0 & \sigma_t^n \end{pmatrix} \quad (3)$$

where $n = i$ or e (for intracellular or extracellular), $c = \cos g(d)$ and $s = \sin g(d)$. Fibre rotation within the cardiac tissue is expressed via the function $g(d)$, where d is the distance through the tissue. Assuming that the fibre direction varies linearly across the heart wall, then the direction of the fibres at a depth d in the ventricular muscle ($d_1 \leq d \leq d_2$) is given by

$$g(d) = \psi_0 + \psi \left(\frac{d_2 - d}{d_2 - d_1} \right) \quad (4)$$

where ψ is the total rotation of the fibre direction from epicardium to endocardium and ψ_0 is the angle between the epicardial fibres and the longitudinal axis of the model. When fibre

rotation is included in the model, the angle of rotation, ψ , is set at 120° . This choice is made based on the fact that in the left ventricle, rotations in fibre direction have been reported in the range of $103 \pm 21^\circ$ [4] up to 180° [5] and to be consistent with previous studies [21, 22, 28].

In terms of this model, the conductivity tensor (3) describes the components of the conductivities acting in the principal coordinate directions, the variable d in equation (4) equates to z and so $d_1 = 0$ and $d_2 = 1$. The region of subendocardial ischaemia in this model is represented by a block region attached to the endocardium, centred on the z axis and extending for a finite distance in the x and y -directions, but not meeting the epicardium in the z -direction. Hence, the ischaemic region can be described as

$$I_s = \{(x, y, z) | -a_x \leq x \leq a_x, -a_y \leq y \leq a_y, a_z \leq z \leq 1\} \quad (5)$$

(see Figure 1). A full description of the model can be found in [21].

To specify an analytic representation for the ischaemic region, the product representation for the transmembrane potential distribution

$$\phi_m(x, y, z) = \Delta\phi_p \Psi(x)\Psi(y)\Psi(1 - z), \quad (6)$$

suggested by Tung [2] is employed, where $\Delta\phi_p$ is the difference in plateau potentials between normal and ischaemic tissue. In any particular direction, t , the shape function, $\Psi(t)$, is defined by

$$\Psi(t) = \begin{cases} \frac{1 - e^{-a_t/\lambda_t} \cosh t/\lambda_t}{1 - e^{-a_t/\lambda_t}} & |t| \leq a_t \\ \frac{e^{-|t|/\lambda_t} \sinh a_t/\lambda_t}{1 - e^{-a_t/\lambda_t}} & |t| > a_t \end{cases} \quad (7)$$

where t is x , y or z . The parameters λ_t , ($t = x, y, z$) govern the width of the ischaemic boundary and have been discussed previously [21]. Note that in equation (7), the argument of the shape function in the z -direction is $1 - z$, to create the ischaemic region near the endocardium ($z = 1$).

To complete the specification of the model and to ensure a unique solution, a set of boundary conditions is required. In this slab model [21], both the cardiac tissue and the blood are

considered infinite in the x and y cartesian directions, hence it is assumed that ϕ_e and ϕ_b tend to zero as $x \rightarrow \pm\infty$ and $y \rightarrow \pm\infty$. As mentioned above, the cardiac tissue is assumed to have unit thickness in the z -direction, with the insulated epicardium at $z=0$ and the endocardium at $z=1$. The tissue is in contact with an infinite blood mass in the positive z -direction, giving rise to the condition that ϕ_b tends to zero as $z \rightarrow \infty$. At the interface between the tissue and the blood, continuity of potential and current is assumed, giving the conditions

$$\text{at } z = 1 : \phi_e = \phi_b \quad \text{and} \quad \sigma_t^e \frac{\partial \phi_e}{\partial z} = \sigma_b \frac{\partial \phi_b}{\partial z} \quad (8)$$

where σ_b is the conductivity of blood.

The form of the transmembrane potential distribution used in this model, equation (6), does not fit exactly with the above boundary conditions, but can be shown to be a good approximation. From [29], the assumption of a constant transmembrane potential distribution near the boundary is acceptable when the width of the tissue region (in this case 1 cm) is much larger than the length constant in the z direction. Based on the assumption that the cells have a radius of approximately $10\mu\text{m}$, with membrane resistance times unit area of $0.91 \Omega\text{m}^2$ and a volume fraction of 0.7 [29] then the length constants corresponding to the conductivities used here are less than 0.5mm. The width of the cardiac tissue (1 cm) is therefore much larger than the length constant and so the approximation used here is reasonable. Krassowska and Neu [30] have argued that $\frac{\partial \phi_i}{\partial z} = 0$ at the boundary, hence it can be concluded that the constant transmembrane potential approximation satisfies the boundary condition (8).

3 Solutions of the governing equations

In order to solve the governing equation (1) for the slab geometry, a technique based on two dimensional Fourier transforms has been previously proposed [21]. Define

$$\Phi_e(k, l, z) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \phi_e(x, y, z) e^{-2\pi i k x} e^{-2\pi i l y} dx dy \quad (9)$$

and

$$\Phi_m(k, l, z) = \int_{-\infty}^{\infty} \int_{-\infty}^{\infty} \phi_m(x, y, z) e^{-2\pi i k x} e^{-2\pi i l y} dx dy \quad (10)$$

In what follows, the notation $\Phi_e(z)$ will be taken to mean $\Phi_e(k, l, z)$ as defined above, with the same notation applying to Φ_m .

Applying these transformations to the governing differential equation (1) yields the following ordinary differential equation in z

$$(M_i^{33} + M_e^{33}) \frac{d^2 \Phi_e}{dz^2} - h(z) \Phi_e = p(z) \Phi_m - M_i^{33} \frac{d^2 \Phi_m}{dz^2} \quad (11)$$

where

$$h(z) = 4\pi^2 k^2 (M_i^{11} + M_e^{11}) + 8\pi^2 kl (M_i^{12} + M_e^{12}) + 4\pi^2 l^2 (M_i^{22} + M_e^{22}) \quad (12)$$

and

$$p(z) = 4\pi^2 k^2 M_i^{11} + 8\pi^2 kl M_i^{12} + 4\pi^2 l^2 M_i^{22} \quad (13)$$

and the M_n^{mj} ($m, j = 1, 2, 3$) represent the elements of the conductivity tensor matrices $\mathbf{M}_n$ ($n = i, e$). It should be remembered that M_n^{11} , M_n^{12} and M_n^{22} ($n = i, e$) are functions of z , through the fibre rotation, yet M_n^{33} ($n = i, e$) are constant.

Note from the definition of $\Psi(1 - z)$, equation (7), that $\Phi_m(k, l, z)$ has the following properties:

$$\Phi_m(k, l, 0) = 0 \quad \Phi_m(k, l, 1) = \Delta \phi_p \quad (14)$$

$$\frac{\partial \Phi_m}{\partial z}(k, l, 0) = 0 \quad \frac{\partial \Phi_m}{\partial z}(k, l, 1) = 0 \quad (15)$$

These properties ensure that the ischaemic border is contained totally within the ventricular muscle. When the ischaemia approaches full thickness and the region of ischaemia breaks through onto the epicardium, the properties described above at $z = 0$ are no longer valid.

4 Simplifying Assumptions

In this section, solutions of equation (11) will be presented for various simplifying assumptions on the conductivity model. These simplifications will, in effect, simplify the expressions (12) and (13), for $h(z)$ and $p(z)$, respectively, and often reduce the governing equation to a form which can be solved using analytic techniques.

4.1 Single Conductivity Assumption

The most significant simplifying assumption is that the cardiac tissue can be electrically described by a single conductivity; that is, $\sigma_t^i = \sigma_t^e = \sigma_l^i = \sigma_l^e = \sigma$, say. In this case, the conductivity tensors are just constant and the fibre rotation disappears. Hence, in the differential equation for the two-dimensional Fourier transform of the extracellular potential (11), the coefficient functions are given by

$$h(z) = 4\pi^2 [2\sigma(k^2 + l^2)] = 2\sigma\alpha^2 \quad (16)$$

and

$$p(z) = 4\pi^2\sigma(k^2 + l^2) = \sigma\alpha^2 \quad (17)$$

where $\alpha^2 = 4\pi^2(k^2 + l^2)$. The differential equation (11) then becomes

$$2\sigma \frac{d^2\Phi_e}{dz^2} - 2\alpha^2\sigma\Phi_e = \sigma\alpha^2\Phi_m - \sigma \frac{d^2\Phi_m}{dz^2} \quad (18)$$

or

$$\frac{d^2}{dz^2} \left(\Phi_e + \frac{\Phi_m}{2} \right) - \alpha^2 \left(\Phi_e + \frac{\Phi_m}{2} \right) = 0 \quad (19)$$

The solution of this differential equation is then

$$\Phi_e = Ae^{\alpha z} + Be^{-\alpha z} - \Phi_m(z)/2 \quad (20)$$

By applying the boundary conditions at $z = 0$ and the continuity conditions at $z = 1$, it can be shown that

$$\begin{aligned} \Phi_e(z) = & \frac{\frac{\Phi'_m(0)}{2\alpha}e^{-\alpha}\left(1 - \frac{\sigma}{\sigma_b}\right) + \frac{\Phi_m(1)}{2} + \frac{\sigma}{\sigma_b}\frac{\Phi'_m(1)}{2\alpha}}{\left(1 + \frac{\sigma}{\sigma_b}\right)e^{\alpha} + \left(1 - \frac{\sigma}{\sigma_b}\right)e^{-\alpha}}e^{\alpha z} \\ & + \frac{\frac{\Phi_m(1)}{2} + \frac{\sigma}{\sigma_b}\frac{\Phi'_m(1)}{2\alpha} - \frac{\Phi'_m(0)}{2\alpha}e^{\alpha}\left(1 + \frac{\sigma}{\sigma_b}\right)}{\left(1 + \frac{\sigma}{\sigma_b}\right)e^{\alpha} + \left(1 - \frac{\sigma}{\sigma_b}\right)e^{-\alpha}}e^{-\alpha z} - \frac{\Phi_m(z)}{2} \end{aligned} \quad (21)$$

where $\Phi_m(1) = \Delta\phi_p$. This represents the two-dimensional Fourier Transform of the extracellular potential distribution as a function of z . Application of the inverse Fourier Transform would give the extracellular potential distribution in an $x - y$ plane, at any depth z , in the cardiac tissue.

Of particular interest is the potential distribution on the epicardium (ie. at $z=0$):

$$\Phi_e(0) = \frac{\Phi_m(1) + \frac{\sigma}{\sigma_b}\frac{\Phi'_m(1)}{\alpha} - \frac{\Phi'_m(0)}{2\alpha}\left[\left(1 + \frac{\sigma}{\sigma_b}\right)e^{\alpha} - \left(1 - \frac{\sigma}{\sigma_b}\right)e^{-\alpha}\right]}{\left(1 + \frac{\sigma}{\sigma_b}\right)e^{\alpha} + \left(1 - \frac{\sigma}{\sigma_b}\right)e^{-\alpha}} - \frac{\Phi_m(0)}{2} \quad (22)$$

The most important observation to be made at this point is that the resulting epicardial potential distribution does not depend on the position of the ischaemic border in the z -direction. In fact, the ischaemic border does not even have to be represented by a sigmoidal type function as described previously [2, 21]. The only necessary condition on the functional representation of the ischaemic region is that related to the values of the transmembrane potential and its derivative at the epicardium and the endocardium.

Given the functional form for the shape of the ischaemic region studied here, equation (7), and including the boundary values, equations (14) and (15), the equation for $\Phi_e(0)$ becomes

$$\Phi_e(0) = \frac{\Phi_m(1)}{\left(1 + \frac{\sigma}{\sigma_b}\right)e^{\alpha} + \left(1 - \frac{\sigma}{\sigma_b}\right)e^{-\alpha}} \quad (23)$$

When the subendocardial ischaemia approaches full thickness, only the derivative of the transmembrane potential on the endocardium will be zero and hence the Fourier Transform of the extracellular potential distribution on the epicardium is given by

$$\Phi_e(0) = \frac{\Phi_m(1) - \frac{\Phi'_m(0)}{2\alpha} \left[\left(1 + \frac{\sigma}{\sigma_b}\right) e^\alpha - \left(1 - \frac{\sigma}{\sigma_b}\right) e^{-\alpha} \right]}{\left(1 + \frac{\sigma}{\sigma_b}\right) e^\alpha + \left(1 - \frac{\sigma}{\sigma_b}\right) e^{-\alpha}} - \frac{\Phi_m(0)}{2} \quad (24)$$

From this it can be concluded that under the assumption of cardiac tissue having a single conductivity, the degree of subendocardial ischaemia does not affect the epicardial potential distribution until the ischaemic border actually reaches the epicardium. Although equation (24) describes the transition from partial thickness ischaemia to full thickness ischaemia, it is not yet clear how $\Phi_m(0)$ and $\Phi'_m(0)$ should be defined in this situation.

4.2 Isotropic Bidomain Approximation

Another approximation is that of the “isotropic bidomain” [25], where the transverse and longitudinal conductivities are defined to be the same in both the intracellular and extracellular spaces. That is, $\sigma_t^i = \sigma_l^i = \sigma^i$ and $\sigma_t^e = \sigma_l^e = \sigma^e$ which again implicitly removes the fibre rotation. In this case,

$$h(z) = 4\pi^2(k^2 + l^2)(\sigma^i + \sigma^e) = \alpha^2(\sigma^i + \sigma^e) \quad (25)$$

and

$$p(z) = 4\pi^2\sigma^i(k^2 + l^2) = \alpha^2\sigma^i \quad (26)$$

Often $\sigma^i + \sigma^e$ is called the bulk conductivity of the myocardium [25]. With these definitions the differential equation (11) becomes

$$(\sigma^i + \sigma^e) \frac{d^2\Phi_e}{dz^2} - \alpha^2(\sigma^i + \sigma^e)\Phi_e = \sigma^i\alpha^2\Phi_m - \sigma^i \frac{d^2\Phi_m}{dz^2} \quad (27)$$

or

$$\frac{d^2}{dz^2} \left(\Phi_e + \frac{\sigma^i}{\sigma^i + \sigma^e} \Phi_m \right) - \alpha^2 \left(\Phi_e + \frac{\sigma^i}{\sigma^i + \sigma^e} \Phi_m \right) = 0 \quad (28)$$

Following the same solution procedure as above, it can be shown that the Fourier transform of the epicardial potential distribution is given by

$$\Phi_e(0) = \frac{2 \frac{\sigma_i}{\sigma_i + \sigma_e} \Phi_m(1)}{\left(1 + \frac{\sigma_e}{\sigma_b}\right) e^\alpha + \left(1 - \frac{\sigma_e}{\sigma_b}\right) e^{-\alpha}} \quad (29)$$

This again shows that the epicardial potential distribution does not depend on the degree of subendocardial ischaemia. As with the previous approximation, the epicardial potential distribution does not change until the ischaemic border touches the epicardium.

4.3 Equal Anisotropy Ratio Approximation

Perhaps the most popular approximation in the use of the bidomain model is that of equal directional anisotropy ratios [17], where it is assumed that

$$\frac{\sigma_l^e}{\sigma_l^i} = \frac{\sigma_t^e}{\sigma_t^i} = q \quad (30)$$

Unlike the previous two approximations, here the fibre rotation is not implicitly removed. Therefore, two separate cases must be considered, one with fibre rotation ignored and one with fibre rotation included.

Firstly, if fibre rotation is ignored, the coefficient functions in the differential equation (11) become

$$h(z) = 4\pi^2(k^2\sigma_l^i + l^2\sigma_t^i)(1 + q) = \beta^2(1 + q) \quad (31)$$

and

$$p(z) = 4\pi^2(k^2\sigma_l^i + l^2\sigma_t^i) = \beta^2 \quad (32)$$

where $\beta^2 = 4\pi^2(k^2\sigma_l^i + l^2\sigma_t^i)$. Therefore, the differential equation (11) becomes

$$(1 + q)\sigma_t^i \frac{d^2\Phi_e}{dz^2} - (1 + q)\beta^2\Phi_e = \beta^2\Phi_m - \sigma_t^i \frac{d^2\Phi_m}{dz^2} \quad (33)$$

or

$$\frac{d^2}{dz^2} \left(\Phi_e + \frac{1}{1 + q} \Phi_m \right) - \frac{\beta^2}{\sigma_t^i} \left(\Phi_e + \frac{1}{1 + q} \Phi_m \right) = 0 \quad (34)$$

In a similar fashion to that used above, the solution to this differential equation at $z = 0$ is given by

$$\Phi_e(0) = \frac{2\frac{1}{1+q}\Phi_m(1)}{\left(1 + \frac{\sigma_t^e}{\sigma_b^e}\right)e^\gamma + \left(1 - \frac{\sigma_t^e}{\sigma_b^e}\right)e^{-\gamma}} \quad (35)$$

where $\gamma^2 = \frac{\beta^2}{\sigma_t^i}$. Hence, for the approximation of equal anisotropy, and ignoring the fibre rotation, the epicardial potential distribution does not depend on the degree of subendocardial ischaemia, except when the ischaemic border touches the epicardium.

Finally, if fibre rotation is included with the assumption of equal anisotropy ratios, it can be shown that the coefficient functions in the differential equation (11) satisfy

$$h(z) = (1 + q)p(z) \quad (36)$$

where the elements in the conductivity tensors satisfy

$$M_i^{mj} + M_e^{mj} = (1 + q)M_i^{mj} \quad (37)$$

for all $m, j = 1, 2, 3$. The governing equation (1) then becomes

$$(1 + q)M_i^{33}\frac{d^2\Phi_e}{dz^2} - (1 + q)p(z)\Phi_e = p(z)\Phi_m - M_i^{33}\frac{d^2\Phi_m}{dz^2} \quad (38)$$

or

$$M_i^{33}\frac{d^2\Phi}{dz^2} - p(z)\Phi = 0 \quad (39)$$

where $\Phi = \Phi_e + \frac{1}{(1+q)}\Phi_m$. In this case, it can also be shown that

$$p(z) = 4\pi^2 (\sigma_l^i - \sigma_t^i) [k \cos g(z) + l \sin g(z)]^2 + 4\pi^2(k^2 + l^2)\sigma_t^i \quad (40)$$

Here, the solution of the governing differential equation (39) is not so straightforward. The coefficient factor $p(z)$ reflects the position of the ischaemic boundary in the z -direction and hence, the epicardial potential distribution (that is, the potential at $z=0$) will depend on this position. This is the first situation where an approximation leads to the this conclusion.

4.4 Reciprocal Anisotropy Ratio Approximation

Another approximation used in the bidomain modelling of cardiac tissue is that of reciprocal anisotropy ratios [24], where it is assumed that

$$\frac{\sigma_l^e}{\sigma_l^i} = \frac{\sigma_t^i}{\sigma_t^e} = q_r \quad (41)$$

As in the previous approximation, fibre rotation is not implicitly removed and so two separate cases must be considered.

Firstly, if fibre rotation is ignored, the coefficient functions in the differential equation (11) become

$$h(z) = 4\pi^2(k^2\sigma_l^i + l^2\sigma_t^e)(1 + q_r) = \delta^2(1 + q_r) \quad (42)$$

where $\delta^2 = 4\pi^2(k^2\sigma_l^i + l^2\sigma_t^e)$. However,

$$p(z) = 4\pi^2(k^2\sigma_l^i + l^2q_r\sigma_t^e), \quad (43)$$

depends on q_r , but not on z . The first thing to notice here is that this approximation leads to the first instance where $h(z)$ is not a simple multiple of $p(z)$. Therefore the differential equation (11) becomes

$$(1 + q_r)\sigma_t^e \frac{d^2\Phi_e}{dz^2} - (1 + q_r)\delta^2\Phi_e = p(z)\Phi_m - q_r\sigma_t^e \frac{d^2\Phi_m}{dz^2} \quad (44)$$

Proceeding as in all previous cases this differential equation can be rewritten as

$$\frac{d^2}{dz^2} \left(\Phi_e + \frac{q_r}{1 + q_r} \Phi_m \right) - \frac{\delta^2}{\sigma_t^e} \left(\Phi_e + \frac{q_r}{1 + q_r} \Phi_m \right) = \left(\frac{p(z) - \delta^2 q_r}{\sigma_t^e (1 + q_r)} \right) \Phi_m \quad (45)$$

A significant difference between this differential equation and similar equations from previous approximations, equations (19), (28) and (34), is that equation (45) is an inhomogeneous differential equation, instead of being homogeneous. The solution of equation (45) can be obtained using a Laplace transform approach, assuming $\Phi_e(0) = A$, for some unknown constant A , to

give

$$\begin{aligned}\Phi_e(z) = & \left[A + \frac{q_r}{1+q_r} \Phi_m(0) \right] \cosh \epsilon z + \frac{q_r}{(1+q_r)\epsilon} \Phi'_m(0) \sinh \epsilon z \\ & + \frac{p(z) - \delta^2 q_r}{\sigma_t^e (1+q_r)} \int_0^z \Phi_m(t) \sinh \epsilon(z-t) dt - \frac{q_r}{1+q_r} \Phi_m(z)\end{aligned}\quad (46)$$

where $\epsilon^2 = \frac{\delta^2}{\sigma_t^e}$. The unknown coefficient A is obtained by matching the boundary conditions at $z = 1$ to give

$$\begin{aligned}A = \Phi_e(0) = & \frac{\alpha \sigma_b \Phi_m(1) + \sigma_t^e \Phi'_m(1)}{\sigma_t^e \epsilon \sinh \epsilon + \alpha \sigma_b \cosh \epsilon} \frac{q_r}{1+q_r} - \frac{q_r}{1+q_r} \Phi_m(0) - \frac{\sigma_t^e \cosh \epsilon + \frac{\alpha \sigma_b}{\epsilon} \sinh \epsilon}{\sigma_t^e \epsilon \sinh \epsilon + \alpha \sigma_b \cosh \epsilon} \frac{q_r}{1+q_r} \Phi'_m(0) \\ & - \frac{p(z) - \delta^2 q_r}{\sigma_t^e (1+q_r) (\sigma_t^e \epsilon \sinh \epsilon + \alpha \sigma_b \cosh \epsilon)} \times \\ & \left\{ \sigma_t^e \int_0^1 \Phi_m(t) \cosh \epsilon(1-t) dt + \frac{\alpha \sigma_b}{\epsilon} \int_0^1 \Phi_m(t) \sinh \epsilon(1-t) dt \right\}\end{aligned}\quad (47)$$

Based on the assumptions concerning the shape of the transmembrane potential distribution, equation (47) further reduces to

$$\begin{aligned}\Phi_e(0) = & \frac{\alpha \sigma_b \Phi_m(1)}{\sigma_t^e \epsilon \sinh \epsilon + \alpha \sigma_b \cosh \epsilon} \frac{q_r}{1+q_r} - \frac{p(z) - \delta^2 q_r}{\sigma_t^e (1+q_r) (\sigma_t^e \epsilon \sinh \epsilon + \alpha \sigma_b \cosh \epsilon)} \times \\ & \left\{ \sigma_t^e \int_0^1 \Phi_m(t) \cosh \epsilon(1-t) dt + \frac{\alpha \sigma_b}{\epsilon} \int_0^1 \Phi_m(t) \sinh \epsilon(1-t) dt \right\}\end{aligned}\quad (48)$$

An analysis of equation (48) shows that the expression for $\Phi_e(0)$ depends (through the integrals) on the complete form of $\Phi_m(z)$, not just the values of $\Phi_m(z)$ and $\Phi'_m(z)$ at $z = 0$ and $z = 1$. In other words, the epicardial potential distribution does depend on the position of the ischaemic boundary, a_z . Hence, changing the degree of subendocardial ischaemia will change the epicardial potential distribution, as will be discussed in the next section.

It can be shown that in equation (45)

$$p(z) - \delta^2 q_r = 4\pi^2 k^2 \sigma_t^e (1 - q_r) \quad (49)$$

Hence, when the $q_r = 1$, the differential equation (45) is again homogeneous and the position of the ischaemic boundary does not affect the epicardial potential distribution.

For the reciprocal anisotropy ratio approximation, including fibre rotation, the coefficient functions in equation (11) become

$$h(z) = 4\pi^2(1 + q_r) [(\sigma_l^i - \sigma_t^e)(k \cos g(z) + l \sin g(z))^2 + (k^2 + l^2)\sigma_t^e] \quad (50)$$

and

$$p(z) = 4\pi^2 [(\sigma_l^i - \sigma_t^e)(k \cos g(z) + l \sin g(z))^2 + q_r(k^2 + l^2)\sigma_t^e] \quad (51)$$

Here, there is no significant simplification to be obtained in terms of a solution of equation (11). Again, the coefficient function $p(z)$ is not a multiple of $h(z)$, with both reflecting the position of the ischaemic boundary and so the epicardial potential distribution will depend on the position of the ischaemic boundary.

5 Results

Here epicardial potential distributions will be presented based on the various simplifications outlined in the previous section. In all cases the epicardial distributions will be presented for a $16\text{cm} \times 16\text{cm}$ slab of cardiac tissue, 1 cm thick, with a $4\text{cm} \times 4\text{cm}$ region of subendocardial ischaemia, of varying severity, centred on the origin. The conductivity data used is based on that presented by Clerc [7] with the conductivity of blood set at 0.0067 S/cm. In all cases the difference in plateau potentials between normal and ischaemic tissue, $\Delta\phi_p$, is set at -30mV. The simulations presented all assume a sharp transition from ischaemic to normal tissue in the three spatial directions with $\lambda_x = \lambda_y = \lambda_z = 0.01$.

5.1 Single Conductivity Assumption

Figure 2 shows the epicardial potential distribution obtained from equation (22) with 50% subendocardial ischaemia and the conductivity, σ , set at 0.00174 S/cm. The figure shows

a set of concentric contours which are more or less square with rounded corners, something that would be expected given the square region of subendocardial ischaemia. Although not presented here, the epicardial distribution shown is identical to distributions obtained at any other degree of subendocardial ischaemia, provided the ischaemic region does not extend to the endocardium. The figure indicates a region of ST depression centred above the region of subendocardial ischaemia and that this does not change as the degree of ischaemia increases.

5.2 Isotropic Bidomain Approximation

Figure 3 shows the epicardial distribution obtained from equation (29) again with 50% subendocardial ischaemia. In this case $\sigma^i = 0.00174$ S/cm and $\sigma^e = 0.00236$ S/cm. The figure is similar to Figure 2, in that it shows a similar set of concentric contours, centred above the region of ischaemia. However, here the potential well is deeper than in the isotropic case, by a factor of about 2. Again, the resulting epicardial potential distribution does not change with an increasing degree of subendocardial ischaemia.

5.3 Equal Anisotropy Ratio Approximation

Figure 4 shows the epicardial potential distribution obtained from equation (35) for three different values of q , all with 50% subendocardial ischaemia. Recall that fibre rotation was ignored in obtaining equation (35). The four conductivity values used were based on choosing $\sigma_l^i = 0.00174$ S/cm and $\sigma_t^i = 0.000193$ S/cm. Again, as suggested by equation (35), there is no change in the epicardial potential distribution as the degree of subendocardial ischaemia increases. The potential distributions shown are obtained with q taking on the values of $\frac{1}{2}$, 1 and 2, respectively. It can be seen that as q increases the depth of the potential well decreases. Hence, increasing the extracellular conductivity, while keeping the intracellular conductivity constant decreases the magnitude of the epicardial potential distribution induced by the subendocardial

ischaemia.

Figure 5 shows the epicardial potential distribution obtained from equation (39), again for three different values of q and 50% subendocardial ischaemia, but here a fibre rotation from the epicardium to the endocardium of 120° is included. Interestingly, the magnitudes obtained in these potential distributions are similar to those obtained in Figure 4 with no fibre rotation.

Further, Figure 6 shows the epicardial potential distribution obtained with $q = 1$ and at increasing degrees of subendocardial ischaemia set at 10%, 40%, 70% and 90%. Note that although the range of the potentials is similar in all cases, it is possible to discern differences in the epicardial potential distribution. For example, in panel (a) (10% ischaemia) the potential distribution is stretched along the line $y = x/4$ and in panel (d) (90% ischaemia) the distribution is stretched along the y -axis. Between these two extremes, the eccentricity of the elliptical potential contours approaches 1 just beyond 50% ischaemia and then decreases again as the contours stretch along the y -axis with increasing ischaemia. However, given that the magnitudes of the potential distributions are similar at all degrees of ischaemia, both with and without fibre rotation, it would appear that the degree of subendocardial ischaemia affects only the orientation of the epicardial potential contours and not the magnitude of the epicardial potentials when fibre rotation is included.

5.4 Reciprocal Anisotropy Ratio Approximation

Figure 7 shows the epicardial potential distribution obtained from equation (47) with $q_r = \frac{1}{2}$ at 10%, 40%, 70% and 90% ischaemia and no fibre rotation. The four conductivity values used were based on choosing $\sigma_t^i = 0.00174$ S/cm and $\sigma_t^e = 0.00236$ S/cm. As suggested by the theory in the previous section, the epicardial potential distributions vary with the degree of subendocardial ischaemia, with the differences becoming more apparent at higher degrees of subendocardial ischaemia. At 10% ischaemia, panel (a), there is a single potential well, as in

the isotropic case, and this is similar to the situation at 40% ischaemia, panel (b). However, by 70% ischaemia, panel (c), there are three potential wells and at 90% ischaemia, panel (d), high potential gradients are observed above the x -direction borders of the ischaemic region.

Similar comments apply when $q_r = 2$, but in this case there is only one potential well at higher degrees of ischaemia. High potential gradients still exist above the x -direction borders as well as moderately high potential gradients above the y -direction borders.

When fibre rotation is included, as in Figure 8 (again with $q_r = \frac{1}{2}$), similar comments may be made to those regarding Figure 7. However, due to the fibre rotation, the patterns are slightly skewed and the high potential gradients at 90% ischaemia, panel (d), are above the ischaemic borders in the y -direction.

5.5 No Approximation

Finally, Figure 9 shows the epicardial potential distribution obtained when equation (11) is solved without any approximations made. The four panels in the figure correspond to 10%, 40%, 70% and 90% subendocardial ischaemia with 120° fibre rotation. For the simulation shown the conductivities used were those obtained from Clerc [7]: $\sigma_l^i = 0.00174$ S/cm, $\sigma_t^i = 0.000193$ S/cm, $\sigma_l^e = 0.00625$ S/cm and $\sigma_t^e = 0.00236$ S/cm. The figure shows that with the full anisotropic behaviour of the tissue included, the degree of subendocardial ischaemia greatly affects the epicardial potential distribution. At 10% ischaemia there is a single well of potential over the ischaemic region and this well has developed three minima at 40% ischaemia. By 70% ischaemia there is significant ST elevation over the borders of the ischaemic region and at 90% ischaemia, there is ST elevation above the region of ischaemia as well as high potential gradients along two of the boundaries of the ischaemic region.

6 Discussion and Conclusions

This paper has presented a study of the effects that simplifying assumptions for the tissue conductivity model have on the epicardial potential distribution, in the context of varying degrees of subendocardial ischaemia. It has been demonstrated analytically and verified numerically that when the tissue is approximated by a single conductivity bidomain, an isotropic bidomain or a bidomain having equal anisotropy ratios with fibre rotation ignored then the epicardial potential distribution is unaffected by the degree of subendocardial ischaemia. The analytical verification follows from the fact that the position of the ischaemic boundary in the z -direction does not explicitly appear in the solution for the Fourier transform of the epicardial potential distributions in equations (23), (29) and (35). This leads to identical epicardial potential distributions as shown in Figures 2, 3 and 4. Even when fibre rotation is included in these models (Figures 5 and 6) it appears that the fibre rotation affects only the orientation of the potential distribution without significantly affecting other aspects of it (for example, magnitude or potential gradients).

However, the above observations are contrary to published experimental data [27, 25] which show a change in epicardial potential distribution with increasing ischaemia. As mentioned in the introduction, the modelling should result in high potential gradients on the epicardial surface as well as both positive and negative potentials. It could thus be concluded that these approximations are inadequate to obtain credible results for this type of modelling.

When the approximation of reciprocal anisotropy ratios is introduced, the epicardial potential distribution does change with the degree of subendocardial ischaemia, even when fibre rotation is ignored (Figure 7). This fact is established by the presence of the position of the ischaemic border in the z -direction in the solution for the Fourier Transform of the epicardial potential distribution, equation (48). With the inclusion of fibre rotation (Figure 8), the epi-

cardial potential distribution patterns appear only to be rotated, corresponding to the degree of fibre rotation. The reciprocal anisotropy approximation does produce higher potential gradients on the epicardium than any of the previous approximations, which is a desired outcome based on experimental observations [27, 25], but it does not reflect the complexity of these experimental observations.

The three sets of experimentally derived conductivity data, which are used most often, are those of Clerc [7], Roberts *et al.* [8] and Roberts and Scher [9]. None of these data satisfactorily fit the approximations for a single conductivity bidomain, an isotropic bidomain or have equal or reciprocal anisotropy ratios (see Table 1). Perhaps the two closest are the data of Roberts *et al.* [8] (closest to the equal anisotropy approximation: $\sigma_l^e/\sigma_l^i = 0.786$ and $\sigma_t^e/\sigma_t^i = 0.5$) and that of Roberts and Scher [9] (closest to the reciprocal anisotropy approximation $\sigma_l^e/\sigma_l^i = 0.353$ and $\sigma_t^i/\sigma_t^e = 0.75$). These data, along with the analytical solutions obtained above, suggest that no approximations to the conductivity model reflect reality in electrocardiographic models.

From the above discussion it is clear that unequal anisotropy ratios must be used to achieve results which in some way explain the published experimental results. Figure 9, derived from the unequal anisotropy ratios published by Clerc [7], shows marked changes in epicardial potential distribution with increasing degree of subendocardial ischaemia, high potential gradients above the borders of the ischaemic region and regions of both positive and negative potential [23].

The results obtained above are equally valid for a previously published cylindrical model of the left ventricle [28]. Expressions for the epicardial potential distributions using this model can be obtained in a similar fashion to that described above, but the algebra involved is somewhat more tedious.

In summary, Figure 9 is in marked contrast to the previous figures shown and clearly demonstrates the problems that can arise when using approximations for the conductivity values in this type of modelling. It also raises speculation as to whether such approximations

could have affected conclusions reached in other applications of the bidomain equations.

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Table Captions

Table 1: Values of bidomain tissue conductivities from the indicated sources (in S/cm) with their corresponding anisotropy ratios and reciprocal anisotropy ratios.

Figure Captions

Figure 1: Cross-section in the $x - z$ plane of the slab model. The hatched region represents the region of subendocardial ischaemia, extending from the Endocardium ($z = 1$) to $z = a_z$ in the z direction and from $x = -a_x$ to $x = a_x$ in the x direction.

Figure 2: Epicardial potential distributions at 50% subendocardial ischaemia for single conductivity cardiac tissue with an ischaemic region of 16 cm^2 . Dotted lines indicate negative potentials. The contour interval is 2.0 mV.

Figure 3: Epicardial potential distributions at 50% subendocardial ischaemia for cardiac tissue under the isotropic bidomain assumptions. Dotted lines indicate negative potentials. The contour interval is 2.0 mV.

Figure 4: Epicardial potential distributions at 50% subendocardial ischaemia for cardiac tissue with various anisotropy ratios and fibre rotation ignored. Dotted lines indicate negative potentials. The contour interval is in each plot is 1.0 mV.

Figure 5: Epicardial potential distributions at 50% subendocardial ischaemia for cardiac tissue with various values of q and fibre rotation included. Dotted lines indicate negative potentials. The contour interval is in each plot is 1.0 mV.

Figure 6: Epicardial potential distributions at varying degrees of subendocardial ischaemia for cardiac tissue for the equal anisotropy ratio approximation with $q = 1$ and fibre rotation included. Dotted lines indicate negative potentials. The contour interval in each plot is 1.0 mV.

Figure 7: Epicardial potential distributions at varying degrees of subendocardial ischaemia for cardiac tissue for the reciprocal anisotropy ratio approximation with $q_r = \frac{1}{2}$ and fibre rotation ignored. Dotted lines indicate negative potentials. The contour interval in each plot is 1.0 mV.

Figure 8: Epicardial potential distributions at varying degrees of subendocardial ischaemia for cardiac tissue for the reciprocal anisotropy ratio approximation $q_r = \frac{1}{2}$ and fibre rotation included. Dotted lines indicate negative potentials. The contour interval in each plot is 1.0 mV.

Figure 9: Epicardial potential distributions at varying degrees of subendocardial ischaemia for anisotropic cardiac tissue with fibre rotation and an ischaemic region of 16 cm². Dotted lines indicate negative potentials and the solid lines present positive potentials. The thick solid line indicates the zero potential. The contour interval in each plot is 0.2 mV.

	Clerc [7]	Roberts <i>et al.</i> [8]	Roberts and Scher [9]
σ_l^i	0.00174	0.0028	0.0034
σ_t^i	0.000193	0.00026	0.0006
σ_l^e	0.00625	0.0022	0.0012
σ_t^e	0.00236	0.0013	0.0008
σ_l^e/σ_l^i	3.59	0.786	0.353
σ_t^e/σ_t^i	12.23	0.5	1.33
σ_t^i/σ_t^e	0.082	2.0	0.75

Table 1:

Figure 1:

Figure 2:

Figure 3:

Figure 4:

Figure 5:

Figure 6:

Figure 7:

Figure 8:

Figure 9: