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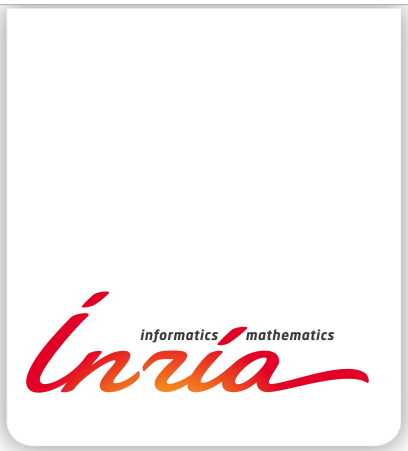

Comment calculer le potentiel extracellulaire de l'électrophysiologie en utilisant un modèle monodomaine augmenté

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Résumé : L'objectif de cet article est de présenter des méthodes efficaces permettant d'obtenir les informations pertinentes pour le calcul d'électrogrammes. Afin d'éviter le coût excessif du modèle bidomaine, on considère ici un modèle monodomaine étendu avec une équation elliptique supplémentaire qui est résolue sur l'épicarde grâce à une équation algébrique ou une formulation intégrale.

Mots-clés : Bidomaine, monodomaine, électrocardiologie

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How to compute the extracellular potential in electrocardiology from an extended monodomain model

Abstract: The objective of this paper is to introduce efficient methods to compute the relevant information required for electrograms simulations. In order to avoid the excessive cost of the bidomain model, we consider an extended monodomain model with an additional elliptic equation which is solved on the epicardium thanks to an algebraic equation or an integral formulation.

Key-words: Bidomain, monodomain, electrocardiology

1 Introduction

The bidomain and monodomain equations are very popular for simulating the electrical activity of the heart. The former models the evolution of both the intra- and extra-cellular potentials, ϕ_i and ϕ_e, while the latter models the evolution of the transmembrane voltage $V = \phi_i - \phi_e$ [5]. On the one hand, the bidomain model ensures a quasistatic balance between the intra- and extra-cellular currents. Hence, it involves solving an ill-conditioned large sparse linear system at each time-step and therefore needs large computing resources. Although it is a favorite choice when an external stimulus is applied (defibrillation), for heart-torso models (e.g. ECG simulations) and when the extracellular potential is needed (e.g. electrogram simulations). On the other hand, the monodomain equations are far simpler to solve but they do not account correctly for any of these situations. Hence they are a favorite choice when faster simulations are necessary, for instance in a clinical context or in order to solve inverse problems, although they lack many important features. Furthermore, in many situations, the monodomain solutions are accurate approximations of the bidomain ones [1, 7] and the difference between the models might even be smaller than the discretization error [3].

The objective of this work is to describe two modeling strategies that will allow fast computations of the extracellular potential in the monodomain context. Based on the transmembrane voltage given by the monodomain model, the extracellular potential ϕ_e is the solution of a quasistatic electrical balance equation. Solving this equation requires large computing resources in general. The first strategy assumes the so-called equal anisotropy ratio which leads to an explicit expression of ϕ_e. Since the values of ϕ_e are only needed on the boundary, the second strategy consists in solving an integral equation. The resulting models should provide a basis for efficient simulations of extracellular surface potential in terms of accuracy and computational cost.

2 The models

The homogenized bidomain equations form the most complete model currently available for the simulation of action potential propagation at the macroscopic level in an excitable tissue. The tissue is represented by a domain $\Omega \subset \mathbb{R}^3$ with boundary $\Sigma = \partial\Omega$. The transmembrane voltage V is the difference between the intra- and extra-cellular potentials ($V = \phi_i - \phi_e$), which are solutions to the *degenerate parabolic system of equations on ϕ_i and ϕ_e*

$$A\left(C\partial_t V + I_{ion}(V,w)\right) = \mathrm{div}(G_i \nabla \phi_i) \tag{1}$$

$$A\left(C\partial_t V + I_{ion}(V,w)\right) = -\mathrm{div}(G_e \nabla \phi_e) \tag{2}$$

coupled to the differential equations $\partial_t w + g(V,w) = 0$ in Ω and for $t > 0$ and with the boundary conditions $G_i \nabla \phi_i \cdot n_\Sigma = G_e \nabla \phi_e \cdot n_\Sigma = 0$ on Σ and for $t > 0$. The parameters A, C, G_i, G_e, I_{ion} and g are, respectively, the ratio of surface of membrane per unit volume, the membrane capacitance per unit area of surface, the intra and extra-cellular electrical conductivity tensors of the tissue, the total ionic current and the function of state of the considered ionic model. Finally, w is the state variable of the cell membrane.

It is important to note that the potentials ϕ_i and ϕ_e are defined up to a constant, while the transmembrane voltage V is defined uniquely (see [2]). *We are only interested in the extra-cellular potential ϕ_e and assume that it is normalized* by

$$\forall t > 0, \quad \int_\Omega \phi_e(x,t)dx = 0. \tag{3}$$

Equations (1) and (2) are equivalent to the *coupled elliptic/parabolic problem on V and ϕ_e*

$$A\left(C\partial_t V + I_{ion}(V,w)\right) = \operatorname{div}(G_i\nabla(V+\phi_e)) \tag{4}$$

$$\operatorname{div}((G_i+G_e)\nabla\phi_e) + \operatorname{div}(G_i\nabla V) = 0 \tag{5}$$

still with homogeneous Neumann boundary conditions. The electrostatic balance of current (5) is uniquely solved thanks to the normalization condition (3).

3 Model 1: monodomain with elliptic equation

The monodomain model is obtained by assuming the *equal anisotropy ratio* $G_i(x) = \lambda G_e(x)$, so that equation (5) reads $\operatorname{div}(G_e\nabla((1+\lambda)\phi_e + \lambda V)) = 0$ in Ω with the boundary condition $G_e\nabla((1+\lambda)\phi_e + \lambda V)\cdot n = 0$ on Σ, which solution is given by

$$\forall t > 0,\ a.e.\ x \in \Omega, \quad (1+\lambda)\phi_e(x,t) + \lambda V(x,t) = f(t). \tag{6}$$

Under this equal anisotropy ratio assumption, the diffusion operator in the evolution equation (4) reads $\operatorname{div}(G_i\nabla(V+\phi_e)) = \operatorname{div}(G\nabla V)$ with

$$G = \left(G_i^{-1} + G_e^{-1}\right)^{-1} = \frac{1}{1+\lambda}G_i = \frac{\lambda}{1+\lambda}G_e. \tag{7}$$

Note that $G_i\nabla(\phi_e+V)\cdot n = 0 \Leftrightarrow G\nabla V\cdot n = 0$ on Σ with $G_e\nabla\phi_e\cdot n = 0$. As a consequence, the monodomain evolution equation is

$$A\left(C\partial_t V + I_{ion}(V,w)\right) = \operatorname{div}(G\nabla V) \tag{8}$$

with the boundary condition $G\nabla V\cdot n = 0$ and the extracellular potential can be computed from equation (6) and the normalization condition (3)

$$\begin{aligned}\forall t > 0, \quad \phi_e(x,t) &= \frac{\lambda}{1+\lambda}\left(\frac{1}{|\Omega|}\int_\Omega V(x,t)dx - V(x,t)\right)\\ &= \frac{\lambda}{1+\lambda}\frac{1}{|\Omega|}\int_\Omega \left(V(y,t) - V(x,t)\right)dy.\end{aligned} \tag{9}$$

Let us point out that this simple formulation is original since the normalization condition is generally not taken into account this way.

4 Model 2: extended monodomain model with an integral representation

The extended monodomain, used in [4, 7], consists in assuming that the transmembrane voltage is solution to the monodomain equation (8) with the

boundary condition $G\nabla V \cdot n = 0$, but without assuming the equal anisotropy ratio (see [2]). Again, the extracellular potential ϕ_e can be directly retrieved from the knowledge of V using the balance equation (5) with the normalization condition (3). As opposed to the previous model, the solution does not express explicitly anymore.

Fortunately, the variables of interest (e.g. electrograms) only involve values of the potential ϕ_e on the boundary Σ. An additional simplification may therefore be made for computing ϕ_e only on Σ in equation (5). The following integral formulation gives a value of $\Phi = \phi_e|_\Sigma$

$$\lambda(x)\Phi(x) + \int_\Sigma \Phi(y)\partial_n\Psi(x,y)dy = \int_H \Big(\mathrm{div}(G\nabla V(y))\Big)\Psi(x,y)dy, \qquad (10)$$

where $\lambda(x) = \lim_{\varepsilon\to 0}\int_{\partial B_\varepsilon} G_e\nabla\Psi(x,y).\mathbf{n}dy$ and Ψ is the fundamental solution associated to the anisotropic Laplace operator $\mathrm{div}\,(G_e\nabla\Psi(x,y)) = \delta(x,y)$. Whenever G_e is a constant, the explicit form of Ψ is given by (see [8])

$$\Psi(x,y) = \Big((x-y)^\top G_e(x-y)\Big)^{-1/2}.$$

The equation (10) can be solved using a classical Boundary Elements Method (see [6] for instance), leading to the resolution of a way smaller linear system involving a full matrix.

Let us emphasize that the right hand side of the variational formulation (10) cannot be reformulated using a divergence theorem since the fundamental solution Ψ lacks regularity. Numerically it implies that the action potential V cannot be discretized with P1-Lagrange elements, which second derivatives vanish. In practice, P3-Hermite elements seem a good choice (gradients are then exactly computed at each vertex).

Now, the solution Φ of equation (10) is not normalized as specified in (3). The normalized solution reads $\Phi + c$ where c is a constant obtained as follows. For $\varphi \in H^2(\Omega)$, Green's formula on (5) gives

$$-\int_\Omega \phi_e\mathrm{div}((G_i+G_e)\nabla\varphi) = \int_\Omega \varphi\mathrm{div}(G_i\nabla V) - \int_\Sigma \Phi(G_i+G_e)\nabla\varphi\cdot n.$$

We choose $\varphi = \frac{1}{6}x^\top(G_i+G_e)^{-1}x$ such that $\mathrm{div}((G_i+G_e)\nabla\varphi = 1$ in Ω. As a consequence

$$c := -\int_\Omega \phi_e\mathrm{div}((G_i+G_e)\nabla\varphi) = \int_\Omega \varphi\mathrm{div}(G_i\nabla V) - \int_\Sigma \Phi(G_i+G_e)\nabla\varphi\cdot n.$$

Finally, let us point out that the hypothesis of space-independent conductivity tensor G_e is only required to get a simple analytical expression of the fundamental solution for the $\mathrm{div}\big(G_e\nabla\cdot\big)$ operator. Indeed, the inhomogeneous case, $G_e := G_e(x)$, leads to an integral expression of the fundamental solution Ψ (see [8] p 317)

$$\Psi(x,y) = w^y(x,y) + \int_\Omega w^z(x,z)\theta(z,y)\ d\mathbf{z},$$

where $w^y(x,y) = \Big((x-y)^\top G_e(y)(x-y)\Big)^{-1/2}$ and θ is a potential verifying a Fredholm equation. In general, θ is difficult to compute. Specifically, it requires

to solve an integral equation for each point of the boundary. However, these equations only depend on the geometry and their solutions can be precomputed. It is also possible to neglect θ, especially if the variation of G_e is not stiff.

The assumption that G_e is constant is therefore made to conserve the simplicity of the method. Though not as crude as the monodomain hypothesis $G_e = \lambda G_i$, its impact has to be determined.

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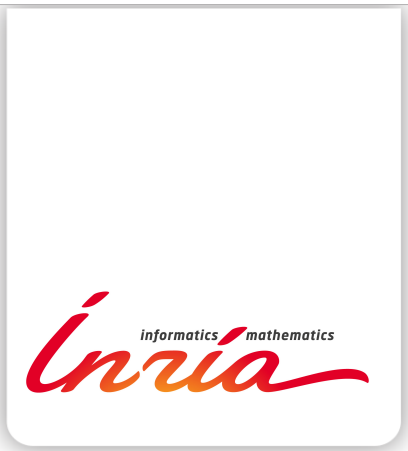

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