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An eikonal-diffusion solver and its application to the interpolation and the simulation of reentrant cardiac activations

Vincent Jacquemet [a,b,*]

[a] *Institut de Génie Biomédical & Département de Physiologie, Université de Montréal, Canada*
[b] *Hôpital du Sacré-Coeur de Montréal, Centre de Recherche, 5400 boul. Gouin Ouest, Montréal, QC H4J 1C5, Canada*

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A B S T R A C T

Electrical propagation of the cardiac impulse in the myocardium can be described by the eikonal-diffusion equation. This equation governs the field of activation times in a domain where conduction properties are specified. This approach has been applied to knowledge-based interpolation of sparse measurements of activation times and to the creation of initial conditions for detailed ionic models of cardiac propagation. This paper presents the mathematical basis, matrix formulation, and compact Matlab implementation of an iterative finite-element solver (triangular meshes) for the eikonal-diffusion equation extended to reentrant activations, which automatically identifies the period of reentry and computes the resulting isochrones. An iterative algorithm is designed to perform Laplacian interpolation of reentrant activation maps to be used as initial estimate for the eikonal-diffusion solver. The performance of the algorithm is analyzed in test-case geometries (ventricular slice and simplified atrial surface model).

1. Introduction

Atrial arrhythmias are rhythm disorders frequently encountered in clinical practice. Current therapies include pharmacological control of the ventricular rate, electrical cardioversion (defibrillation) and catheter ablation (creation of lesions in the atrial tissue using radio frequency or cryo catheter electrodes). Catheter ablation involves exploration of atrial endocardium with intracardiac electrodes recording electrical signal (electroanatomical mapping). Local activation time can usually be extracted from these intracardiac electric signals. In combination with cardiac imaging data, this procedure can provide a description of the dynamics of the arrhythmia through activation maps. Spatial resolution is, however, often limited.

To investigate the basic mechanisms of atrial arrhythmias and guide the development of diagnostic and therapeutic tools, computer models of atrial electrophysiology have been developed [1–6]. In these models, propagation of the electrical impulse in the myocardium is governed by a reaction-diffusion equation [7]. To improve the clinical relevance of model results, patient-specific information needs to be incorporated. This information can be local (cell electrophysiology, cell-to-cell coupling) or global (dynamics of the arrhythmia, pathways of reentry). Local, microscale data are natural parameters in the bottom-up approach typically used in cardiac modeling. Global, macroscale data such as activation maps are often easier to obtain but more difficult to integrate in the model.

* *Correspondence address*: Hôpital du Sacré-Coeur de Montréal, Centre de Recherche, 5400 boul. Gouin Ouest, Montréal, QC H4J 1C5, Canada. Tel.: +1 514 338 2222x2522.
E-mail address: vincent.jacquemet@umontreal.ca
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Lines et al. proposed to add a non-local forcing term to the reaction-diffusion equation to synchronize a reentrant activity with experimental or synthetic signals recorded at sparse locations during atrial flutter [8]. More recently, we developed a method for creating an initial condition for the reaction-diffusion system from a reentrant pathway [9]. This method was based on the eikonal-diffusion equation [10–12], a partial differential equation for the activation time. Activation maps computed using this approach showed good correspondence with those simulated using the reaction-diffusion system, at a much lower computational cost. In addition, the initial condition created from an activation map enabled the simulation of reentries along prescribed anatomical or functional reentrant pathways in the reaction-diffusion model [9].

In this paper, an efficient iterative solver for the eikonal-diffusion equation applied to reentrant activity is described. Numerical methods from [9] are reformulated to facilitate and optimize Matlab implementation. An alternative, more robust algorithm for the interpolation of activation times (used as initial estimate for the iterative solver) is proposed. Compact Matlab code is provided and explained. A theoretical analysis of the algorithm is presented that enables automatic computation of the period of the reentry, thus reducing the number of required input parameters. Performance and accuracy is assessed using test case problems.

2. Background

2.1. Problem statement

Activation time is the time $t_a(\mathbf{x})$ at which an electrical impulse (cardiac wave front) passes through the point $\mathbf{x}$. The field $t_a(\mathbf{x})$ forms an activation map. Stable reentry consists in single or multiple self-sustained activation waves propagating periodically in the cardiac tissue. To emphasize the periodic nature of a reentrant activity and exhibit its topological features, the scaled activation time τ is defined as

$$\tau(\mathbf{x}) = 2\pi\, t_a(\mathbf{x})/T \mod 2\pi, \tag{1}$$

where T is the period of the reentry. For the moment, T is assumed to be known. Later, methods will be presented to derive its value from conduction properties (Sections 2.3 and 4.5).

Two problems will be considered in this paper:

1. *Interpolation*: From a set of known scaled activation times $\tau(\mathbf{x}_i)$, $\mathbf{x}_i \in \Gamma$, interpolate an activation map $\tau(\mathbf{x})$ while taking into account its periodic nature. The set Γ can be a discrete set of points (interpolation from a finite number of measurements, for example catheter electrodes) or closed curves describing observed pathways of reentry.
2. *Simulation*: Reconstruct activation maps using *a priori* knowledge about wave front propagation (local curvature-dependent conduction velocity). Adjust activation maps obtained from problem 1 to satisfy hypothesized conduction properties of the tissue substrate.

Both problems will be solved using a partial differential equation based on the eikonal-diffusion equation for the field τ.

2.2. The eikonal-diffusion equation for a reentry

Derived from the monodomain propagation equations [7] using singular perturbation techniques [12], the eikonal-diffusion equation in the domain Ω (with boundary $\partial\Omega$) governs the shape of activation wave fronts [10,9,11,12]:

$$\|\mathbf{c}\nabla\tau\| = 1 + \nabla\cdot(\mathbf{D}\nabla\tau) \qquad \mathbf{x}\in\Omega, \tag{2}$$

$$\mathbf{n}\cdot\mathbf{D}\nabla\tau = 0 \qquad \mathbf{x}\in\partial\Omega. \tag{3}$$

where the tensors $\mathbf{c}$ (scaled propagation velocity in cm/rad, which means conduction velocity in cm/s $\times T/2\pi$) and $\mathbf{D}$ (scaled diffusion tensor in cm^2) are symmetric positive definite, $\|\cdot\|$ is the euclidean norm and $\mathbf{n}$ is a unit vector normal to the boundary $\partial\Omega$. In the isotropic case with $D\to 0$, it reduces to the eikonal equation $c\|\nabla\tau\| = 1$ stating that the propagation velocity of the wave fronts is constant [13]. Diffusion of activation times introduces wave front curvature-dependent propagation velocity [10]. In the purely diffusive limit $\mathbf{D} = \lambda\hat{\mathbf{D}}$ with $\lambda \to +\infty$, the equation becomes the diffusion equation

$$\nabla\cdot(\hat{\mathbf{D}}\nabla\tau) = 0 \qquad \mathbf{x}\in\Omega\setminus\Gamma, \tag{4}$$

$$\mathbf{n}\cdot\hat{\mathbf{D}}\nabla\tau = 0 \qquad \mathbf{x}\in\partial\Omega\setminus\Gamma, \tag{5}$$

$$\tau(\mathbf{x}) = \tau_0(\mathbf{x}) \qquad \mathbf{x}\in\Gamma. \tag{6}$$

The Dirichlet boundary condition on Γ (6) was added to formulate a Laplacian interpolation problem [14]. Interpolation of activation times is therefore a limit case of the eikonal-diffusion problem.

Note, however, that τ may contain 2π jumps anywhere, which makes it more difficult in this formulation to numerically compute the gradient [15]. To handle this phase unwrapping problem, a phase function transform $\phi = \exp(i\tau)$ is applied. The transformed eikonal-diffusion equation reads [9]:

$$\|\mathbf{c}\nabla\phi\| = 1 + \mathrm{Im}\,\nabla\cdot(\phi^*\mathbf{D}\nabla\phi) \quad \mathbf{x}\in\Omega, \tag{7}$$

$$|\phi| = 1 \quad \mathbf{x}\in\Omega, \tag{8}$$

$$\mathbf{n}\cdot\mathbf{D}\nabla\phi = 0 \quad \mathbf{x}\in\partial\Omega, \tag{9}$$

where the symbol 'Im' denotes the imaginary part and the star ($*$) means the conjugate (when applicable) transposed vector/tensor.

2.3. Parameter identification

The parameters $\mathbf{c}$ and $\mathbf{D}$ will be selected to reproduce activation patterns that would be observed in a monodomain model with conductivity tensor $\boldsymbol{\sigma}$ (mS/cm), membrane surface-to-volume ratio β (cm^{-1}), and membrane capacitance per unit membrane area C_m ($\mu\text{F/cm}^2$). The derivation of the