Simulation of Fractionated Electrograms at Low Spatial Resolution in Large-Scale Heart Models

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Abstract

To compute extracellular potentials from transmembrane potentials an elliptic boundary-value problem must be solved. This must be done at a spatial resolution of 0.2 mm or better to avoid artefacts in the form of large spikes before and after major deflections. For macroscopic heart models, this leads to very large linear systems.

Artefacts in low-resolution solutions are related to the restriction operator that is used to translate the sources from high to low resolution. Typically, this restriction is done by injecting transmembrane potentials. We propose to use transmembrane current as a source, with weighted summation rather than simple injection.

We tested this method in a model of the human ventricles. We found that using the proposed scheme, a good visual match could be obtained between electrograms computed at 1-mm and 0.2-mm resolution, even in regions where strong sub-millimeter heterogeneity in tissue conductivity was present.

1. Introduction

Computation of extracellular potentials from transmembrane potentials is a common problem in cardiac electrophysiology [1, 2]. It is part of many bidomain reaction-diffusion models, and is also used to compute (intracardiac) electrograms from membrane potentials simulated by monodomain models [3, 4]. Computation of extracellular potentials requires the solution of an elliptic boundary-value problem which, when discretized, can be written as a system of linear equations. Because extracellular potentials must be solved at a spatial resolution of 0.2 mm or better to avoid spike artefacts [5], these linear systems can have tens or hundreds of millions of equations for a whole-heart model [3,6]. Such large systems are hard to solve and require in the order of 10–100 GB memory. Faster and less memory-intensive solutions are often desirable.

Artefacts in low-resolution solutions are related to the restriction operator that is used to translate the source data from the high-resolution to the low-resolution mesh. Typically, this restriction is done by injecting transmembrane potentials. We propose to use transmembrane current as a source, with regional summation rather than simple injection. The summation algorithm must fulfill the following criteria:

- No contribution may be lost, otherwise a solution for the linear problem would not exist.
- Contributions should remain as local as possible.
- The summation should not introduce artefacts.

We tested the performance of a summation method with trilinear weighting to fulfill these criteria.

2. Methods

An anatomic model of a human heart and torso was created from MRI data as described earlier [7]. This model described torso surface, myocardium, intracavitary blood masses, and lungs. A detailed cardiac anatomic model was manually fitted to the cardiac outlines obtained from MRI. The resulting model represented the subject's heart with 50 million cubic elements having sides of 0.2 mm. To each element, a local fiber orientation and cell type (subendocardial, subepicardial, or M cell) were assigned.

Propagating action potentials (AP) were simulated with a monodomain reaction-diffusion equation, using software that has been described previously [3]. Ionic currents were computed with the TNNP model for the human ventricular myocyte [8]. Sinus rhythm was mimicked by stimulating the ventricles at the early activation sites published by Durrer et al. [9, 10].

Computation of extracellular potentials (electrograms) from the simulated membrane potentials was based on the bidomain model for cardiac tissue [11, 12], which approximates the myocardium with two continuous domains. The "intracellular domain" represents the interior of myocytes and gap junctions, while the "extracellular domain" represents the interstitium. Intracavitary blood and connective tissue are handled as an extension of the extracellular domain [3]. The electric conductivity is represented by conductivity tensor fields $\mathbf{G}_\mathrm{i}$ and $\mathbf{G}_\mathrm{e}$ in the intracellular and

extracellular domains, respectively. The bidomain model leads to the following expression for the extracellular potential, $\phi_e(\mathbf{x}, t)$, at position $\mathbf{x}$ and time t:

$$\nabla \cdot [\mathbf{G}_i(\mathbf{x}) + \mathbf{G}_e(\mathbf{x})] \nabla \phi_e(\mathbf{x}, t) = I(\mathbf{x}, t) \quad (1)$$

where

$$I(\mathbf{x}, t) = -\nabla \cdot \mathbf{G}_i(\mathbf{x}) \nabla V_m(\mathbf{x}, t). \quad (2)$$

We evaluated $I(\mathbf{x}, t)$ at the full 0.2 mm resolution of the reaction-diffusion model.

Uniform finite-difference meshes were used for both the simulation of propagation and for the computation of $\phi_e(\mathbf{x}, t)$.

To solve equation (1) at 1-mm resolution, transmembrane current $I(\mathbf{x}, t)$ was taken from the high-resolution propagation model and summed over 1-mm^3 volumes. Each fine-mesh (F) node contributed to 1, 2, 4, or 8 coarse-mesh (C) nodes, depending on whether it coincided with a node, an edge, or a face of the low-resolution mesh, or with none of these. The weight of each contribution was

$$w = \begin{cases} 0, & \text{if } \Delta x \geq N \vee \Delta y \geq N \vee \Delta z \geq N \\ (N - \Delta x)(N - \Delta y)(N - \Delta z)/N^6, & \text{otherwise} \end{cases}$$

where N is the ratio of fine to coarse grid resolution ($N = 5$ in this paper) and Δx, Δy, Δz is the number of fine-mesh edges between the C node and the F node along the x, y, and z axis, respectively. Thus, both the sum of all weights for a single C node and the sum of the weights for a single F node were unity.

To obtain a unique solution to equation (1), ϕ_e was defined to be zero at a reference site on the top of the right atrium. Thus, $\phi_e(\mathbf{x}, t)$ is equivalent to the unipolar electrogram at site $\mathbf{x}$ with a reference electrode on the top of the right atrium.

Electrograms were computed at 1-mm resolution both for the isolated heart and for the in-situ heart. These simulations were performed with 1 million and with 42 million nodes, respectively. To test the validity of the low-resolution results, electrograms were also computed at the full 0.2-mm resolution in the isolated heart; this took 113 million nodes. Simulations were performed on 32–128 processors of an SGI Altix 4700 supercomputer.

To create a situation where inhomogeneous tissue caused fractionated electrograms, fibrofatty replacement and Na-channel block were simulated as in previous work [4]. Fibrosis was simulated by introducing barriers with a thickness of 0.2 mm in the outer 50 % of the right ventricular wall. In these barriers, no intercellular coupling was present. In bidomain terms, $\mathbf{G}_i = 0$ but $\mathbf{G}_e$ had the normal value for myocardium. In the barriers, gaps of 0.2×0.2 mm were made in which intracellular coupling was one third of its normal value, to mimick even smaller gaps. The conductivity of the fast Na current was set to 30 % of its normal value, in the entire heart.

3. Results

Figure 1 shows electrograms computed at low and high resolution. Panels A and B show the simulated geometry, activation isochrones, and locations from where the displayed electrograms were taken. Panel C shows electrograms computed at high resolution, and panel D those computed at low resolution, from the same simulated transmembrane currents. The electrograms computed at low resolution were visually indistinguishable from those computed at high resolution.

Figure 2 shows three electrograms computed for the same position (needle electrode C5 in figure 1). The black signal was computed at a resolution of 1 mm in an isolated-heart model. The red signal at a resolution of 0.2 mm, also in an isolated heart. The blue signal was computed at 1-mm resolution in a model of the heart embedded in the torso. Differences between the first two signals are minor. The electrogram computed for an in-situ heart is much attenuated, as expected, due to the conductivity of the torso. However, it still shows the same fractionation pattern as the signals computed in the isolated heart.

4. Discussion and conclusions

We have shown that using regionally summated transmembrane current as a source, electrograms may be computed at a resolution as low as 1 mm in a model of the human ventricles without introducing visible artefacts. Assuming that the transmembrane current itself is computed with a reaction-diffusion model at 0.2-mm to 0.1-mm resolution, this reduces the computational load associated with electrogram simulation by at least a factor 125 to 1000.

The proposed method is easy to implement in an existing bidomain solver. It worked well even in the presence of sub-millimeter heterogeneity in tissue conductivity. The method is probably less accurate in small-scale simulations, where most of the electrogram shape originates from nearby tissue. We consider it useful for whole-heart and whole-body models of large mammals, especially man. It may also be valuable as a restriction operator in (geometric) multigrid methods.

Acknowledgements

Computational resources for this work were provided by the Réseau québécois de calcul de haute performance (RQCHP).

The anatomic model used in this study was prepared by Dr André Linnenbank and Dr Pieter Postema at the Academic Medical Center of the University of Amsterdam. The representation of fibrotic myocardium was developed in collaboration with Dr Mark Hoogendijk, from the same institution.

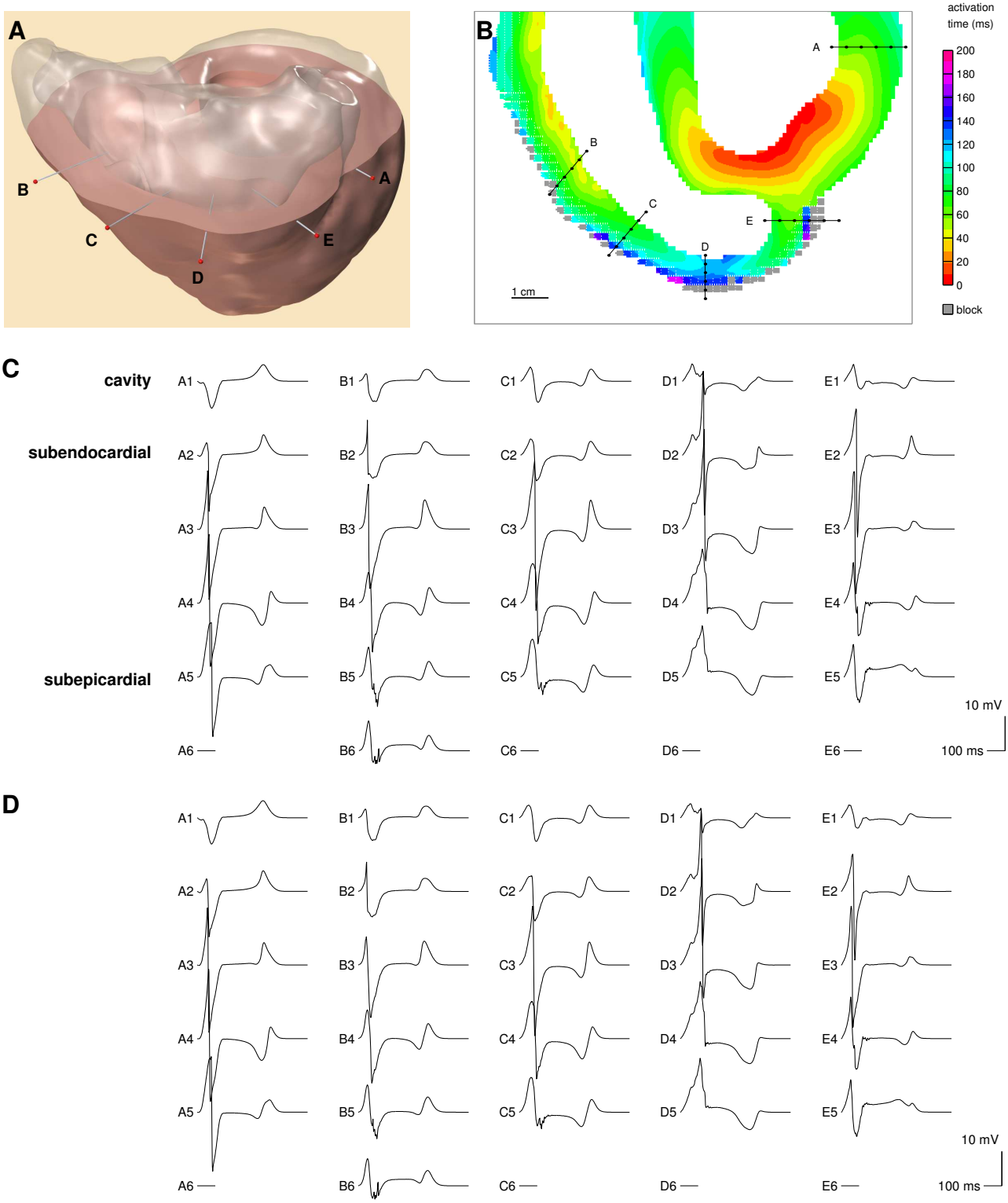

Figure 1. **A.** Three-dimensional model of the human ventricles, the top part rendered transparently to show the plane and virtual needle electrodes from which data are shown. **B.** Activation times in a single plane of the three-dimensional heart model, with positions of the virtual needle electrodes. **C.** Simulated electrograms at the positions of the needle electrodes, computed at high (0.2-mm) resolution. **D.** Simulated electrograms at the same positions as in panel C, computed at low (1-mm) resolution.

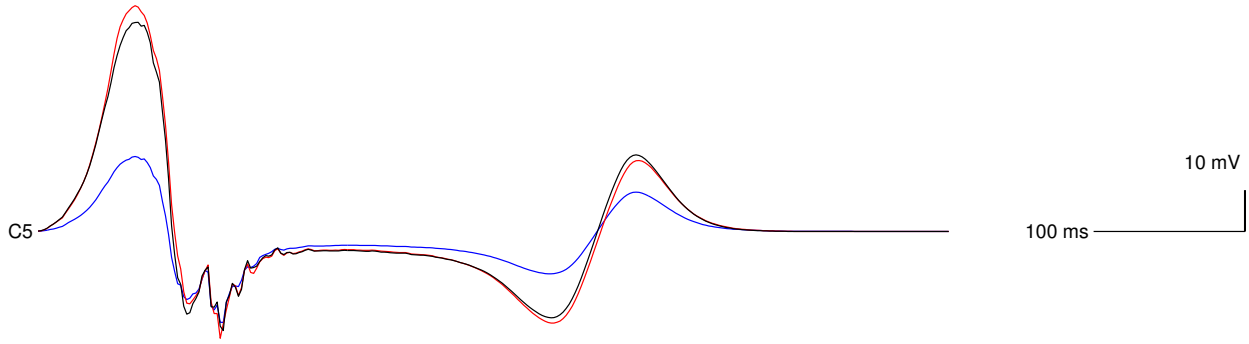

Figure 2. Simulated electrograms at the position of needle electrode C5 (see figure 1). Black, computed at a resolution of 1 mm; red, computed at a resolution of 0.2 mm, both in an isolated heart with blood in the cavities. The blue signal was computed at 1-mm resolution in a model of the heart embedded in the torso.

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