

3D Cardiac Electrical Activity Model

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Original scientific paper

The aim of this study is to develop a new, computationally-efficient, anatomically-realistic 3D bidomain cardiac electrical activity model using widely available software and standard low-cost hardware. The model incorporates whole-heart embedded in a human torso, spontaneous activation of sinoatrial node and specialized conduction system with heterogeneous action potential morphologies. The model is capable of generating realistic body surface electrocardiograms (ECGs) and is proposed as a useful tool for investigating some major issues in heart pathophysiology and in stimulation; such as simulating and optimizing synchronized electrical cardioversion, defibrillation and pacing stimulation.

Key words: Bidomain model, cardiac simulation, ECG, whole-heart

3D model električne aktivnosti srca. Cilj studije je razviti računalno efikasan, anatomski realističan 3D model električne aktivnosti cijelog ljudskog srca na široko dostupnoj računalnoj opremi. Model uključuje cijelo srce okruženo plućima i postavljeno unutar ljudskog torza, sa spontanom aktivacijom sinus-atrijskog čvora i specijaliziranim vodljivim putevima s heterogenim morfologijama akcijskih potencijala. Model omogućuje simuliranje elektrokardiograma (EKG) realističnog oblika te ga je moguće koristiti za istraživanje srčanih patofiziologija, simuliranje i optimizaciju sinkronizirane električne kardioverzije, defibrilacije ili simulacije različitih srčanih stimulacija.

Ključne riječi: Dvodomenski model, simulacija srčanog ritma, EKG, model srca

1 INTRODUCTION

Application and benefits of computational cardiac models range from predicting the effects of intervention of medical treatments, to providing the only conceivable alternative to animal experimentation [1].

State-of-the-art of the computational cardiac modeling and simulation is oriented today towards personalized, individualized, patient-specific or pathology-specific human heart models, highly detailed, but still ventricular-only or atria-only models.

Recently ended European euHeart project have gathered 16 relevant industrial, clinical and academic partners from 6 European countries and with an outcome of more than 300 conference and journal publications [2]. Models in euHeart project have incorporated cutting-edge experience and knowledge of cardiac modeling and their results give excellent contemporary overview and state-of-the-art of the European and world cardiac modeling.

The euHeart consortium targeted four important aspect of cardiovascular diseases (CVD): (a) congestive heart failures due to abnormal activation or due to structural abnormalities leading to abnormal hemodynamic and loading,

(b) cardiac arrhythmias (treated by radiofrequency ablation), (c) abnormal myocardial tissue perfusion in coronary artery disease and (d) abnormalities in hemodynamic and loading due to valvular or aortic disease, etc., although not everything with equal depth and quality.

All presented cardiac models were either ventricular-only or atria-only models, focused on the very specific application or pathology. Furthermore the project did not address the problem of simulating and optimizing methods of synchronized electrical cardioversion, defibrillation or pacing stimulation. Some euHeart models have handled only: (a) cardiac hemodynamics (fluid mechanics), the others (b) myocardial mechanical contractions (solid mechanics) and the third (c) electrical activity.

Some major issues in heart pathophysiology and stimulation, like simulating and optimizing synchronized electrical cardioversion, defibrillation and pacing stimulation require integrated, whole-heart model of cardiac activity. Today, generalized, whole-heart electrical activity models embedded in the torso, with spontaneous activation and ECG generation, are relatively rare [3,4].

In general computational modeling of cardiac electrical activity is performed from the heart cell, tissue and

organ levels through to the body surface level, formulating the forward problem of the whole-organ system within the body [1]. To simplify this very complex system, most cardiac modelers adopt a bidomain framework with two continuum (volume-averaged), interpenetrating domains: intracellular and extracellular domains, and third passive extra-myocardial region for modeling the torso [1,5,6].

Therefore, the main objective of this study is to integrate some of the above mentioned and fragmented sub-models into one, unified, integrated, new and realistic whole-heart model of cardiac electric activity.

2 METHODS

2.1 Geometry

The anatomically-realistic 3D model geometry of: (a) whole-heart embedded in torso with lungs (Figure 3) and (b) whole-heart geometry with atrial and ventricular cavities and specialized heterogeneous conduction pathway (Figure 4) was assembled from manually segmented 155 CT tomographic images with resolution 512 by 512 pixels at 3 mm intervals per slice, where each pixel is made up of 12 bits of grey tone, and where voxel size is 0.9mm x 0.9mm x 3mm, obtained from the Visual Human Project male digital image dataset (Figure 1) [7]. There are 1871 CT cross-sections and only torso sections 192:347 were used for assembling the 3D model geometry.

2.2 Segmentation

CT images from Visual Human Project are not readily segmented or labeled, therefore inner organs of the Visible Human Male had to be segmented and labeled manually image by image (Figure 2). The following regions were segmented and labeled as: torso, lungs, bones, left & right atrium cavity, left & right ventricle cavity, arch of aorta, ascending aorta, superior vena cava, inferior vena cava, pulmonary arteries, pulmonary veins, sinoatrial node (SAN), atrial myocardium, atrioventricular node (AVN), His bundle, bundle branches, Purkinje fibers, ventricular myocardium.

2.3 Mesh

A volumetric tetrahedral mesh (Figure 5) was created from the 3D volumetric images (Figure 3 and Figure 4) using Computer Graphical Algorithms Library (CGAL 3.5) 3D mesher for direct mesh generation. The resulting mesh was imported into the Comsol Multiphysics 4.2a (COMSOL AB, Sweden) finite element solver (Figure 6).

Complete mesh (heart, lungs and torso) consisted of 298.728 elements (tetrahedrons), 308.070 triangles and 86.288 nodes (Figure 5).

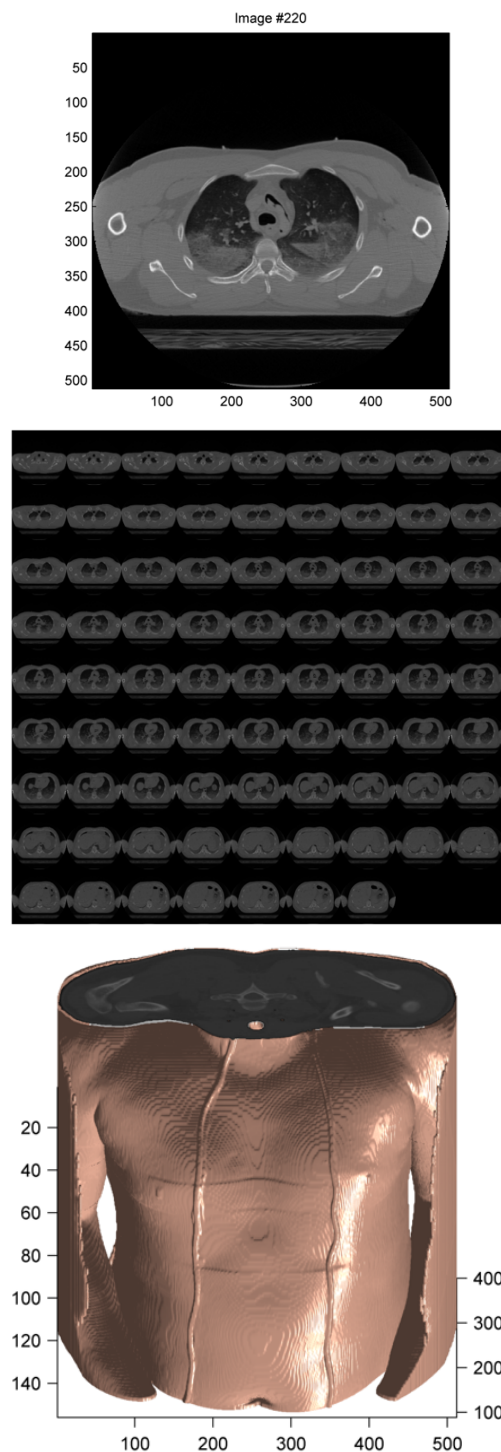


Fig. 1. Visual Human Project male digital image dataset: (top) CT image sample, (middle) tomographic CT images at 3 mm intervals per slice, (bottom) montage of torso from tomographic CT images.

2.4 Equations

Due to large number of mesh elements and therefore computational complexity of realistic 3D whole-heart model we used computationally efficient and simple equations for cellular activation - modified FitzHugh–Nagumo (FHN) equations to simulate action potentials in different subdomains / regions of the heart [10,11].

Outside the myocardium the governing equation for the extracellular voltage V in the passive volume conductor domains was given by the Laplace formulation

$$\nabla \cdot (-\sigma_o \nabla V) = 0$$

where σ_0 is the electrical conductivity of respective outside-heart domains (torso, lungs, muscles, blood, fat, and bones) with values given in Table 1 [6,8]. All exterior boundaries of the torso were set to be electrically insulating (zero normal component of current density), and all interior boundaries in contact with the heart were set to $V=V_e$ where V_e is the extracellular voltage in the myocardial walls.

From the surface of the torso (Figure 6) three Einthoven leads V_I , V_{II} , and V_{III} from the standard 12-lead system were calculated as: $V_I = V_L - V_R$, $V_{II} = V_F - V_R$, $V_{III} = V_F - V_L$, but other lead systems can be obtained, if desired, by placing additional 6 electrodes on the torso (for the precordial leads) or by implementing additional calculations (for the Goldberger-augmented leads) or by placing additional 7 electrodes (for the orthogonal X, Y, Z leads of vectorcardiogram) as described in details in [9].

2.5 Subdomains

The heart itself was divided into 7 subdomains or regions (sinoatrial node - SAN, atria - ATR, atrioventricular node - AVN, His bundle - HIS, bundle branches - BNL, Purkinje fibers - PKJ, ventricles - VEN) with heterogeneous cardiac cell properties and tissue conductivities (Table 2) representing specialized cells of the conduction system and the myocardium. An electrical isolation gap exists between the atria and ventricles except at a junction in the septum that links the atrioventricular node with the His bundle.

The bidomain model of cardiac activation, including the SAN, was defined at the cellular level by three dependent variables: V_e – the extracellular potential, V_i – the intracellular potential, and u – a recovery variable governing cellular refractoriness. The bidomain equations were based on modified FitzHugh-Nagumo equations [10,11]. For the

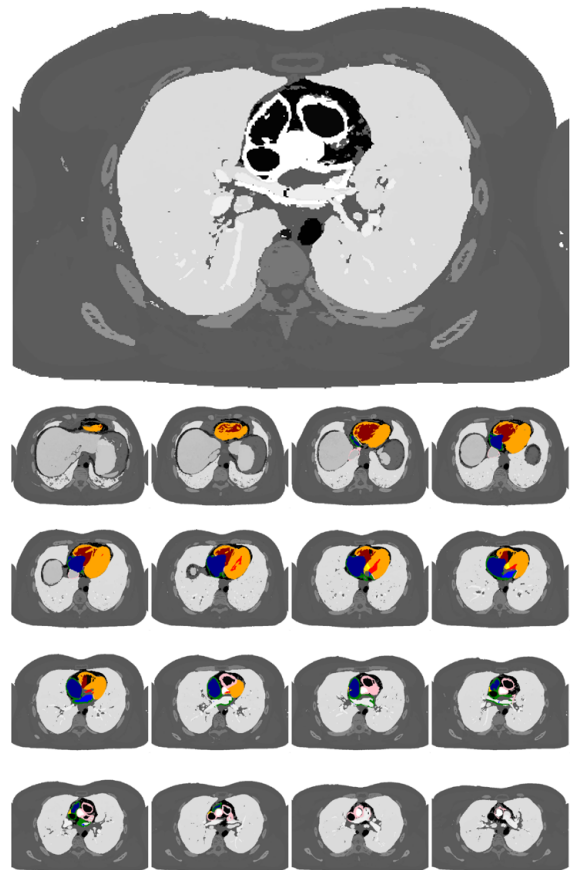


Fig. 2. Segmented tomographic CT images of the heart regions, lungs and torso.

Subdomain	Conductivity (S/m)[8]	Conductivity (S/m)[6]	Conductivity (S/m) Present study
Heart	0.054	0.400* ^c 0.179* ^d	0.05
Blood	0.7	0.625	0.7
Lungs	0.203* ^a 0.039* ^b	0.050	0.04
Muscle	0.202	0.526* ^e 0.076* ^f	n/a
Fat	0.012	0.040	n/a
Bone	0.000975* ^g	0.006	n/a
Torso	n/a	n/a	0.2

*a deflated, *b inflated, *c longitudinal, *d transversal, *e parallel, *f normal, *g marrow.

Table 1. Electrical conductivity values for various model tissues.

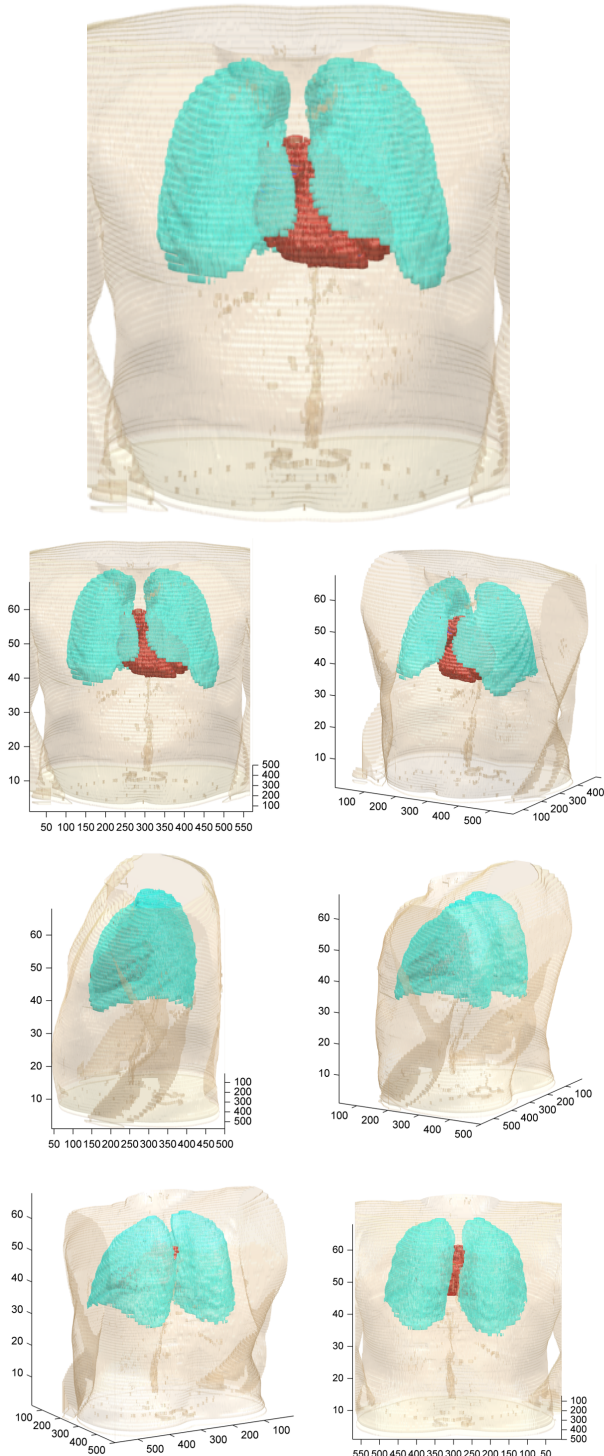


Fig. 3. Torso geometry. Whole-heart geometry including atrial and ventricular cavities is shown embedded in the torso with lungs.

Table 2. Table 2. Model parameters and model initial values (V_i, V_e, u) by 7 subdomains/regions.

	SAN	ATR	AVN	HIS	BNL	PKJ	VEN
a	-0.60	0.13	0.13	0.13	0.13	0.13	0.13
b	-0.30	0	0	0	0	0	0
c₁	1000	2.6	2.6	2.6	2.6	2.6	2.6
c₂	1.0	1.0	1.0	1.0	1.0	1.0	1.0
d	0	1.0	1.0	1.0	1.0	1.0	1.0
e	0.0660	0.0096	0.0132	0.0050	0.0022	0.0047	0.0056
A	0.0330	0.2800	0.2800	0.2800	0.2800	0.2800	0.2800
B	-0.022	-0.085	-0.085	-0.085	-0.085	-0.085	-0.085
k	1000	1000	1000	1000	1000	1000	1000
σ_e	0.5	8	0.5	10	15	35	8
σ_i	0.5	8	0.5	10	15	35	8
V_i	-0.060	-0.085	-0.085	-0.085	-0.085	-0.085	-0.085
V_e	0	0	0	0	0	0	0
u	0	0	0	0	0	0	0

each region of the heart they were defined according to:

$$\begin{aligned} \frac{\partial V_e}{\partial t} - \frac{\partial V_i}{\partial t} + \nabla \cdot (-\sigma_e \nabla V_e) &= i_{ion} \\ \frac{\partial V_i}{\partial t} - \frac{\partial V_e}{\partial t} + \nabla \cdot (-\sigma_i \nabla V_i) &= -i_{ion} \\ \frac{\partial u}{\partial t} &= ke \left[\frac{(V_m - B)}{A} - du - b \right] \end{aligned}$$

with σ_e, σ_i denoting the extracellular and intracellular conductivities respectively, $V_m = V_i - V_e$, and $a, b, c_1, c_2, d, e, k, A, B$ are region-specific parameters, whilst i_{ion} is defined according to:

$$\begin{aligned} i_{ion} &= kc_1 (V_m - B) \left[a - \frac{(V_m - B)}{A} \right] \left[1 - \frac{(V_m - B)}{A} \right] \\ &\quad + kc_2 u \end{aligned}$$

within the SAN and

$$\begin{aligned} i_{ion} &= kc_1 (V_m - B) \left[a - \frac{(V_m - B)}{A} \right] \left[1 - \frac{(V_m - B)}{A} \right] \\ &\quad + kc_2 u (V_m - B) \end{aligned}$$

within the walls of the atria, ventricles, AVN, His bundle, bundle branches and Purkinje fibers. Parameters of the model with region-specific values, along with initial variable values are listed in Table 2.

Boundary conditions on all interior boundaries in contact with the torso, lungs and cardiac cavities are zero-flux for V_i , therefore $-n \cdot \Gamma = 0$ where \mathbf{n} is the unit outward normal vector on the boundary, and Γ is the flux vector through that boundary for the intracellular voltage, equal to $\Gamma = -\sigma_i \cdot \partial V_i / \partial n$. For the variable V_e , the inward flux on these boundaries is equal to the outward current density \mathbf{J} from the torso / chamber volume conductor, therefore $-\sigma_e \cdot \partial V_e / \partial n = n \cdot J$.

2.6 Simulation

The realistic 3D cardiac model was simulated using Comsol Multiphysics 4.2a (COMSOL AB, Sweden) finite

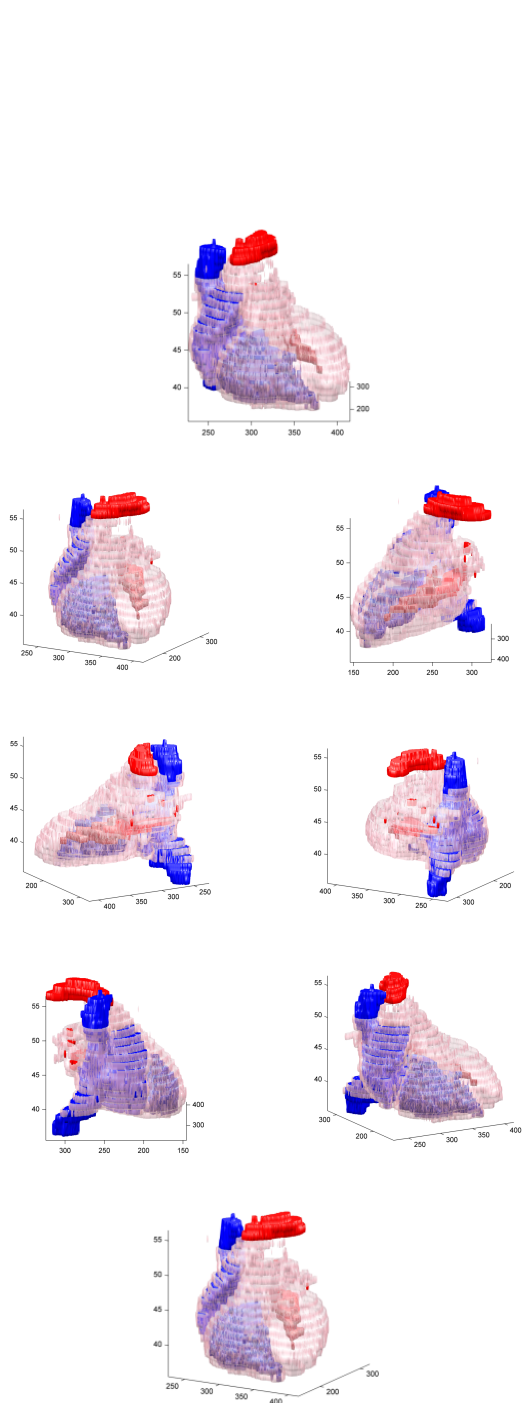


Fig. 4. Heart geometry. Whole-heart is shown with atrial and ventricular cavities inside the transparent heart.

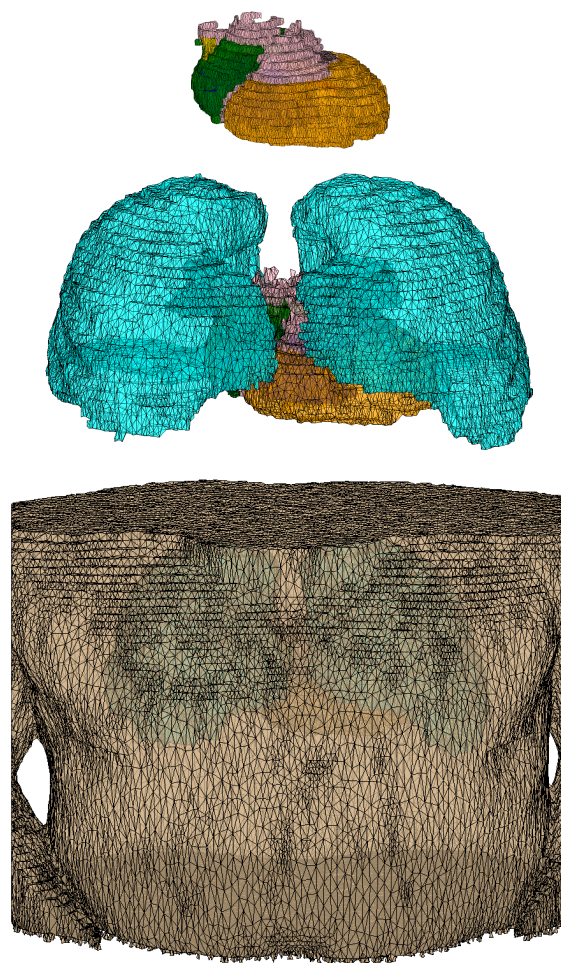


Fig. 5. Finite element mesh layout for: (top) the heart, (middle) the heart and lungs and (bottom) the heart and lungs embedded in the torso.

element software. The resulting finite element mesh consisted of 298,728 tetrahedral elements (of minimal 1x1x1 mm size) with 682,768 degrees of freedom (DoF) solved at each time step. The simulations were performed on an Intel Core i7-970 processor workstation with 24 GB of memory, 2x6 cores and processing power of about 100 Gflops.

The accuracy and stability of the model were tested for finer mesh resolutions, and it was found that for finer spatial and temporal discretizations the model ECG converged to the same solution.

3 RESULTS

The model is capable to simulate and generate realistic electrocardiogram (ECG) morphologies (Figure 7) under normal state (Figure 8 and Figure 9) and also pathological heart states like myocardial infarcts in [9]. The time

Table 3. Comparison of three torso-embedded whole-heart models developed by our group in: [9], [12] and present study.

	Simplified* 2D	Simplified** 3D*	Realistic*** 3D
Tetrahedral Elements	8.174	21.106	298.728
DoF	28.403	51.680	682.768
Simulation Time (Isec @ 1ms)	~ 5 min	~ 1 h	~ 12 h

*all three models developed in Comsol Multiphysics 4.2a are available through the following link: <http://hr.linkedin.com/in/ssovilj>

dependent solver took about 12 hours to solve 1 simulated second of ECG with 1 ms time resolution (Figure 7).

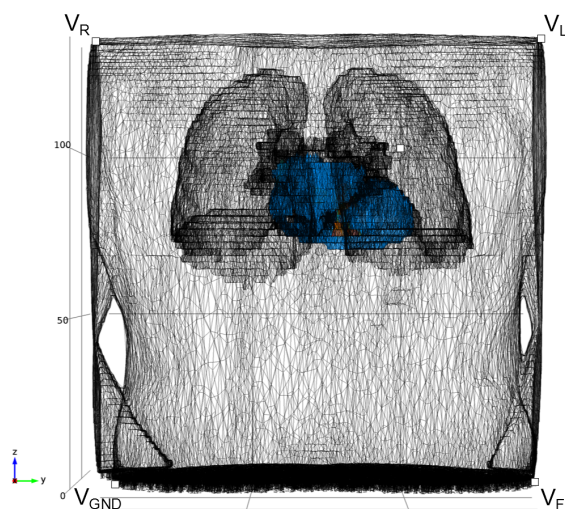


Fig. 6. Simulation of heart electrical activity with position of ECG electrodes (V_R , V_L , V_F and V_{GND}) in Comsol Multiphysics 4.2a.

In all simulations, spontaneous and periodic rhythmic activation occurred in the SAN pacemaker region, located in the right atrial wall of the heart (Figure 8 and Figure 9). The electrical activation impulse then spread throughout the atria and through the atrial septum before reaching the AVN, where the excitation wave front was delayed until the atria were entirely activated. Subsequently, the AVN activated the His bundle from where the activation spread to the bundle branches, the Purkinje fibers and the whole ventricles (Figure 9).

4 CONCLUSION

We have developed an anatomically-realistic 3D cardiac model using widely available commercial finite element software that could run on relatively standard and affordable computer hardware and software.

In previous work [9,12] we have developed simplified whole-heart torso-embedded models in 2D and 3D that can

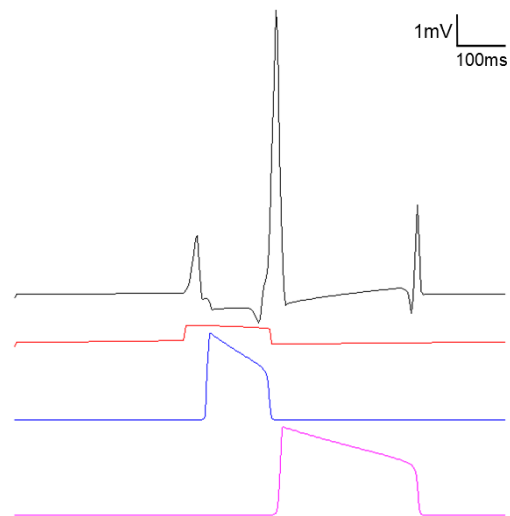


Fig. 7. Simulated lead II ECG and action potentials of: SAN, atria and ventricles (the most distant and last activated points). Amplitude of action potentials is scaled-down 100 times.

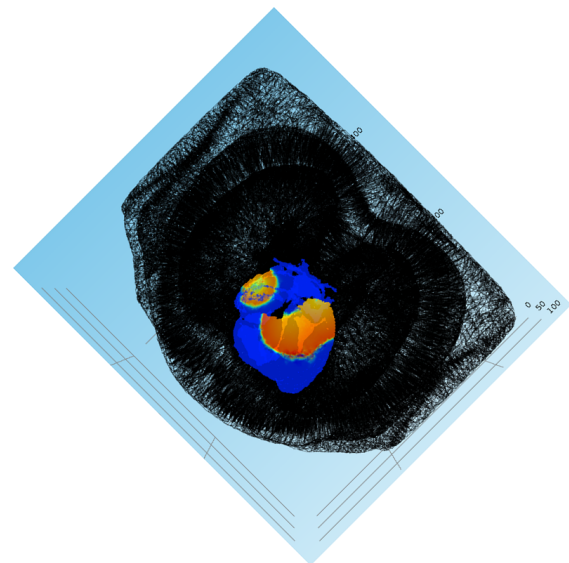


Fig. 8. View from the top of torso. This view was mostly used for the simulation monitoring of the heart electrical activity.

be utilized as a starting point for the rapid a priori formulation, testing and refinement of this realistic 3D model. Table 3 gives a comparison between these three models in sense of computational burden and complexity. It is not always necessary to use high dimensional, all-inclusive, highly detailed cardiac models to gain insights into cardiac function. Even so, the lowest possible dimension models

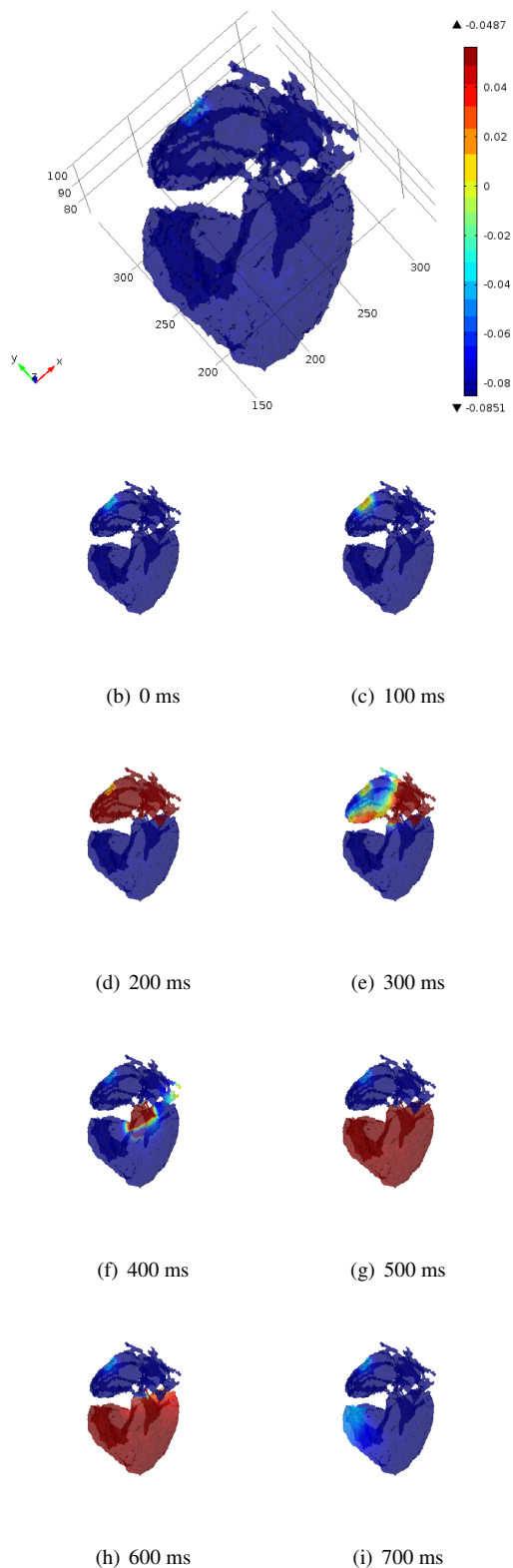


Fig. 9. Top view of the transparent heart with electrical activity in 100 ms time steps.

like [9,12] should be developed first and progressively expanded to higher dimensional and more complex models like the one presented in this study.

Even though the model was able to reproduce realistic ECG morphologies, the shape of the T wave tended to be narrower than commonly observed. This property of the model was due to the nature of the uniform action potential (AP) implemented throughout the ventricles, such that repolarization occurred nearly simultaneously at all points throughout the ventricular myocardium. The T wave duration could be widened by introducing some heterogeneity in ventricular AP parameters (such as parameter e) which would lead to heterogeneous AP durations and a spread in ventricular repolarization times.

We believe the model has multilateral application potentials in education, research and in the clinical practice since it can be used as a simulator for various arrhythmias, including atrial / ventricular fibrillation, as well as able to simulate the effects of changes in tissue conductivity, action potential duration or shape on ECG morphology, with the aim of developing new ECG diagnostic algorithms, methods and tools that are predictive, preventive, personalized like in [12-14].

Since the model is capable of inducing various cardiac arrhythmias, as a continuous bidomain model, it also allows simulation of synchronized electrical cardioversion, defibrillation and pacing stimulation, that would be useful in medical practice as suggested by researchers from Medtronic, Inc. in [15].

In future development stages, the model could be further improved with: (1) finer geometry resolution and finer anatomical details, also with (2) patient-specific geometry and body surface potentials, then cardiac electrical function could be inversely assessed, and (3) more detailed cell models could be used.

It is envisioned that the current cardiac electrical activity model could be improved by coupling with other electro-mechanical and blood flow models [which incorporates both (4) heart hemodynamics and (5) mechanical contraction] into a new, state-of-the-art, torso-embedded, whole-heart, fully-coupled model of cardiac fluid-solid mechano-electric activity which is not currently available in the field yet.

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