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Refining the Eikonal Model to Reproduce the Influence of Atrial Tissue Geometry on Conduction Velocity

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Abstract: Atrial fibrillation is responsible for a significant and steadily rising burden. Simultaneously, the treatment options for atrial fibrillation are far from optimal.
Personalized simulations of cardiac electrophysiology could assist clinicians in the risk stratification and therapy planning for atrial fibrillation. However, the use of personalized simulations in clinics is currently not possible due to either too high computational costs or non-sufficient accuracy. Eikonal simulations come with low computational costs but cannot replicate the influence of cardiac tissue geometry on the conduction velocity of the wave propagation. Consequently, they currently lack the required accuracy to be applied in clinics. Biophysically detailed simulations on the other hand are accurate but associated with too high computational costs.
To tackle this issue, a regression model is created based on biophysically detailed bidomain simulation data. This regression formula calculates the conduction velocity dependent on the thickness and curvature of the heart wall. Afterwards the formula was implemented into the eikonal model with the goal to increase the accuracy of the eikonal model without losing its advantage of computational efficiency.
The results of the modified eikonal simulations demonstrate that (i) the local activation times become significantly closer to those of the biophysically detailed bidomain simulations, (ii) the advantage of the eikonal model of a low sensitivity to the resolution of the mesh was reduced further, and (iii) the unrealistic occurrence of endo-epicardial dissociation in simulations was remedied.
The results suggest that the accuracy of the eikonal model was significantly increased. At the same time, the additional computational costs caused by the implementation of the regression formula are neglectable. In conclusion, a successful step towards a more accurate and fast computational model of cardiac electrophysiology was achieved.

Keywords: cardiac modelling, eikonal model, conduction velocity, wall thickness, tissue curvature, atrial fibrillation

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1 Introduction

Atrial fibrillation (AFib) is responsible for an increase of morbidity and mortality and its prevalence is expected to increase further, due to the rising life expectancy of humans and age being a major risk factor [1]. At the same time the treatment options available for AFib are far from optimal. Personalized simulations of cardiac electrophysiology could assist clinicians in the risk stratification and therapy planning for AFib [2].

Bidomain simulations are detailed but computationally too expensive to be used in clinical time frames. The eikonal equation can be used as an efficient way to calculate local activation times (LATs) of wavefronts in the myocardium. Due to the computational efficiency, eikonal simulations have the potential to be applied in clinical time frames. However, eikonal simulations lack accuracy, because of their inability to capture certain electrophysiological effects like source sink mismatches or reentry. A fast and accurate model is needed to make personalized simulations applicable in clinics. [3]

Whereas previous work addressed the wavefront curvature in eikonal simulations [4], this work is about the influence of tissue curvature and wall thickness on local conduction velocity (CV). Hereby, Information obtained with bidomain simulations is used to create a regression model for the CV. The formula is then implemented into the eikonal model to increase its accuracy in a computationally efficient way.

2 Methods

2.1 Software

The following software was used:
- Myokit's [5] data extractor to obtain information from graphs
- openCARP [6] to run bidomain simulations
- MATLAB [7] to run eikonal simulations (anisotropic, homogeneous, fast iterative method), generate the mesh, find the best approach for the regression formula, and optimize the parameters of the regression formula.

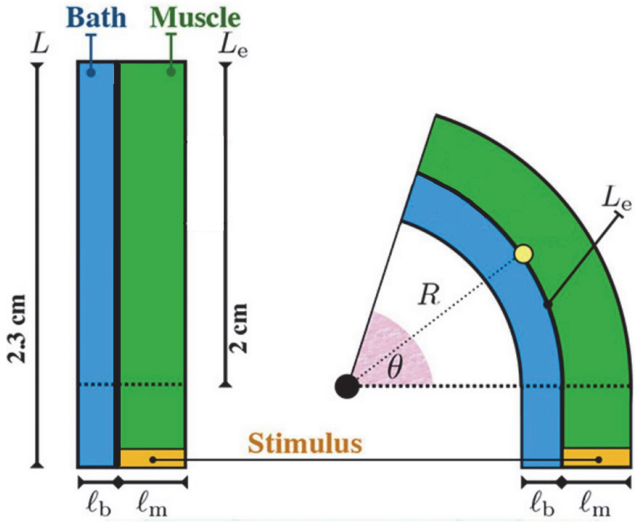

Fig. 1: Idealized model of myocardial tissue. The tissue (green) length in the endocardium L_e is fixed at 2 cm, whereas the length of the epicardium changes depending on the curvature. The curvature κ_{endo} is equal to the inverse of the radius R in the endocardium and is applied to the upper 2 cm of the muscle. The lower 3 mm of the tissue remain straight to initialize a bottom up stimulus (yellow). The wall has a thickness of l_m. Reproduced from Rossi et al. [8] under the CC BY license.

2.2 Myocardial Tissue Model and Mesh Generation

The methods in this section were chosen to be as similar as possible to the methods used in Rossi et al. [8], where the influence of atrial tissue geometry such as wall thickness and curvature on CV was studied using a 2D mesh. A similar mesh was created based on the myocardial tissue model shown in Figure 1. The mesh was then bent to a certain curvature κ_{endo} in the endocardium. This was achieved by editing the coordinates of the nodes in the straight mesh using the trigonometric formula presented in Rossi et al. [8]. The sign of the curvature indicates the direction the mesh was bent to. A positive curvature κ_{endo} means the block is bent towards the left and vice versa.

2.2.1 Fiber Direction

The fiber direction has an influence on CV in all anisotropic cases [9]. Therefore the implementation of the information about the fiber direction into the mesh is crucial to correctly study the impact of geometrical factors on CV. A vector was assigned to each node of the mesh representing the fiber direction. These fiber vectors were calculated in a way that they stay aligned with the longer borders of the mesh for all curvatures.

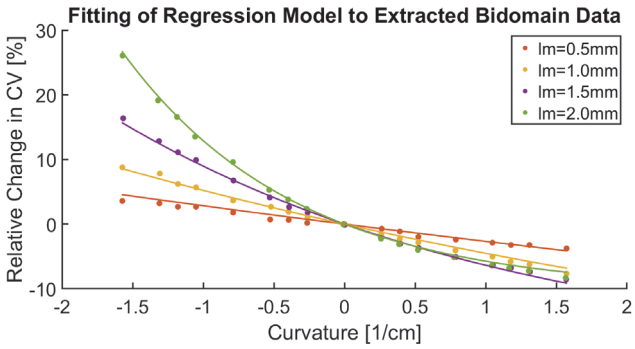

Fig. 2: The relative changes in CV for different curvatures and wall thicknesses are compared for the results of the regression formula (lines) and the extracted bidomain simulation data (points) from Rossi et al. [8]. Each colour represents a certain wall thickness.

2.3 Regression Model Creation

Based on the bidomain data about the influence of wall thickness and curvature on conduction velocity published in Rossi et al. [8], a regression model was created. This regression model describes the relative change in CV depending on the wall thickness l_m in mm, the curvature κ_{endo} in cm^{-1} to a reference CV in straight tissue:

$$CV_{rel} = (p_1 \cdot l_m + p_2) \cdot e^{-p_3 \cdot e^{p_4 \cdot l_m} \cdot \kappa_{endo}} - (p_1 \cdot l_m + p_2) \quad (1)$$

The four parameters were optimized by minimizing the RMSE towards the locally calculated CV of the bidomain solution, which resulted in the following values: p_1=-0.23, p_2=0.57, p_3=0.03 and p_4=1.73. The resulting match of the regression model to the bidomain data can be seen in Figure 2.

2.4 Implementation of the Regression Model into the Eikonal Model

In the eikonal simulation, every node is assigned a so called local speed function (LSF) that corresponds to the local CV along the longitudinal fiber direction. At first, the employed eikonal model neglects the influence of geometrical factors on CV, because a constant CV in the longitudinal direction is assumed in case homogeneous tissue is modeled. This means that the LSF has the same value in every node of the mesh in non-fibrotic tissue. To implement the influence of atrial tissue geometry on CV into the eikonal model, the LSF has to be calculated in every node according to the regression formula. The difficulty hereby is to define the curvature for each node. In our case the curvature in endocardium κ_{endo} is known and the curvature in the epicardium κ_{epi} can be calculated using equation 2:

$$\kappa_{epi} = -\frac{1}{\frac{1}{\kappa_{endo}} + l_m} \quad (2)$$

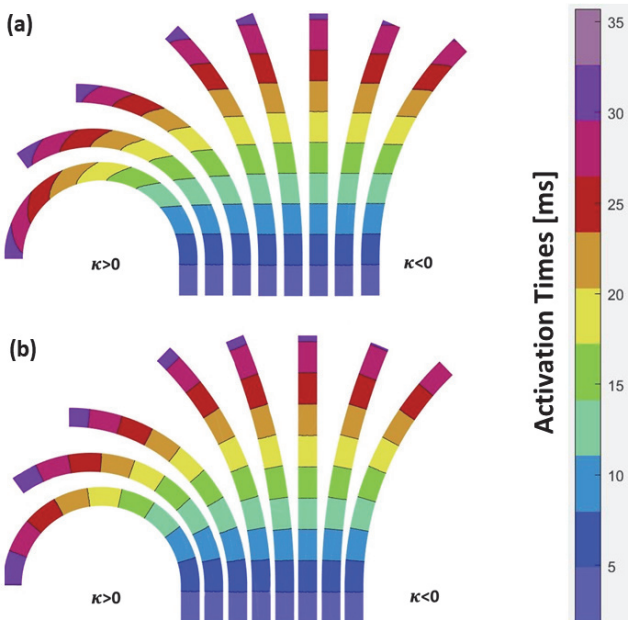

Fig. 3: LATs at different endocardial curvatures for a wall thickness of 1.5 mm obtained by eikonal simulations in (a) without the regression model and in (b) with the regression model implemented.

Alternatively, it is possible to determine the curvature in an anatomically realistic mesh. The LSF of the remaining nodes, which are in between the endo- and epicardium, was estimated by a linear interpolation of the calculated CV between the endo- and epicardium.

3 Results

The LATs and wavefront shapes of eikonal simulations in curved tissue can be seen in Figure 3. In Figure 3a it can be observed that during the propagation through curved tissue the wavefront becomes increasingly curved and endo- epicardial dissociation (EED) builds up. The inside arc of the curved geometry is always shorter than than the outside arc, but the LSF is constant in all nodes of the mesh. As a consequence, the electrical activity in the longer arc lags behind the activity in the shorter arc. The changes caused by the implementation of the regression model can be seen in Figure 3b. It can be noted that negative curvatures (shorter arc) now slow down the CV and positive curvatures (longer arc) speed up the CV. Consequently, no more significant EED occurs.

To quantify the changes made by the regression model, eikonal simulations were compared to accurate bidomain simulations. Once before the implementation of the regression model and again afterwards. Overall 24 geometries with varying wall thicknesses and curvatures were analysed. The deviation of the eikonal simulations to the bidomain simulations was quantified by the root mean square error (RMSE) of the LATs.

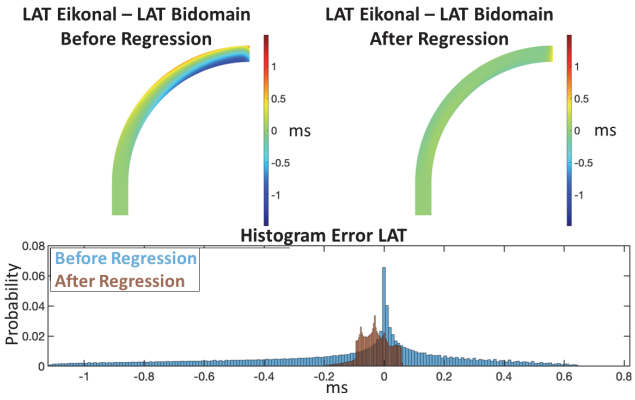

Fig. 4: LATs of eikonal simulations before and after the regression model was implemented minus the LATs of bidomain simulations for a myocardial tissue with a curvature of $-\pi/4\,\mathrm{cm}^{-1}$ and a wall thickness of 1.5 mm.

To show the improvements obtained with the regression model the geometry with a curvature of $-\pi/4\,\mathrm{cm}^{-1}$ and a wall thickness of 1.5 mm is shown in Figure 4. A positive value (red) means that the eikonal simulation has a higher LAT at the same node compared to the bidomain simulation. The stimulus in eikonal simulations propagates slower than in the bidomain simulations in red areas. On the other hand, a negative value (blue) means that the eikonal simulation has a lower LAT than the bidomain simulation indicating a higher CV in the blue areas. In green areas the differences in LATs between eikonal and bidomain simulations are small and show that the eikonal model matches the bidomain simulations well in these areas. The histogram in the bottom of Figure 4 shows that after the implementation of the regression model the error distribution is significantly smaller. To test the influence of the mesh resolution two eikonal simulations are compared for the same muscle tissue geometry but with different mesh resolutions.

Tab. 1: RMSE of LAT eikonal - LAT bidomain before and after the implementation of the regression model for 24 different geometries in terms of wall thickness l_m in mm and curvature κ in cm^{-1}. RMSE in ms before regression $\rightarrow$ RMSE in ms after regression.

	l_m			
κ_{endo}	0.5	1	1.5	2
$\pi/2$	$0.32 \rightarrow 0.06$	$0.54 \rightarrow 0.07$	$0.62 \rightarrow 0.17$	$0.60 \rightarrow 0.34$
1	$0.20 \rightarrow 0.05$	$0.33 \rightarrow 0.06$	$0.40 \rightarrow 0.11$	$0.40 \rightarrow 0.18$
$\pi/4$	$0.16 \rightarrow 0.05$	$0.27 \rightarrow 0.06$	$0.32 \rightarrow 0.09$	$0.24 \rightarrow 0.23$
$-\pi/4$	$0.18 \rightarrow 0.05$	$0.31 \rightarrow 0.07$	$0.39 \rightarrow 0.07$	$0.43 \rightarrow 0.14$
-1	$0.22 \rightarrow 0.06$	$0.37 \rightarrow 0.07$	$0.46 \rightarrow 0.10$	$0.50 \rightarrow 0.24$
$-\pi/2$	$0.35 \rightarrow 0.08$	$0.58 \rightarrow 0.11$	$0.70 \rightarrow 0.27$	$0.74 \rightarrow 0.71$

Tab. 2: RMSE of LAT high-resolution mesh - LAT low-resolution mesh obtained with eikonal simulations once before and once after the implementation of the regression model for different geometries with varying muscle thickness l_m in mm and curvature κ in cm^{-1}. The high-resolution mesh has an element size of $50\,\mu$m and the low-resolution mesh has an element size of $100\,\mu$m. RMSE in µs before regression → RMSE in µs after regression.

	l_m			
κ_{endo}	0.5	1	1.5	2
$\pi/2$	$17 \rightarrow 7.5$	$23 \rightarrow 6.8$	$27 \rightarrow 5.4$	$34 \rightarrow 16$
1	$12 \rightarrow 7.4$	$15 \rightarrow 6.2$	$17 \rightarrow 5.0$	$22 \rightarrow 13$
$\pi/4$	$11 \rightarrow 7.5$	$12 \rightarrow 6.1$	$12 \rightarrow 4.9$	$18 \rightarrow 13$
$-\pi/4$	$10 \rightarrow 7.3$	$11 \rightarrow 5.6$	$12 \rightarrow 5.1$	$17 \rightarrow 13$
-1	$12 \rightarrow 7.2$	$14 \rightarrow 5.7$	$16 \rightarrow 5.3$	$20 \rightarrow 13$
$-\pi/2$	$16 \rightarrow 7.2$	$26 \rightarrow 5.9$	$26 \rightarrow 6.1$	$30 \rightarrow 14$

The RMSE of the LATs between the eikonal simulations with different mesh resolution is calculated to quantify the mesh sensitivity before and after the implementation of the regression model. This procedure was done twice, once before and once after the implementation of the regression model. Table 2 shows that the RMSE decreased in all geometries after the implementation of the regression model.

4 Discussion

Figure 3 shows that the implementation of the regression model removes the unrealistic occurrence of EED in eikonal simulations with no epicardial fibrosis present. Additionally, the increasingly curved wavefront shapes in Figure 3b indicate that transmural propagation from the shorter to the longer arc took place due to the increasing EED. Removing these unrealistic conduction patterns from the simulation is important due to the role of EED in the maintenance of AFib [10].

The quantitative comparison of the LATs to accurate bidomain simulations in Figure 4 and Table 1 leads to the conclusion that the accuracy of the eikonal model was significantly increased by the regression model. Even the smaller improvements for a wall thickness of l_m=2 mm can be explained by differences in the wavefront shapes instead of CV mismatches. The implementation of the regression model into the eikonal model did not result in a markedly increase of the simulation run time. At the same time, a decrease of the mesh resolution showed that the eikonal model kept its advantage of a low sensitivity towards the mesh resolution (Table 2).

A limitation of the used methods is that the bending of the mesh affects the element size of the mesh. There are more parameters that have an effect on CV than wall thickness and curvature (e.g. wavefront curvature, bath size, diastolic interval). The influence of these parameters was neglected in this study because the creation of an analytical formula becomes significantly more challenging with each additional parameter considered. To tackle this issue, future research could use other methods of regression like machine learning techniques.

In conclusion a successful step towards a more accurate and fast computational model of cardiac electrophysiology was achieved. The creation of a regression formula turned out to enable significant improvements in the accuracy of eikonal simulations.

Author Statement

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