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Modelling of patient-specific Purkinje activation based on measured ECGs

Abstract: The Purkinje system is part of the fast-conducting ventricular excitation system. The anatomy of the Purkinje system varies from person to person and imposes a unique excitation pattern on the ventricular myocardium, which defines the morphology of the QRS complex of the ECG to a large degree. While it cannot be imaged in-vivo, it plays an important role for personalizing computer simulations of cardiac electrophysiology. Here, we present a new method to automatically model and customize the Purkinje system based on the measured electrocardiogram (ECG) of a patient. A graph-based algorithm was developed to generate Purkinje systems based on the parameters fibre density, minimal distance from the atrium, conduction velocity, and position and timing of excitation sources mimicking the bundle branches. Based on the resulting stimulation profile, the activation times of the ventricles were calculated using the fast marching approach. Prescribed action potentials and a finite element lead field matrix were employed to obtain surface ECG signals. The root mean square error (RMSE) between the simulated and measured QRS complexes of the ECGs was used as cost function to perform optimization of the Purkinje parameters. One complete evaluation from Purkinje tree generation to the simulated ECG could be computed in about 10 seconds on a standard desktop computer. The measured ECG of the patient used to build the anatomical model was matched via parallel simplex optimization with a remaining RMSE of 4.05 mV in about 16 hours. The approach presented here allows to tailor the structure of the Purkinje system through the measured ECG in a patient-specific way. The computationally efficient implementation facilitates global optimization.

Keywords: Excitation system, Purkinje system, Modelling, Optimization, ECG.

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1 Introduction

Representing the individual activation pattern of the ventricular myocardium is a challenging task in patient-specific cardiac computer simulations. The anatomical cause for this unique pattern is the Purkinje system which is not visible in imaging techniques. Having a large effect on the morphology of the QRS complex of the ECG, several approaches have been published from handpicking stimulation points to generating systems with respect to user specified parameters [1–3]. A fast and automatic method to model the technically invisible Purkinje system is still missing. This paper presents a new method to adjust a parameterized tree to an individual ventricle geometry based on the measured ECG.

2 Methods

We developed a software implementing the workflow shown in figure 1 consisting of two major steps. First, we calculate an ECG resulting from the ventricle activation caused by a Purkinje system generated from a set of specifiable parameters. Secondly, we compare the simulated with the measured ECG and use the resulting RMSE as cost function to perform a parameter optimization to match the measured ECG.

2.1 Fast ECG calculation

The fast calculation of the ECG was implemented in three separate tasks. First, the Purkinje system was generated with a modified Prim algorithm [5] with respect to a set of pre-described parameters: node density, atrial distance (see figure 2 A), conduction velocity, and positions and time offsets of the root nodes. After that, the activation times of the ventricular myocardium were calculated via a fast marching simulation. At last, the forward calculation was solved with the lead field approach to obtain the simulated ECG efficiently via matrix multiplication.

Figure 2 A shows an example ventricle model represented as an unstructured grid. In the first step to obtain the parameterized Purkinje system, vertices on the endocardium of the left ventricle (LV) and right ventricle (RV) were separately selected without specific order while keeping a predefined min-

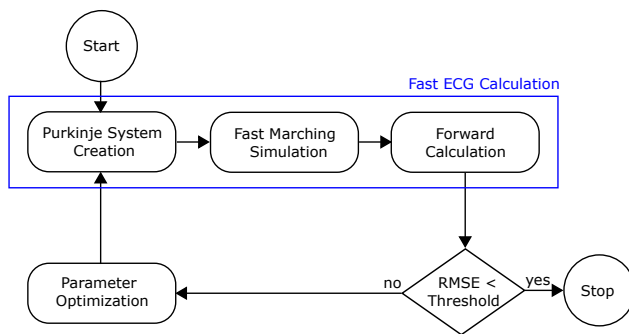


Figure 1: Flowchart showing the main concept: Calculate an ECG based on a Purkinje parameter vector as fast as possible and use the RMSE between the calculated and measured ECG as cost function for optimization.

imal distance to each other and to the atrium. The distance to the atrium was calculated based on a principle component analysis of the LV. Afterwards, multiple vertices were chosen as root nodes for the graph algorithm to mimic the ends of the bundle branches. Based on the selected vertices and root nodes, a graph as shown in figure 3 was created to generate a system as shown in figure 2 B.

Figure 3 shows the modified Prim algorithm in the case of two root nodes with the resulting trees. To create the graph, the weights of the graph's edges were set to the Euclidean distance $d_{i,j}$ between the two vertices represented by the nodes i and j that are connected by the edge. Afterwards, the node-root-distances $S_{i,r}$ to all root nodes r were calculated with Dijkstra's algorithm [5]. The distances were then added to the corresponding edge resulting in one weight for each root node per edge. The modified Prim algorithm was then executed like the classic one [5], except the tree contained all the root nodes at the start and considers the minimum of the multiple edge weights while growing. This way, multiple trees can be generated and they are growing outwards more evenly because of the growing weight with increasing distance to the corresponding root point.

The stimulation times t_a at the points representing the Purkinje-muscle junctions (PMJ) were calculated by detecting the leafs of the tree. To receive the path distance d the edge distances of the path from the individual leaf to the root were added up. With the time offset t_{offset} of the root node and the conduction velocity v_p the activation times t_a were calculated: $t_a = \frac{d}{v_c} + t_{offset}$. Figure 2 B shows a generated Purkinje system.

The resulting stimulation profile was then used as a trigger point list in a fast marching simulation with a fixed anisotropic myocardial conduction velocity v_m of $800 \frac{mm}{s}$ to obtain the activation times of the ventricles as seen in figure 2 C. The fast marching algorithm is a graph-based algorithm to solve the Eikonal equation with the anisotropy tensor G :

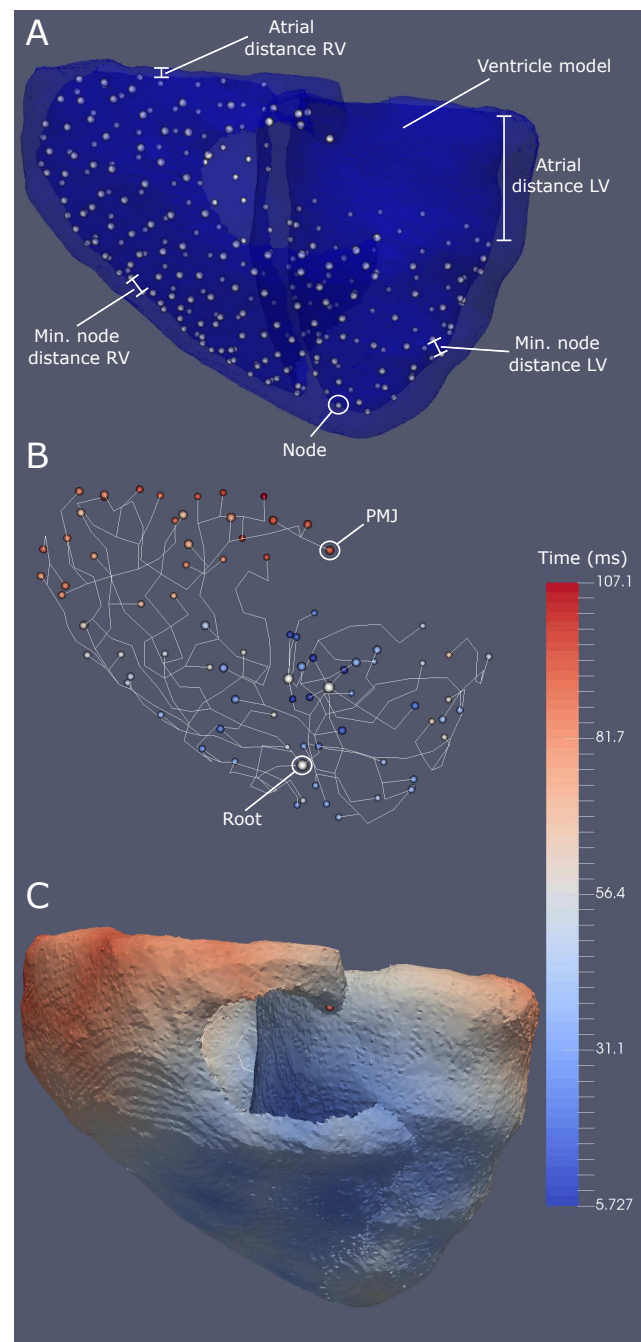


Figure 2: A: The ventricle model (blue) with distributed nodes (white) according to the parameters atrial distance and node distance. B: Generated Purkinje system with the root nodes (white) and PMJs with activation times (red-blue color scale) determined through the parameters conduction velocity and time offset of the root. C: Activation times of the ventricular myocardium obtained through fast marching simulation.

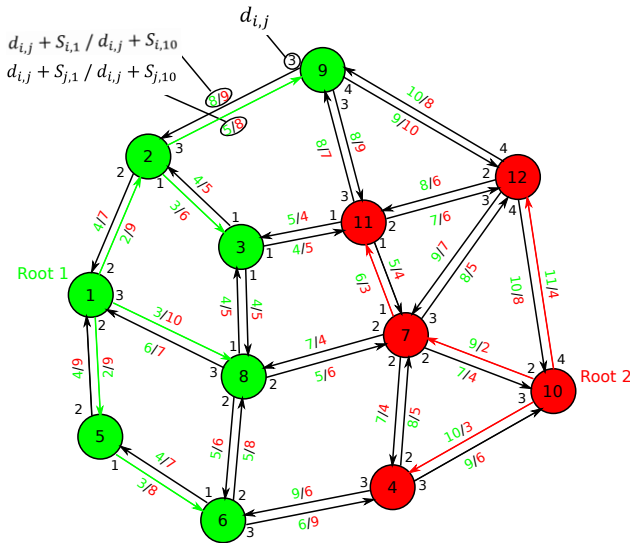


Figure 3: A graph consisting of nodes 1-12 with the chosen root nodes 1 (green) and 10 (red). The multiple edge weights are the result of adding the minimal path of each node to each root to the outgoing edges of the node. After execution of the modified Prim algorithm, the results are two trees grown outwards from root 1 and root 2.

$v_m \sqrt{\nabla t_a G \nabla t_a} = 1$, which describes the excitation wave. The algorithm is efficient because it takes advantage of the causality relationship between nodes [4].

The gradient of the membrane voltage V_m induces a volume current which is the source of the extracellular surface potential measured as the ECG. V_m was modelled with pre-described ventricular action potentials triggered for each vertex on the unstructured grid at the calculated activation time. The ECG was calculated with the finite element method. A lead field matrix was generated by solving the problem for all possible sources. This way, the forward problem could be reduced to a matrix multiplication.

2.2 Parameter optimization

With the described fast method to calculate the simulated ECG with a set of parameters, several optimization algorithms were tested with the cost function of the RMSE between the simulated and measured 12-lead ECG. The problem has several constraints, as for example the atrial distance must be smaller than the ventricle height. To leverage unconstrained parameter optimization algorithms, a parameter transformation was applied. All parameters could be transformed into the constraints with a closed interval $[a, b]$ transformation [7]: $y = \frac{a+b}{2} + \frac{a-b}{2} \cdot \sin(x)$.

Simplex algorithms [6] could be successfully executed but ended in different local minima due to the non-convex na-

ture of the problem. An improvement of the result could be achieved through repetitive multithreaded execution of simplex algorithms starting from random initial parameters.

3 Results

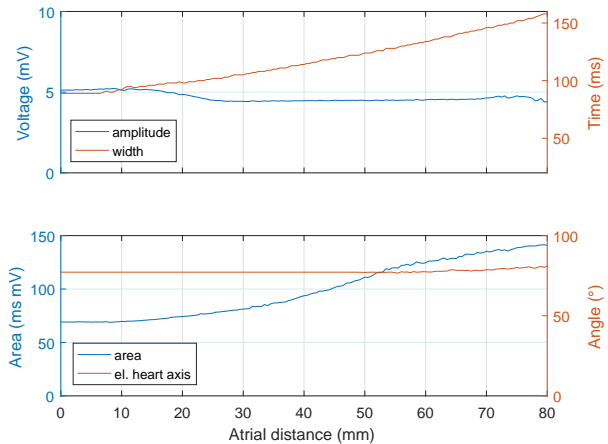


Figure 4: Atrial distance parameter effect on the amplitude, width and area of the the simulated QRS complex as well as on the electrical heart axis.

To study the effects of the Purkinje parameters on the morphology of the ECG, a reference system was generated and the ECG amplitude, width, absolute area, and electrical heart axis were computed as a function of the parameters. The main effects observed were:

- (i) Increased atrial distance caused higher width and area of the ECG (figure 4)
- (ii) Increased conduction velocity caused higher amplitude and lower width
- (iii) Root positions had some effect on the amplitude and the electrical heart axis

Our method required about 10 seconds for one cost function evaluation on a standard desktop machine. Simplex algorithms [6] were run successfully, were multithreaded and repetitively executed with one root on the endocardium of the LV and two on the RV as seen in figure 2 B. The system is the result of the optimization. The results were compared to compensate for the non-global nature of the simplex algorithm. Figure 5 shows the convergence behaviour and indicates the non-convex nature of this problem. Figure 6 shows the simulated and optimized 12-channel ECG in comparison to the

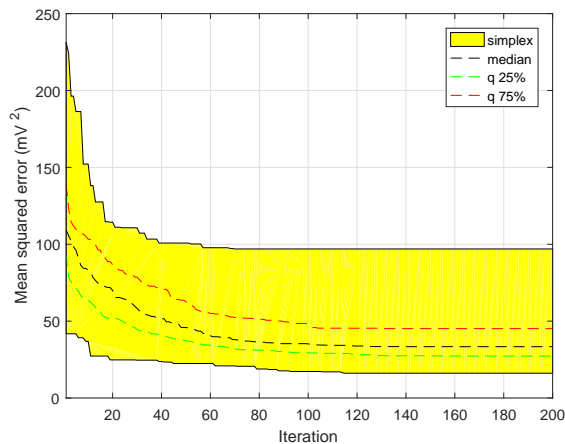


Figure 5: Convergence of 120 simplex algorithm executions (yellow) with median (black) and 25% (green) and 75% (red) quantiles.

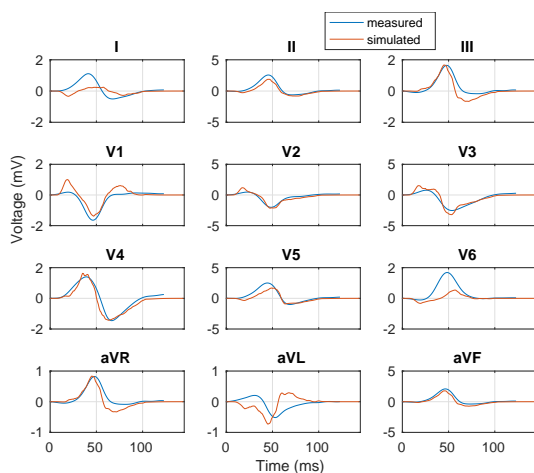


Figure 6: Optimized 12-channel QRS complex (red) in comparison with the original measured QRS complex (blue).

measured ECG. It is the result of 120 simplex runs and has a remaining RMSE of 4.05 mV. The calculation time was 16 hours on a 12-core machine.

4 Discussion

We successfully extended the previously published approach of tailoring Purkinje activation with a graph-based genera-

tion of parameterized trees [1]. The algorithm was modified to achieve more realistic trees by including the Dijkstra algorithm. This way, the trees do not shape as many meandering paths, which can lead to PMJs with activation times which occur later than the myocardial activation time. While single executions of simplex-based algorithms yielded bad results, a multithreaded work-around improved the results. Other global optimization algorithms like particle swarm weren't considered because of the conceivable very long execution time. A point to improve may be to add the conduction velocity of the myocardium as a parameter; this was not implemented because of the software architecture. All in all, our tool is suitable to automate and accelerate the time consuming process of modelling and customizing patient-specific Purkinje activation.

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