

# Inverse Estimation of Ventricular Purkinje Tree Pathways from Sequences of Depolarization

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## Abstract

*The electrical activation of the heart is a complex process that is essential for the understanding and treatment of several cardiac dysfunctions, such as ventricular tachycardia. Patient-specific local activation times (LAT) are usually obtained using electro-anatomical maps, however unveiling the underlying fast pathways formed by the Purkinje network remains a complex problem. We present a method based on differential geometry to estimate from a set of endocardium LATs, the locations on the endocardium with a potential number of Purkinje myocardial junctions, and the corresponding Purkinje branching structure. We evaluate our method on biophysical simulations using several Purkinje configurations. LAT errors of estimated Purkinje trees are in the order of 6 ms.*

## 1. Introduction

The information about the electrical sequence of activation of the heart of a given patient is crucial to evaluate its condition and plan several complex therapies such as cardiac resynchronization therapy, or radio frequency ablation [1]. Clinical doctors have tools such as electro-anatomical mapping systems to register the activity within the cavities of the heart and stratify patients to optimally plan the interventions [2]. Voltage maps and local activation time maps are among the most useful clinical sources of information. However information in those maps is often limited to a set of scattered measurements on the endocardium (< 300-900 samples). Computer simulations of cardiac electrophysiology are a novel technology that can help in the understanding of cardiac diseases and provide additional information about the patient's heart condition [3], [4]. Nowadays, it is possible to reconstruct the patient-specific 3D cardiac geometry from MR or CT scans. In addition, specific cell and tissue models of cardiac electrophysiology allow simulating the electrical activity of the heart in normal and pathological

conditions. Still, an important challenge in cardiac modeling is that some key structures of the heart such as the cardiac conduction system (CCS) cannot be reconstructed from in-vivo data. The CCS has a primary role in the sequence of activation of the ventricles and is involved in several cardiac diseases such as fascicular ventricular tachycardia (VT) [5], [6], or left bundle branch block. For that reason researchers have developed methods to incorporate generic CCS in their ventricular models in order to improve the realism of their simulations. Among the techniques used to build the CCS there are: manual delineation of branches, fractal models [7], rule based models [8] or segmentation of free-running sections from high-resolution ex-vivo images [9]. Others have developed rule-based CCS models constrained by population ex-vivo animal data to construct realistic geometries [8]. None of these techniques provide a patient specific CCS model from in-vivo clinical data that will be very useful to plan clinical interventions.

In this paper we present a novel methodology to estimate the Purkinje tree (PKT) conduction pathways from endocardial LAT maps. The methodology is based on differential geometry principles. The method first estimates the location and number of Purkinje-myocardial junctions (PMJs) that are the only connection points between the CCS and the working myocardium. Following, it estimates the PKT structure taking into account the geometry of the endocardium, the LAT map and the estimated PMJs. To validate the technique four biophysical simulations with different CCS configurations were constructed. LAT maps obtained from simulations were used to estimate the original PMJs and PKTs. Results show that estimations were in agreement with the original data.

## 2. Material and methods

### 2.1. Estimation of Purkinje trees

Given an electrophysiological map consisting of a set of points on a mesh for which the local activation time (LAT) is known, we inversely estimate the location of

PMJs and the structure of a potential PKT.

Let define the surface mesh  $S$ , a Riemmanian manifold, and the LAT map,  $\psi_{z_i}: S \rightarrow R$ , which is a point distance field from the points  $z_i$  to  $\psi_{z_i}$ . Points  $z_i$  are the PMJs that can be modeled as a special type of points called *critical points*. These points are those where the lines following the gradient of  $\psi_z$  converge (sink points) or diverge (source points), or where there is a singularity (see Figure 1). Therefore, they can be detected by exploiting their non-differentiability.

In particular, we will calculate the discrete lateral derivatives in our discretized mesh and check that at critical points they differ more than a threshold  $\epsilon$ .

Once critical points are detected, i.e. PMJs, we estimate a PKT that can produce an activation similar to that observed in the data. In particular, we define a weighted map  $\psi(x) \forall x \in S$  and search for the shortest geodesic weighted paths that will form the branches between PMJs of the PKT. More formally we define the shortest geodesic path from  $y$  to a set of points  $z_i$  as,

$$\Gamma_{\psi, z_i, y} = \underset{\gamma}{\operatorname{argmin}} \{L_{\psi}(\gamma) : \gamma(0) = y, \gamma(1) \in \{z_i\}\},$$

where the curves are parameterized in the interval  $[0, 1]$  by the parameter  $s$ , and  $L_{\psi}(\gamma)$  is the weighted length of the curve  $\gamma$ ,

$$L_{\psi}(\gamma) = \int_0^1 \psi(\gamma(s)) \|\gamma'(s)\| ds$$

Finally,  $\Gamma_{\psi, z_i, y}$  can be obtained as the set of points that satisfy the ordinary differential equation (backtracking equation),

$$\frac{d}{ds} \Gamma_{\psi, z_i, y}(s) = \nabla_S \phi(x),$$

with Dirichlet boundary conditions  $\Gamma_{\psi, z_i, y}(0) = y$ ,  $\Gamma_{\psi, z_i, y}(1) = z$ , where  $z$  is the closest point to  $y$  among all  $z_i$ , and where  $\nabla_S \phi$  denotes the gradient computed on the surface points). Note that the critical points, PMJs, will be mainly used as starting or end points for  $\nabla_S \phi$ .

The PKT is therefore constructed connecting first the earliest PMJ detected to a point manually defined at the His Bundle, and then connecting each detected PMJs to the previous ones, or to the already constructed tree, traversing them in ascending chronological order. As explained above, each connection is performed computing geodesic paths.

Since the PMJs location and the corresponding LAT map will influence the paths of the PKT branches, the weighted maps can be adapted to indicate how much we rely on their underlying information. Here we choose as weighted map  $\psi_{ref}(x)$  the inverted LAT map normalized in the interval  $[0, 1]$ . Therefore, PKT branches will be attracted to regions with lower LAT, which are those activated earlier.

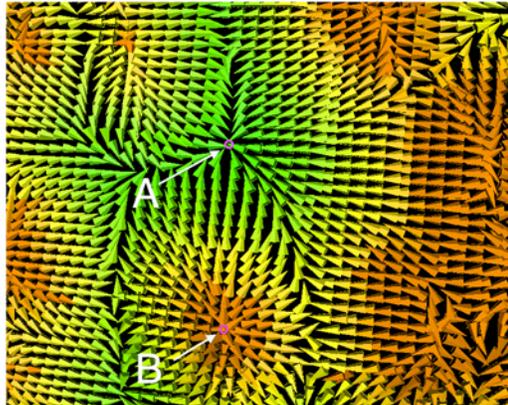


Figure 1. Small patch of the endocardium. Critical points detected are marked with white arrows. A corresponds to a sink critical point and B to a source critical point. The remaining arrows display the vector field calculated from the LAT map at every node of the endocardial mesh.

## 2.2. Biophysical modelling

A ventricular model was built to produce realistic electrophysiological maps that served as an input for the CCS estimation algorithm. The geometry was segmented from a CT scan of an adult human with non-structural disease. A biventricular mesh of triangles was obtained and subsequently meshed with linear hexahedral elements (voxels) with a resolution of 0.4 mm. Following the fibre orientation was calculated at the centroid of each element using an equation based on Streeter's findings [10]. Four different Purkinje networks were grown on the endocardium of the model using the approach described in [8]. The rules used to construct the Purkinje networks were varied to produce different configurations and test the accuracy of the estimation algorithm. Once the geometrical model was constructed, we simulated the electrical activation with the solver Elvira [11] using the monodomain formulation, coupled to the Ten Tusscher model for the cellular ion kinetics in the working myocardial cells and the Stewart model for the Purkinje cells. A single stimulus was given to the His Bundle, which rapidly propagated through the CCS (2-4 m/s) and passed to the working myocardium at PMJ junctions, synchronously activating most of the endocardium. Finally the LAT map for each node in the model was obtained. Figure 2 shows the resulting simulation in a biventricular mesh, where only the endocardium is displayed together with the CCS. Early activated areas correspond to regions with PMJs, being those closer to the His bundle the ones that activated first. The base of the left ventricle is the latest activated region.

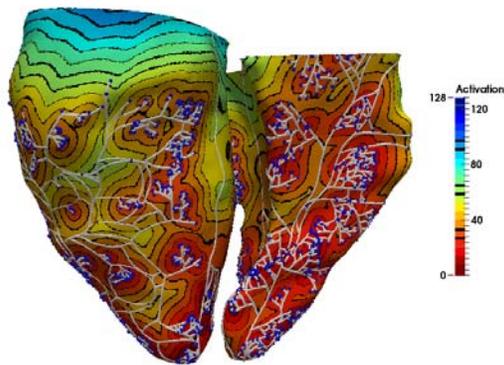


Figure 2. Endocardium of a biventricular human heart model including a CCS automatically generated (white lines) and PMJs (blue spheres). Colours correspond to local activation times in milliseconds.

### 3. Results

Four different simulations were performed to obtain the LAT maps required for the estimation procedure. The method did not require any information regarding location of original PMJs or branches of the CCS, with exception of the approximate position of the His Bundle. Only information of LATs on the endocardium was provided, and the rest of the volumetric information was only used for validation purposes (see Figure 4).

Firstly, the PMJs were estimated from the LAT maps. Different values of the threshold  $\epsilon$  were used, and the distance from the original PMJs to the estimated ones measured. The best results were obtained for values of  $\epsilon$  in the range [60, 80], with errors around 0.1 cm on average. In all the cases there was a clear trend, the number of PMJs recovered was around half the number in the original tree.

Following, the algorithm connected the detected PMJs taking into account the underlying geometry of the endocardium, the LAT map and the location of the His Bundle. Figure 3 shows the PMJs and the PKTs estimated from the LAT map displayed. The original PMJs and PKT can be observed in Figure 2. As can be observed the PKTs joined the PMJs following the red areas (earliest activated), and generated several branches among isolated regions. The morphology of the estimated PKT differed from that of the original CCS, although the location of PMJ dense regions was properly estimated.

Once all the PKTs were estimated, new simulations were performed with those trees and the LAT maps were compared with the original ones.

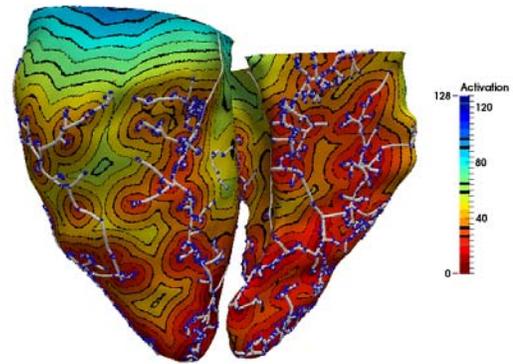
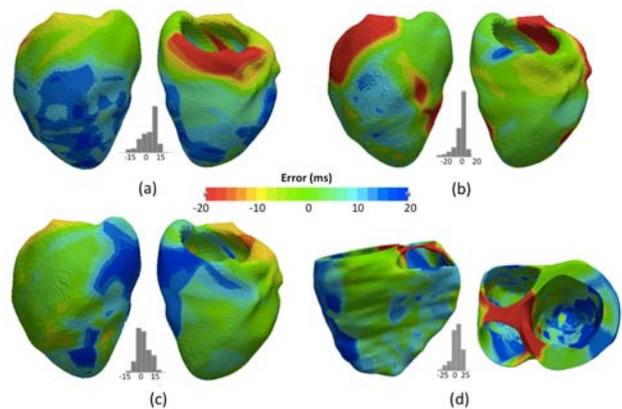


Figure 3. Estimation of the CCS. Blue spheres are the PMJs estimated from the underlying original LAT map. White branches correspond to the optimal PKT encountered for the combination of LAT and PMJs estimated.

Although only information about the endocardial LATs was used for the estimation, both the endocardium and epicardium LATs were used to check the estimation error. Figure 4 shows the LAT errors (only epicardium visible) of the four models using a colormap, together with the corresponding histogram distribution. Errors were centered in zero and had a maximum absolute difference error between original and estimated case of 20 ms (either earlier or later). Basal regions showed the highest errors for all the CCS models estimated.



4: Errors in the endocardium and epicardium of electrical simulations performed in four geometrical models with estimated CCS. Colors correspond to the difference between original LAT and the LAT obtained after simulating with the estimated CCS. Times are in milliseconds.

## 4. Discussion and conclusions

The method presented for the estimation of preferential conduction pathways, PKTs, and the connection of them to the myocardium, PMJs, successfully estimated the underlying CCS from different LAT maps. The resulting trees were not equal to the original ones, since this is a pose inverse problem in which different CCS configurations could produce the same resulting LAT map. However, the estimated PKTs could reproduce functionally the LAT maps of the original simulations. This solution can provide better results than the use of generic CCS models that do not correspond to a specific patient. Errors were in the order of 10 ms with maximum values of 20 ms. The location of the PMJs was correctly estimated, although they were systematically underestimated with a ratio 2:1. This effect is due to the close distance between the PMJs in the original tree, which makes many of them functionally “invisible”, and has a very small impact in the activation sequence.

It is important to point out that estimations were performed with highly dense LAT maps where accurate information at every point in the endocardium is available. When applied to real clinical data, only a few points will have real data, while most of the information will be interpolated. This is expected to impact the precision of the PMJ detection and the subsequent construction of the PKTs. In addition, this method is only able to construct tree configurations, and it is known that the CCS forms extensive redundant networks.

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