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Reintegration of an endocardial Purkinje system into an anatomically realistic 3D rabbit ventricular geometry

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Abstract

A major contributor to the formation and maintenance of cardiac arrhythmias is strongly suspected to be the specialized conduction system of the ventricles, referred to as the Purkinje system (PS). The PS is known to be potentially pro-arrhythmic under various conditions, e.g. shock-induced arrhythmogenesis or failure of defibrillation. Surprisingly, most experimental, as well as computational studies neglect the effects of the PS. Experimental techniques are hampered to resolve the electrical behavior confined to the depth of the ventricles with sufficient spatio-temporal accuracy. Anatomically realistic cardiac computer models have been developed recently, however, without the specialized conduction system. Computer models might bridge the gap between experimental observations and electrical events occurring at the ventricular myocardium or within the ventricular walls. The objective of this research is to provide a mathematical framework to incorporate an existing, literature-based Purkinje topology into a recent anatomically realistic geometry of the rabbit ventricles. An affine transformation matrix was determined on the basis of four manually selected vertices in the existing Purkinje network and their pendants in the target geometry. The entire Purkinje network was then transformed for each cavity separately and finally mapped onto the underlying myocardial grid employing an octree based method.

1 Introduction

The Purkinje system (PS) is an accumulation of specialized cells which form a network-like structure within the endocardial ventricular surfaces. The electrical pacemaker signals are channeled and rapidly distributed in the heart which permits its organized electrical activity. The network is electrically isolated from the myocardium except at discrete endpoints (Purkinje-myocardial junctions).

Cardiovascular diseases are the most frequent cause of death in the industrialized world; in the vast majority of the cases the cause of death is attributed to an arrhythmogenic event. A major factor in the formation and maintenance of cardiac arrhythmias is the specialized conduction system of the ventricles, the PS. The PS is known to be potentially pro-arrhythmic under various conditions including shock-induced arrhythmogenesis, failure of defibrillation shocks or arrhythmias induced by focal activation. Despite decades of research, today's clinically available and therapeutical options are, at best, sub-optimal. Almost all therapies are rather palliative than curative and, depending on the metrics used, such as improvement in quality of life, increase of life expectancy, severeness of detrimental side effects or cost effectiveness, a poor performance is common to all approaches. Depending on the classification of an arrhythmia [1] various outcomes are possible ranging from moderate impairments of quality of life to immediately life-threatening conditions such as ventricular fibrillation with sudden cardiac death as endpoint. Hence, it is not surprising, that cardiac arrhythmias are among the most important causes for medical interventions in European countries [2] and the most frequent reason for hospitalization in the US [3].

Surprisingly, most studies, both experimental as well as computational, quite often neglect the PS effects. While recent advances in experimental methodology have provided new characterizations of tissue responses to externally applied electric fields, mechanistic inquiry into the biophysics of arrhythmogenesis or defibrillation is hampered by the inability of current experimental techniques to resolve, with sufficient accuracy, the electrical behavior confined to the depth of the ventricles or in the PS. Computer models quite naturally suggest themselves as a surrogate technique to bridge the gap between experimental observations, typically recorded at the epicardial surface of the heart, and electrical events occurring within the PS, at the ventricular endocardium or within the depth of ventricular walls. Despite major recent advancements in modeling technology [4], integrating topologically realistic models of the PS with anatomically realistic models of the ventricles remains to be challenging.

The overall goal of this research is, to bring a new level of understanding of the topological organization of the PS in the rabbit ventricles and its role in the formation of arrhythmias. Acquiring experimental data of the PS requires highly skilled techniques and has not yet been available. However, there is a simplified model of the rabbit ventricles available (see Figure 1, left) [8], which incorporates a literature-based PS [5].
As an intermediate step, a mathematical modeling method is developed to reintegrate the existing endocardial PS

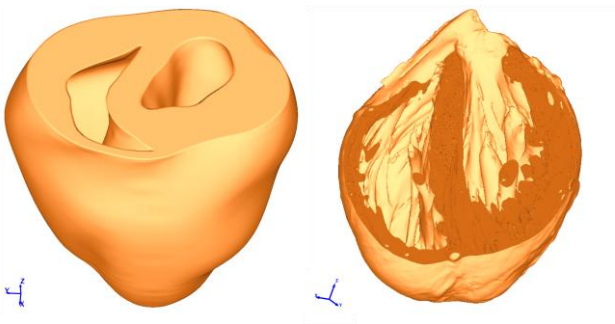

Figure 1 The Purkinje system (not shown here) developed for a less-detailed computer model of the San Diego rabbit ventricles [8] (left) served as the basis for the transformation into a recent anatomically highly realistic and electrophysiologically more significant computer model (right) [6].

into an anatomically highly detailed and thus more significant representation of rabbit ventricles [6, 7] (see Figure 1, right).

2 Materials and Methods

2.1 Computer Modeling

The mathematical technique to integrate an endocardial PS into a different finite element model of the same mammalian is based on the following datasets:

2.1.1 Computer Model with Simplified Geometry

The myocardial mesh was a re-meshed version of the San Diego rabbit ventricles [8], which had been used in numerous studies [9,10]. The intracellular domain, representing cardiac tissue, comprised 547,680 nodes. The extracellular domain, representing bath, blood, and interstitial fluid, was made up of 862,515 nodes. Minimum, mean and maximum discretization of the finite elements were 37.1 µm, 279.0 µm and 635.1 µm, respectively [10].

The PS model used was a branching network of 1D cubic Hermite elements (1712 nodes) separated by discrete gap junctions [5]. Each segment of the PS was represented as a pair of two numbers forming a line segment. The underlying PS served as the basis for the reiteration into the consecutively described finite element mesh.

2.1.2 Anatomically Realistic Computer Model of Rabbit Ventricles

Based on high-resolution structural and diffusion tensor magnetic resonance (DTMR), an anatomically realistic computer model of rabbit ventricles was developed in a previous study [6]. The intracellular and the extracellular domain comprised 4.233,818 nodes and 6.775,307, respectively. Minimum, mean and maximum discretizations of the finite elements were 3.1 µm, 102.0 µm and 243.4 µm, respectively.

The free-running PS and points where the PS entered the myocardium were identified and incorporated into the computer model [7]. Due to the image acquisition modality, DTMR imaging, the reconstruction of the endocardial PS was not possible and remained missing.

2.2 Transformation of the Purkinje Network between Arbitrary Grids

Although the cardiac anatomy of the same mammalian heart was present, the inter-subject variability with respect to the shape of the ventricles required the implementation of a general affine transformation. Such transformation

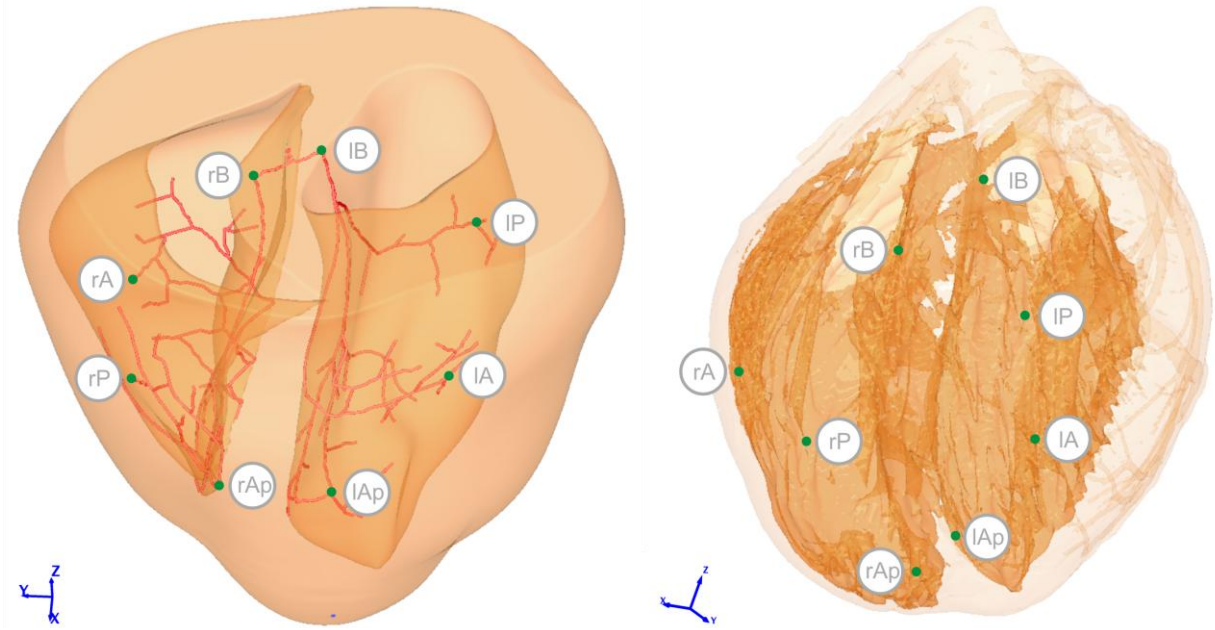

Figure 2 Four vertices in the published Purkinje network of a rabbit ventricular geometry (left) and their counterparts in the target coordinates system (right) were manually selected to sufficiently determine the affine transformation between both finite element grids. '*r**' and '*l**' denote the right and left endocardial cavity; vertices were selected at the apex (**Ap*), the base (**b*), the anterior (**A*) and posterior (**P*) endocardial wall.

matrix has the following form:

$$\begin{bmatrix} P'_{1x} & P'_{2x} & P'_{3x} & P'_{4x} \\ P'_{1y} & P'_{2y} & P'_{3y} & P'_{4y} \\ P'_{1z} & P'_{2z} & P'_{3z} & P'_{4z} \\ 1 & 1 & 1 & 1 \end{bmatrix} = \begin{bmatrix} a_{11} & a_{12} & a_{13} & a_{14} \\ a_{12} & a_{22} & a_{23} & a_{24} \\ a_{13} & a_{23} & a_{33} & a_{34} \\ 0 & 0 & 0 & 1 \end{bmatrix} . \begin{bmatrix} P_{1x} & P_{2x} & P_{3x} & P_{4x} \\ P_{1y} & P_{2y} & P_{3y} & P_{4y} \\ P_{1z} & P_{2z} & P_{3z} & P_{4z} \\ 1 & 1 & 1 & 1 \end{bmatrix},$$

$$\boldsymbol{P}' = \boldsymbol{A} \cdot \boldsymbol{P},$$

where **P** is the matrix of selected vertices in the source coordinates system and **P'** the matrix of vertices in the target coordinates system after transformation; **A** denotes to the transformation matrix.

Four vertices were manually selected at positions near to the base, near to the apex, at the anterior wall and at the posterior endocardial wall within the left and the right ventricle (see Figure 2, left). The corresponding counterparts were manually determined in the anatomically realistic computer model (see Figure 2, right).

Employing basic matrix inversion,

$$\boldsymbol{A} = \boldsymbol{P}' \cdot \boldsymbol{P}^{-1},$$

yielded in the transformation matrix **A**, which subsequently was applied to the entire Purkinje network in the source coordinates system.

2.3 Octree-Based Mapping onto Underlying Finite Element Grid

The coordinates forming the segments of the PS were, after the transformation, merged into the finite element grid employing an octree as the basic data structure. Each cell of the octree cell represented a cube in 3-D space, which was refined till the discretization fell below the mean discretization of the finite elements in the target grid. Intrinsic to the data structure is the ability to quickly find neighboring vertices and elements. Thus, the transformed Purkinje network was mapped onto the high-resolution computer model of the rabbit ventricles.

3 Results

A literature based Purkinje network [5], which was previously implemented for the San Diego rabbit ventricles [8], was successfully transformed into an anatomically realistic computer model of the same species employing general affine transformations in 3D and finally mapped onto the underlying grid making use of an octree method (see Figure 3).

4 Discussion

The PS is of particular interest in the treatment of ventricular arrhythmias. Clinical techniques, e.g. clinical mapping are currently limited in their ability to determine the underlying mechanisms with sufficient spatiotemporal discretization. 3D computer models of the heart have increased their complexity steadily [4, 7]. However, an important feature which describes the electrical activation pathways has been missing so far or has solely been available for anatomically less significant geometries.

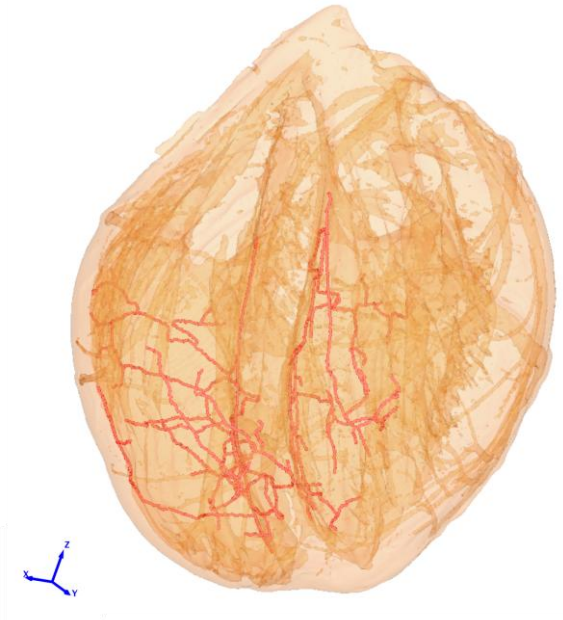

Figure 3 Semi-transparent surfaces of the high resolution computer model of the rabbit ventricles unveil the Purkinje system mapped from literature-based source data.

The proposed research provides a mathematical method to overcome this shortcoming and describes the reintegration of an existing endocardial PS into arbitrary 3D ventricular geometries.

It has to be noted, that general affine transformations not only apply rotation and translation with respect to an object, the object also might be exposed to shearing and scaling. Consequently, lengths and angles between Purkinje segments might be altered by the affine transformation. However, the important topology of the network remains preserved.

Obtaining the endocardial PS from histological images is being focused on in the ongoing research. Since the data has not been available yet, subsequent computer studies will rely on the PS developed as described above.

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