Interactive Simulation of the Activation Sequence: replacing Effect by Cause

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Abstract

Electrocardiographic wave forms during the QRS interval reflect the activation sequence of the heart. This can be demonstrated in ECGSIM, an interactive software package aimed to support ECG education and research. When using this package, the timing of activation may be changed interactively, either locally or globally. The resulting QRS changes are displayed instantaneously.

We describe a new feature which permits the user to interactively change of the spatial distribution of the propagation velocity. This new feature enhances the teaching and research capabilities of ECGSIM, e.g. for simulating the activation under ischemic circumstances or during ectopic activation, and investigate the interaction between the Purkinje system and the myocardial tissue.

1. Introduction

An important feature of the electrical activation sequence of the heart is the sites of initial activity (foci). During normal activity the locations of the foci are the bundle branches and the terminal points of the Purkinje system. The subsequent spread of activation is governed by the propagation velocity within the myocardium, which is largely a passive tissue property reflecting the electric cell to cell coupling [1].

In a recent paper [2], we have shown that highly realistic activation sequences can be generated by defining a limited numbers of initiation (focus-like) sites in a numerical model of the propagation within the myocardium. The propagation was simulated by the fastest route algorithm (FRA), in which the spatial distribution of the (anisotropic) propagation velocity was taken to be uniform. Since then, we have tested an additional feature that enables the user to interactively define the propagation velocity locally or globally, and consequently the effect: the timing of activation. This new feature will be implemented in ECGSIM (version 2.2.0). ECGSIM can be downloaded, free of charge, from www.ecgsim.org.
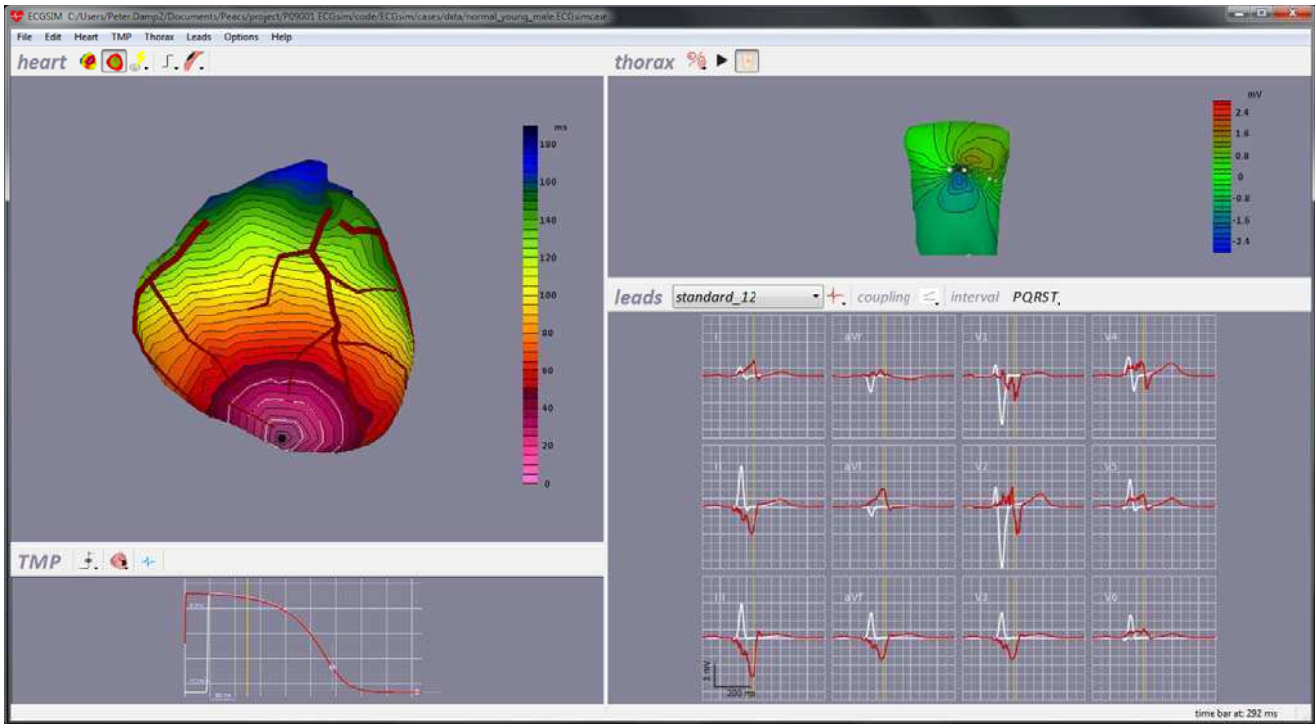
2. Methods

ECGSIM is based on a biophysical model that links the local transmembrane potential (TMP) at the surface bounding the myocardial tissue to the ECG. It includes atrial, ventricular and torso geometries, reconstructed from human magnetic resonance images [3, 4].

The source model used is the equivalent double layer (EDL). This expresses the entire electrical activity within the atria or ventricles by means of a double layer source situated on the closed surface bounding either the atrial or the ventricular myocardium. For any position on the surface (node), the time course of the local EDL source strength is taken to be proportional to the TMP, $V_m(t)$, of the nearby myocytes [5,6]. Any of 7 parameters are used to describe the TMP analytically. All of these, including the local timing of local depolarization, can be changed interactively.

The propagation is implemented by means of the FRA. as described by van Dam et al. [2]. In short: the FRA is based on an adjacency matrix comprising all connections between the nodes of the model heart. Given the lengths of the connections, and by assigning the propagation velocity along them, the traveling time along each connection is specified. Subsequently the shortest path algorithm [7] is used to compute the timing of activation at all nodes initiated from just one or several foci, in which the activation initiated from multiple sites is found from the rule: first come first served.

In release 2.1.0 of ECGSIM the values of the propagation velocities along each connection were spatially uniform. This paper demonstrates the results of the implementation in which their spatial distribution can be changed interactively, essentially in the same manner as for the source parameters.

Each node can be marked as focus (see Figure 2). The activation time of the focus can be adjusted. Two specialized buttons are available to the user: 1) by using the *ectopic* button an activation wave is generated that originates only from the selected node. 2) The button "*activate transmural*" activates a focus on the opposite
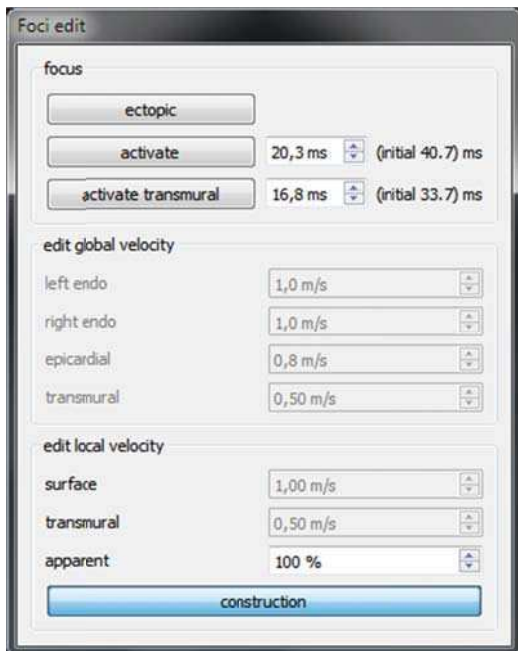
Figure 2. Floating Foci edit window: The parameters used to add or remove foci or change the propagation velocity globally or locally (within the zone indicated by the white circles in the upper-left panel of Figure 1). The operation mode can be switched between construction/manipulation.
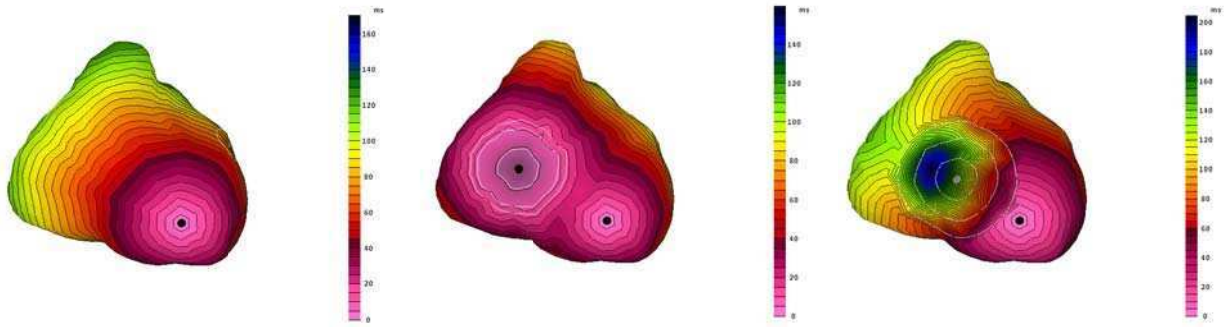
a focus on the opposite wall. This button enables the user to investigate the influence of activation from either an endo- or epicardial node at the same region.

In addition to the ECGSIM mode in which the user manipulates the local activation times, the new version ECGSIM has two new modes: the *construction* and the *adaptation* mode.

In the *construction* mode ECGSIM a simple propagation model is used to construct the activation times from foci set by the user (see Figure 2). In this mode the default (global) intrinsic, cell coupling-based, propagation velocity can be set for the left endocardial, right endocardial or epicardial surface, as well as transmuraly. Subsequently, the velocities can be modified locally within a selected zone (white circles Figure 3).

In the *adaption* mode ECGSIM reconstructs foci and propagation velocities between nodes that reproduce a given activation sequence [2], from whatever source (e.g. inverse computations [8]). The user can than manipulate the local propagation velocity and observe the resulting activation sequence.

The apparent propagation velocities that result from this method are reconstructed by this method do not necessarily correspond to the intrinsic tissue-based values. For instance, 2 adjacent nodes might be activated by the Purkinje system at approximately the same time. In

the implementation shown in this paper, percentile changes in the apparent velocity were introduced.

3. Construction of activation

The construction of an activation wave requires the definition of at least one focus, and the velocity for each connection within the triangulated geometry of the heart. Figure 3 shows three examples of the basic principles of the construction of activation waves. The most simple activation pattern is generated by a single focus with a fixed propagation velocity (Figure 1 left panel). The middle panel shows the result when a focus is added. The area near the second focus is given a propagation velocity of 2 m/s resulting in more rapid spread of activation in the selected zone. In the last panel the propagation velocity is drastically reduced in the selected zone, resulting in an activation washing around the selected area and changing also the activation outside the selected area. Note that the latest activated area is not in the center of the zone, which is as expected because the activation enters the zone from one side.
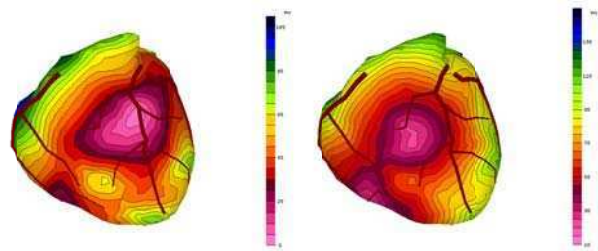
4. Adaptation of activation

Two examples of the use of the adaptation mode are given in this section. In the first example the original activation has been modified by just deactivation of the foci reconstructed in the left ventricle. This situation mimics the left bundle branch block situation (see Figure 4). This only changes the activation in the left ventricle, because the activation is now initiated only by the foci that were reconstructed in the right ventricle. In this example no velocity values were changed.

In the second example the activation is adapted such that a typical Brugada syndrome (BrS) ECG is obtained [8]. The underlying pathophysiological mechanisms responsible for BrS ECG patterns are still debated [9]. Here the hypothesis was tested that a locally delayed activation causes the typical ECG patterns. We selected an area on the epicardium of the outflow tract (near V2, see Figure 5). In this area (radius 18 mm) the propagation velocity was reduced by 80%, resulting in a significant later activated area on the epicardium. The action potential duration was maintained, i.e. the local timing of repolarization was delayed too. The resulting ECG shows a clear ST shift in lead V2 and a negative T wave.

Figure 5. The simulation of Brugada syndrome ECGs based on the delayed activated hypothesis. In a limited area the propagation velocity was reduced by 80% (area indicated by white circles). The remaining part of the heart was kept at the original, apparent propagation velocity. The action potential duration was kept constant. In lead V2 the ST shift and negative T wave are clearly visible (red lines in the ECG). The reference ECG is indicated in black.

5.   Discussion

This paper focuses on changing the local activation parameter in a physiological manner, i.e. manipulation of the propagation velocity instead of the sole the timing of depolarization.

Where earlier versions of ECGSIM only allowed the user to manipulate existing activation patterns, the new version enables the user to construct activation patterns, originating from several foci and the manipulation of the local propagation velocity. In this way the dynamic properties of the propagating activation wave can be taken into account, such as the wave washing around an ischemic zone with reduced propagation velocity.

We hope this new feature will help researchers and teachers to visualize the complex interplay between the activation of the heart and the resulting ECG.

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