

# Clustering of Re-entry Close to Scar Boundaries in Ventricular Tissue during Simulated Ventricular Fibrillation

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## Abstract

*Scar tissue in the ventricles can act as a source of anatomical re-entry. However, the interaction of scar with complex activation during ventricular fibrillation (VF) is not well understood. In this study we investigated how simulated scars influence clustering of re-entry filaments in simplified computational models. In a slab geometry representing the ventricular wall, the number of filament voxels spiked to around 5 times the mean value in normal tissue close to the scar boundary. In a surviving epicardial layer, the number of filament voxels was around one fifth of the mean. In contrast, the number of epicardial phase singularities showed no spike close to the boundary. In an ellipsoid geometry we observed more clustering of filament voxels when the radius of the scar is increased. This study shows that the scar is able to pin re-entrant filaments, but that this effect may not be manifest as clustering of phase singularities on the tissue surface.*

## 1. Introduction

Ventricular Fibrillation (VF) is a cardiac arrhythmia, which is a medical emergency. Early experimental studies provided evidence that the mechanism of VF is consistent with multiple waves of re-entry [1]. Re-entry forms spiral waves of activity in 2D and scroll waves in 3D. In 2D the core of a spiral wave is a point of phase singularity (PS) and in 3D it is a line of phase singularity called a filament. The complexity of the wave patterns during VF can be understood by knowing the behaviour, motion, and configuration of filaments.

Many patients with VF have pre-existing scar resulting from a prior myocardial infarction. Scar tissue in the ventricles can act as a source of anatomical re-entry, and to pin re-entrant filaments [1], but the effect of scar tissue on filament stability is not well understood and is difficult to investigate experimentally. The aim of this study was therefore to use a computational model of cardiac tissue electrophysiology to examine how simulated scars influence the clustering of re-entrant filaments.

## 2. Methods

### 2.1. Cell model

A simplified model of human ventricular electrophysiology [2] was used. This phenomenological model was chosen because it reproduces the action potential shape, action potential duration (APD), and rate dependence of APD. These are compatible with ionic models based on Hodgkin Huxley formulations, and also with experimental studies. An important advantage of the phenomenological model is that it is much less time consuming to solve compared with detailed ionic models [3].

For endocardial cells the parameter set described in the original paper [2] was used. Two variants of the epicardial cell model were used, based on the parameters in the original paper [2]. The first variant (epiMod1) supported unstable re-entry, but had relatively flat action potential duration (APD) restitution. The second variant (epiMod2) had steeper APD restitution resulting in more unstable re-entry. For the variant epiMod1 the parameter  $\tau_{v1}$  was changed from 60.0 to 10.0, and  $\tau_{v2}$  was changed from 1150.0 to 20.0. In epiMod2,  $\tau_{v1}$  and  $\tau_{v2}$  were changed as for epiMod1, and in addition  $\tau_{s01}$  was changed from 30.0181 to 28.0, and  $\tau_{s2}$  from 16.0 to 40.0.

### 2.2. Tissue model and numerical method

We used a monodomain tissue model [3] with anisotropic diffusion. The diffusion coefficients were  $0.001 \text{ cm}^2\text{ms}^{-1}$  along fibres and  $0.00025 \text{ cm}^2\text{ms}^{-1}$  across fibres. The membrane capacitance was set to  $1 \text{ }\mu\text{Fcm}^{-2}$ . The model was solved using an explicit finite difference method with no-flux boundary conditions imposed on each face. The time step to solve the model was 0.005 ms and the space step 0.02 cm.

Two 3D tissue geometries were used; a rectilinear slab (8.0 x 8.0 x 1.2 cm) representing a section through the wall of the left ventricle, and a half ellipsoid representing the left ventricle (base-apex 9.0 cm, wall thickness 1.1

cm). Both geometries incorporated the orientation of fibers, with  $120^\circ$  rotation between endocardial and epicardial surfaces. The rectilinear slab incorporated a layer of endocardial cells and a layer of epicardial cells, which were had either epiMod1 or epiMod2 parameters. The half-ellipsoid had uniform epicardial cells. A simulated scar region was incorporated in both geometries as described below.

The initial condition for each simulation was a single re-entrant wave with a transmural filament, implemented by stacking Archimedean spirals. Filaments were identified and tracked using methods described previously [4,5]. Each simulation had a duration of 2 s.

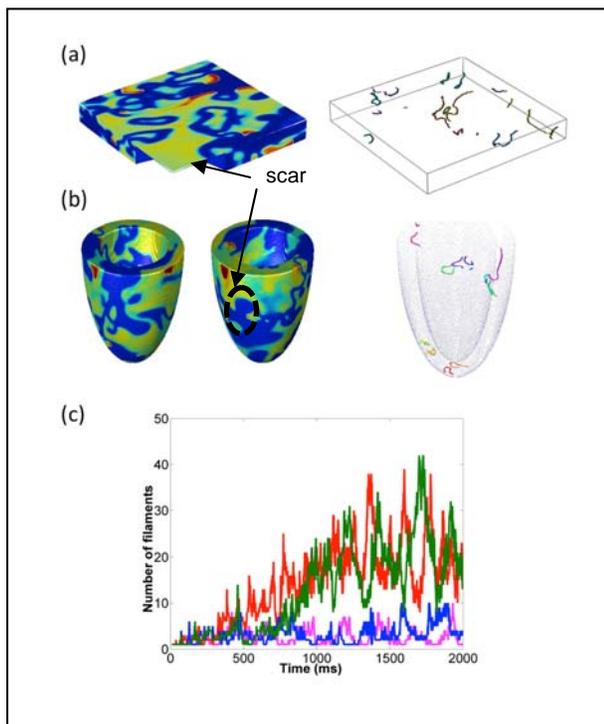


Figure 1. Snapshots of re-entry and corresponding filaments in (a) slab with epiMod2 dynamics at 1520 ms, (b) ellipsoid with half depth scar and epiMod2 dynamics at 1550ms, views of front and back. (c) Change in number of filaments over time (ms) for slab (red, pink) and ellipsoid (green, blue) with epiMod1 dynamics (pink, blue) and epiMod2 dynamics (red, green).

### 2.3. Scar region

Regions of scar were represented by a region of inexcitable but diffusively coupled tissue. In the slab geometry, this region was a quarter cylinder extending from the endocardium, with a thin layer of surviving

epicardial tissue. In the ellipsoid geometry, scars with full and half depth were represented by a cylindrical region of inexcitable but diffusively coupled tissue located in the middle of the wall (Figure 1).

## 3. Results

In each simulation the initial re-entrant wave broke up, resulting in complex re-entry typical of VF. The number of filaments and complexity of re-entry was higher for simulations with epiMod2 dynamics compared to those with epiMod1 dynamics, with an average of 13.4 filaments for slab and 15.5 for ellipsoid in epiMod2 (Figure 1). In both slab and ellipsoid geometries simulations with epiMod2 dynamics had a greater number of filaments than epiMod1 dynamics.

The density of filament voxels was computed by summing the filament voxels along an axis and through time, from snapshots taken every 2 ms throughout the 2000 ms simulation. In the slab geometry, filament voxels were distributed uniformly in normal tissue. However, close to the scar boundary in the slab geometry, the number of filament voxels spiked to around 5 times the mean value in normal tissue (Figure 2). In the surviving epicardial layer, the number of filament voxels was around one fifth of the mean. In contrast, the number of phase singularities on the epicardial surface showed no spike close to the boundary. A similar trend was observed in ellipsoid geometry (Figure 3), with greater clustering with a half depth scar compared to a full depth scar.

Increasing the radius of the half depth scar with epiMod2 dynamics resulted in more clustering near the scar region (Figure 4).

These observations show that the simulated scar is a potent focus for re-entrant filaments during simulated VF.

## 4. Discussion and conclusions

In this study, we have used a computational model of human cells and tissue to examine how re-entrant activity during simulated VF is modified by the presence of scar. In a slab geometry representing a section through the ventricular wall, and an ellipsoid geometry representing the left ventricle, re-entrant filaments tended to cluster close to the boundary between scar tissue and normal tissue. However, if there was a surviving region of tissue, this clustering was not always evident on the epicardial surface.

This study has several limitations resulting from our simplified model of structure and function. We used a simplified model of cardiac anatomy, with smooth

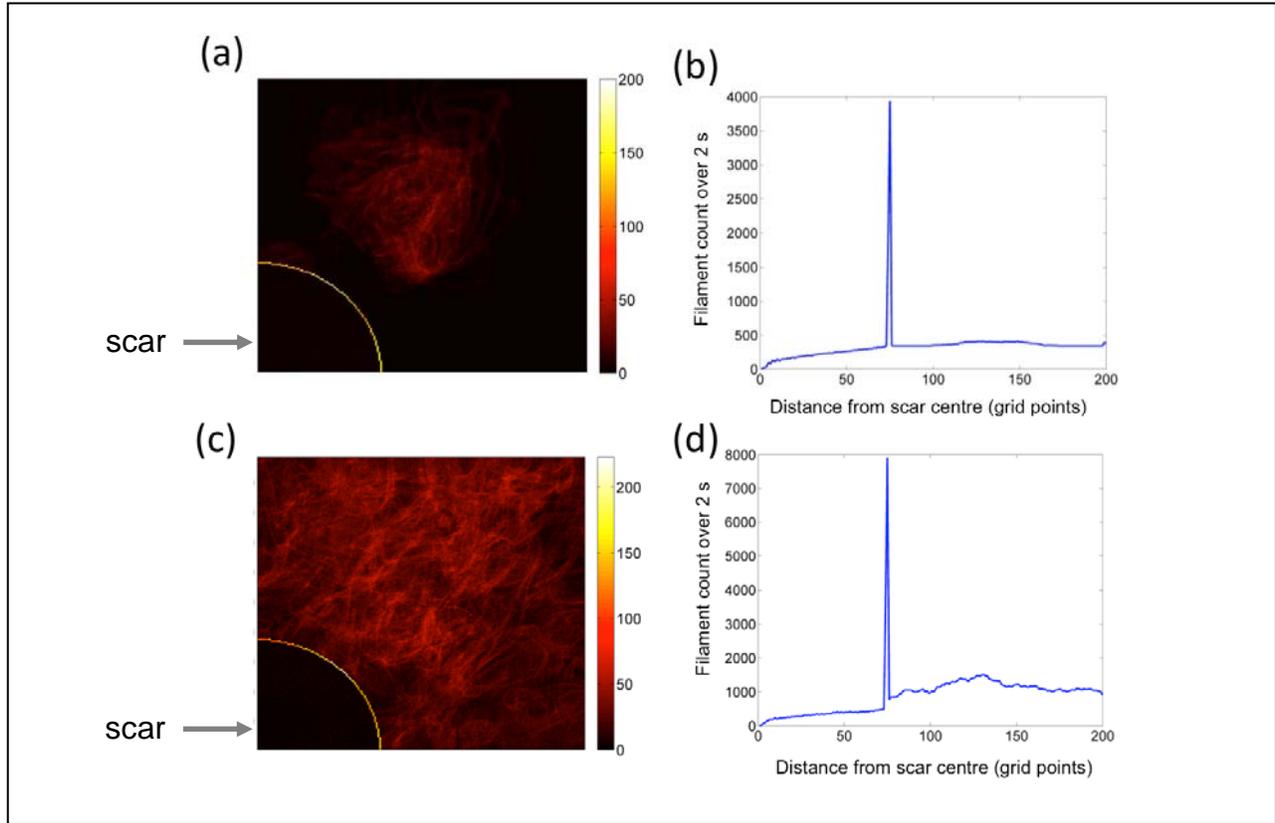


Figure 2. Clustering of filaments in slab geometry with simulated scar in (a) epiMod1 dynamics (c) epiMod2 dynamics. Color bar shows the total number of filament voxels summed over the transmural axis, and over 2 s. Panels (b) and (d) show how the total number of filament voxels changes with distance from centre of the scar, for epiMod1 (b) and epiMod2 (d) dynamics.

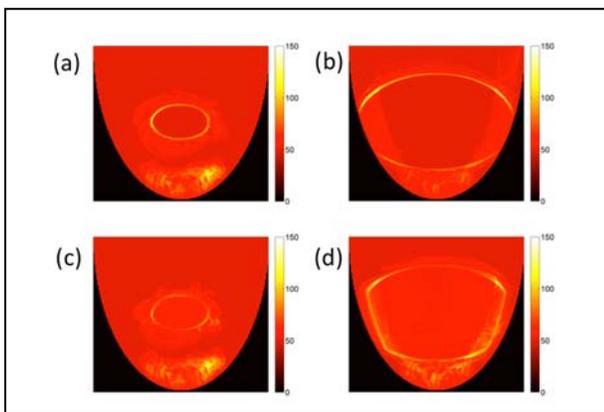


Figure 3. Clustering of filaments in ellipsoid geometry with incorporated simulated scar with EpiMod1 (shallow APDR) dynamics (a) Full depth scar, (b) full depth scar with increased radius, (c) half depth scar, (d) half depth scar with increased radius. Color bar shows the sum of filament voxels over the y-axis and over 2 s.

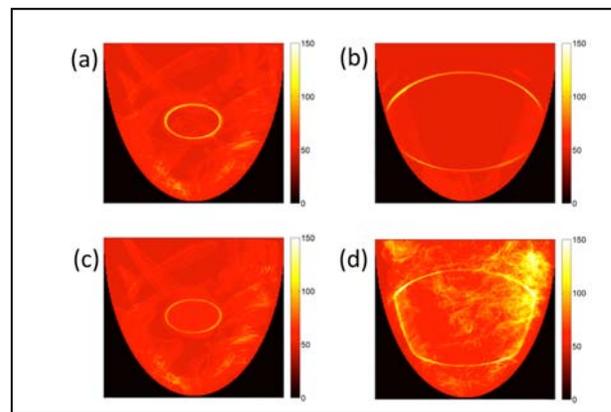


Figure 4. Clustering of filaments in ellipsoid geometry for EpiMod2 (steep APDR) dynamics. Each panel shows same information as in Figure 3.

cylindrical regions of scar. While this enables us to look at the effect of obstacles without the added complication of anatomical structures, in real tissue regions of scar have irregular edges as well as a border zone where regions of scar interdigitate with regions of surviving tissue. These features might be expected to make an important contribution to VF dynamics in the region of the scar. Further studies will examine the contribution of these features to activation during VF.

Despite these limitations, we have shown that the presence of a simulated scar region can have an important effect on the behavior of filaments, and hence on the dynamics of electrical activation during VF.

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