

The Effect of Critical Point Location and Membrane Kinetics on VF Induction by T-wave Stimulation

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Abstract

A strong stimulus delivered in the T-wave of a normal cardiac cycle can induce ventricular fibrillation. The critical point mechanism is thought to be responsible for this phenomenon. However, rapid pacing can cause an otherwise benign strong T-wave stimulus to induce VF. In this paper, we examine an extension of the critical point hypothesis which can explain the effect of rapid pacing. Specifically, we hypothesize that a critical point must form a minimum distance from an anatomical obstacle to establish VF. Furthermore, we suspect that this minimum distance depends on the pacing rate prior to the stimulus. The FitzHugh-Nagumo membrane kinetics and advanced solving techniques (EZ-Spiral) were used to simulate the dynamics of spiral waves and critical points in excitable media. The model confirms a distance / pacing rate interaction, but also indicates a subtle difference in the form of reentry initiated after rapid pacing.

1. Introduction

It is well known that a stimulus delivered in the T-wave of a normal cardiac cycle can induce ventricular fibrillation (VF) [1]. It has been shown that irregular wave propagation and the discreteness of cardiac tissue might be pertinent to the mechanism of cardiac arrhythmias. The onset of spiral waves in the heart has been demonstrated both experimentally and numerically [2]. It is also widely accepted that cardiac tissue can be considered as a generic excitable medium. Cellular automata methods can be applied for modeling purposes [2]. According to traditional theory, premature stimulation results in temporary, unidirectional conduction block in areas of later recovery with the spread of activation towards areas of earlier recovery, thus favoring the development of reentry, or the formation of spiral waves, and VF [3]. The purpose of this study is to use a model to determine if the critical point hypothesis holds true once the critical point is moved a

certain distance from the object and to study its effect with regard to rapid pacing.

2. Methods

2.1 The Model

The FitzHugh-Nagumo membrane kinetics and advanced solving techniques (EZ-Spiral) were used to simulate the dynamics of spiral waves and critical points in excitable media. The model reaction - diffusion equations for the FitzHugh equations are [4]:

$$\begin{aligned}\delta u / \delta t &= \nabla^2 u + \varepsilon^{-1} u(1-u)(u-U_{th}(v)) \\ \delta v / \delta t &= D_v \nabla^2 v + g(u,v)\end{aligned}$$

where

$$u_{th}(v) = (v + b)/a \quad \text{and} \quad g(u,v) = u-v$$

so that a , b , and ε are the parameters of the reaction membrane kinetics. D_v is the ratio of diffusion coefficient and for cellular automata this parameter is set equal to zero. Because of the value used for ε , the u field takes on one of two states almost everywhere: quiescent ($u = 0$, dark gray) and excited ($u = 1$, light gray) [5]. In Figures 2,3,4 and 5, black is the region where u is neither 0 nor 1, it is the thin interface, or reaction zone, that separates the two regions [5].

The experiment simulated here is the “cross-field” stimulation protocol, assumed by Malkin [1], and used extensively by Frazier. The initial conditions of the model were set to mimic the graded response theory for reentry as proposed by Frazier, where the initial conditions of the model contain direct excitation, graded response, and no effect as seen in Figure 1 [3].

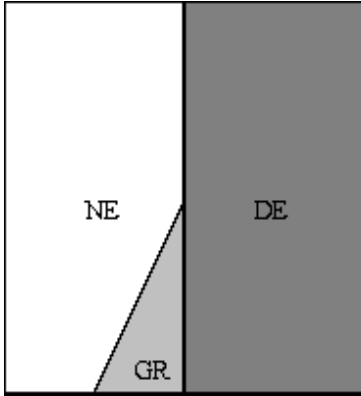


Figure 1. The initial conditions of the model as extrapolated from the experimental results of Frazier [3].

For the purpose of this paper, the critical point is described as the point where the NE, DE, and GR regions intersect. The u and v parameters for the initial conditions were set as follows: For the NE region, u was set equal to 0 and v decayed from 1 on the left to 0 on the right of the region. For the DE region, u was set equal to 1 and v was set equal to 0. For the GR region, u was set to 0 and v was the gradient again starting at 1 at the boundary with the NE region, with the same rate of decline as in the NE region.

2.2 Membrane kinetics for rapid and normal pacing

We calibrated the FitzHugh parameters to approximate measurements of conduction velocity (QRS duration) and effective refractory period (peak of T-wave). In order to determine the appropriate parameters to be used for this experiment, various combinations were tried in an attempt to understand the effect each had on the formation of the spiral wave. The u and v fields were plotted at specific

time steps using the EZ-Spiral program. The effective refractory period and the conduction velocity were matched to a variety of combinations of effects, including normal and rapid pacing. It was found that the parameters for normal pacing were as follows: $a = 0.9$, $b = 0.005$, $1/\epsilon = 120$ and those parameters for rapid pacing were found to be as follows: $a = 0.7$, $b = 0.005$, $1/\epsilon = 120$.

4. Results

In order to determine the effect the critical point had on the formation of the spiral waves, the critical point was progressively moved towards a non-conducting obstacle in 3mm steps, noting spiral formation at each step. The effect of the movement of the critical point was observed for both rapid and normal pacing. The results of the movement of the critical point are noted in Table 1 where “yes” means that a spiral clearly formed and “no” means that a spiral did not form. Figure 2 and Figure 3 are examples of spiral formation and failure to form, respectively.

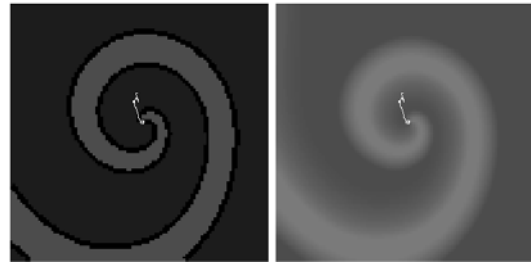


Figure 2. The clearly formed spiral wave following cross-field stimulation after rapid - pacing.

Distance from obstacle (mm)	$a = 0.7$		$a = 0.9$	
	$b = 0.03$ $1/\epsilon = 35$	$b = 0.005$ $1/\epsilon = 120$	$b = 0.03$ $1/\epsilon = 35$	$b = 0.005$ $1/\epsilon = 120$
-3	yes	yes	yes	yes
-6	no	yes	yes	yes
-9	no	yes	no	yes
-12	no	yes	no	yes
-15	no	no	no	no

Table 1. The determination of whether or not spiral waves formed for the given membrane kinetics while changing the distance of the critical point from the object. Notice that the closest distance a spiral wave can form depends on the membrane kinetics. “Yes” means that a spiral formed as in Figure 2 and “no” means that spiral formation failed as in Figure 3.

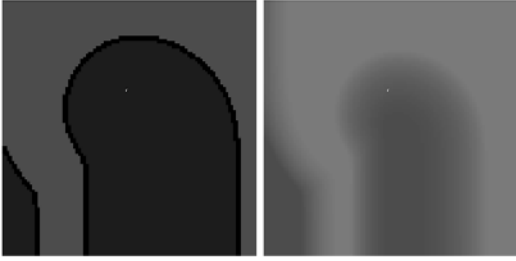


Figure 3. The wave that results after cross-field stimulation following normal pacing. No spiral formation is seen.

In addition to the sensitivity to the distance from the obstacle, another feature about the spiral waves that formed was the first few milliseconds after cardiac stimulation. It appears from Figures 4 and 5 that the determination of VF and the formation of reentrant spiral waves is subtly determined within the first few milliseconds of activation. It is barely noticeable in these two figures that the formation is different from each other. These two figures eventually go on to form the very different figures seen in 2 and 3 respectively, despite their model similarity.



Figure 4. The spiral wave at 50 time steps after cross-field stimulation following rapid pacing.



Figure 5. The spiral wave at 50 time steps after cross-field stimulation following normal pacing.

From Table 1 it is clear that the pacing rate virtually has only a subtle effect on whether or not the spiral wave forms. It should be noted, however, that the time required for the wave to reenter was longer for normal pacing spiral waves as compared to those following rapid pacing. The faster formation of spirals following rapid pacing may make them more likely to form before the heart's intrinsic activity "resets" the heart.

It is also seen in Figures 4 and 5 that the determination of where a particular cross-field stimulation will degrade to VF is made is within the first few hundred milliseconds. In fact, from these figures it is clear to see that a difference in their formation is seen, though subtly, almost directly after activation of the tissue. Further experimental work should focus on the first few hundred milliseconds after stimulation.

References

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4. Discussion and Conclusion