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# Areas of Effectiveness of Defibrillating Pulse in the Energy/Phase Diagram for the Fibrillation Cycle on the Cardiomyocyte Model

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## Introduction

The use of implantable, remote monitoring devices might help to avert hospitalization by detecting early evidence of HF decompensation, thus allowing implementation of outpatient interventions. Implantable remote monitoring devices include implantable cardioverter-defibrillators (ICDs) or cardiac resynchronization therapy defibrillators (CRT-D), which can be used to monitor intrathoracic or intracardiac electrical impedance, respiratory rate, physical activity, rhythm abnormalities, and heart rate variability [1]. The main function of the ICD and CRT-D is passing the electrical pulse (defibrillation pulse) through the myocardium in case of the ventricular fibrillation. The optimal form of the defibrillation pulse and the level of the defibrillation energy is still an open question for the researchers. The aim of this work is to study the areas of effectiveness of defibrillating pulse in the energy/phase diagram for the fibrillation cycle on the cardiomyocyte model.

The hypothesis about the role of refractory period extension of cardiomyocytes during cardiac defibrillation was put forward on the basis of experimental data in the early 1990s [2–4]. In 1997, the results of experiments on isolated rabbit hearts confirming this hypothesis were published [5]. It was also confirmed on a two-dimensional model of the myocardium [6]. In the study [7] performed on the human ventricular cardiomyocyte model, energy/phase diagrams of the lower energy threshold of a rectangular depolarizing pulse extending its refractory period were constructed. The diagrams were constructed based on the assumption of the lower threshold only, i.e. the value of energy below which the refractory period does not lengthen. However, when modeling was performed, the existence of upper thresholds was also noted at high values of the pulse energy, i.e. values of energy above which the refractory period does not extend. This led to a more detailed study of the response to the impact of the depolarizing pulse on the cardiomyocyte, which is under the influence of fibrillation waves.

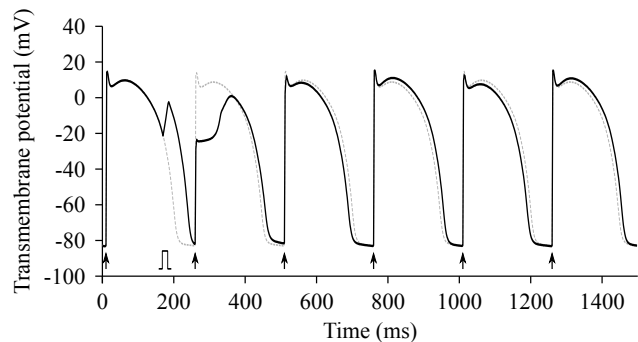
## Materials and Methods

The study was carried out in the BeatBox simulation environment [8] on the human heart ventricle myocyte model ten Tusscher-Panfilov 2006 [9]. The response of a cardiomyocyte in a state of imitative fibrillation to the effect

of a depolarizing current pulse was evaluated. Imitation of fibrillation was caused by excitation impulses of 0.5ms duration with a frequency of  $240\text{min}^{-1}$  (the limiting frequency, perceived by the model of a cardiomyocyte). The details of materials and methods are presented in [7].

The extension of refractoriness of the cardiomyocyte was detected visually, from the time diagram displayed during the simulation. As an example on fig. 1 is a time diagram of the transmembrane potential under the action of a depolarizing rectangular pulse of 15ms duration with a delay of 160ms from the excitation impulse and a prethreshold amplitude of  $2.104\mu\text{A}/\text{cm}^2$ , on fig. 2—with a threshold amplitude of  $2.105\mu\text{A}/\text{cm}^2$ , which causes extension of refractoriness. The arrows indicate the moments of action on the cardiomyocyte excitation impulses, the dotted line shows the transmembrane potential at the excitation rhythm frequency of  $240\text{min}^{-1}$ .

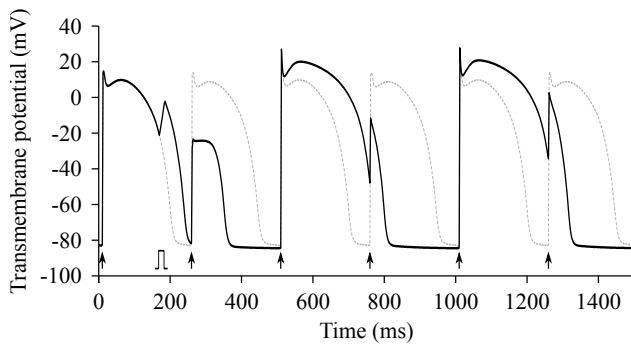
All the materials and experimental data in the article are presented in the online resource ResearchGate [10].



**Figure 1:** Time Chart of the Transmembrane Potential under the Influence of a Rectangular Depolarizing Pulse Duration of 15ms with a Delay from the Excitation Impulse of 160ms and an Amplitude of  $2.104\mu\text{A}/\text{cm}^2$

## Results

The results are presented on the diagrams for the depolarizing pulse durations of 15, 30 and 45ms respectively (fig. 3–5). Phases of the imitation fibrillation cycle are represented on the diagrams in delays from the end of the excitation impulse caused by the fibrillation wave. The depolarizing



**Figure 2:** Time Chart of the Transmembrane Potential under the Influence of a Rectangular Depolarizing Pulse Duration of 15ms with a Delay from the Excitation Impulse of 160ms and an amplitude of  $2.105\mu\text{A}/\text{cm}^2$

pulse causes a long-term extension of refractoriness of the cardiomyocyte at the efficiency areas (numbered from 1 to 5). At any level of energy of the depolarizing pulse it is impossible to provide an extension of refractoriness at all phases of the fibrillation cycle, but at a certain energy level, refractoriness is prolonged in 90% of the cardiomyocytes in different phases of the fibrillation wave cycle (according to the diagrams on the fig. 3-5). For example, at an energy ratio of  $147.3\mu\text{A}^2\cdot\text{ms}/\text{cm}^4$  of a rectangular depolarizing pulse with a duration of 15ms, the refractoriness is prolonged by delays from the excitation impulse from 0 to 215.8ms and from 240.4 to 250ms, which is 90.2% of the fibrillation phases cycle.

The upper thresholds of region 1 and 5 are a consequence of a one-step increase of the duration of the refractory period, with an increase in the energy of the depolarizing pulse. In this case, the duration of the current refractory period may exceed the period of the fibrillation excitation impulses. The time diagram of the transmembrane potential change under the influence of a depolarizing pulse in efficiency area No 5 with a delay from the end of the excitation impulse of 40ms is shown in fig. 6.

## Discussion

At high energy levels of the depolarizing pulse, the duration of the current refractory period of all myocardial myocytes may exceed the repetition period of the fibrillation excitation impulses (fig. 6). This should lead to the cessation of the spread of the fibrillation wave. Presumably this is the second defibrillation mechanism, apart from long-term extension of refractoriness at lower energy levels of the depolarizing pulse.

## Conclusions

At any energy levels, the depolarizing pulse does not provide a long-term extension of refractoriness of all heart cardiomyocytes in different phases of the excitation wave cycle, but at a certain energy level, refractoriness is extended in 90% of the cardiomyocytes in different phases

of the fibrillation wave cycle.

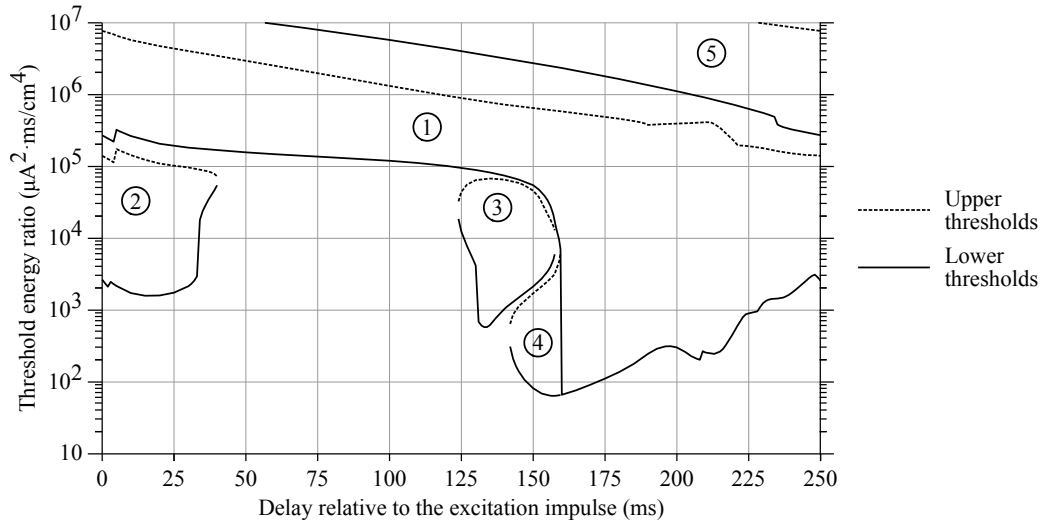
At high energy levels, the impact of the depolarizing pulse leads to a one-step increase in the duration of the refractory period of cardiomyocytes to values exceeding the duration of the fibrillation wave period.

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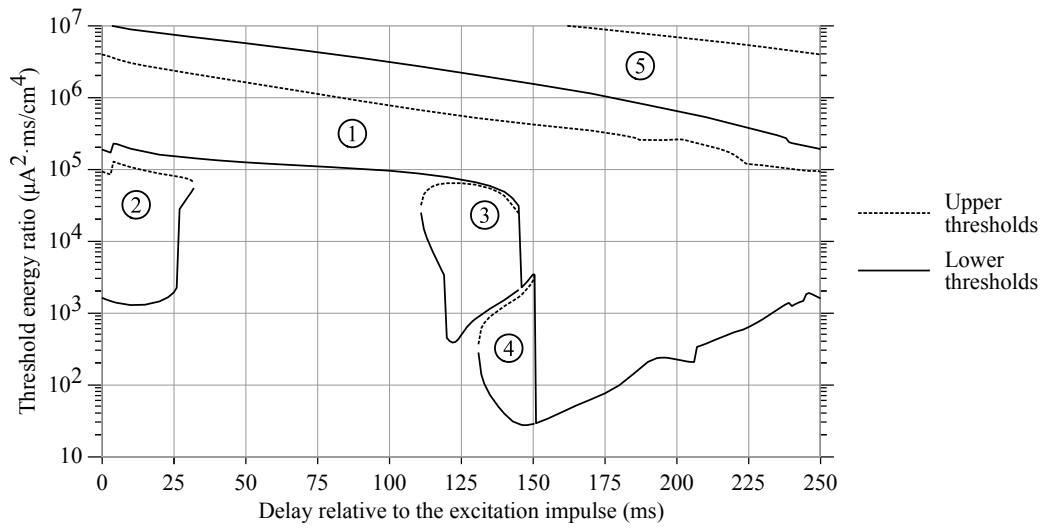
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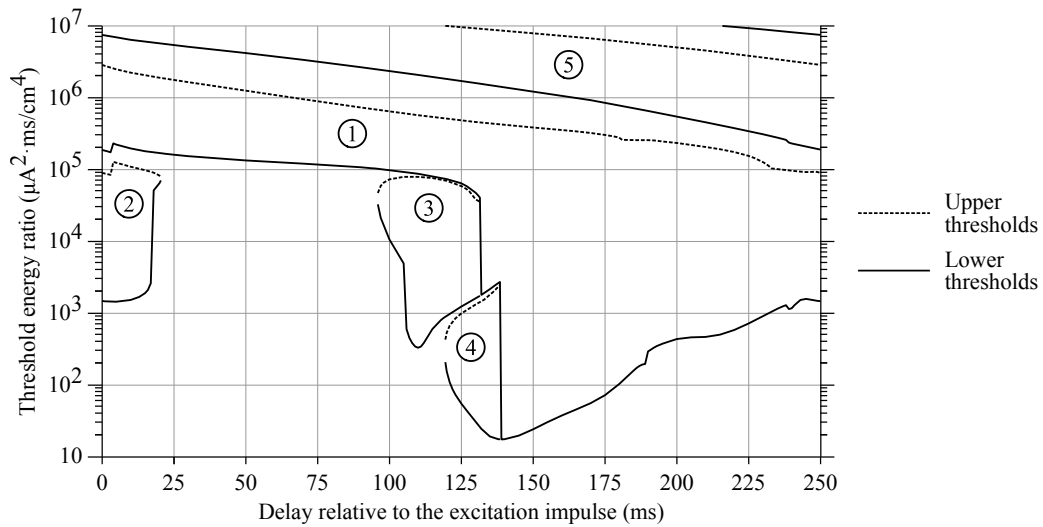
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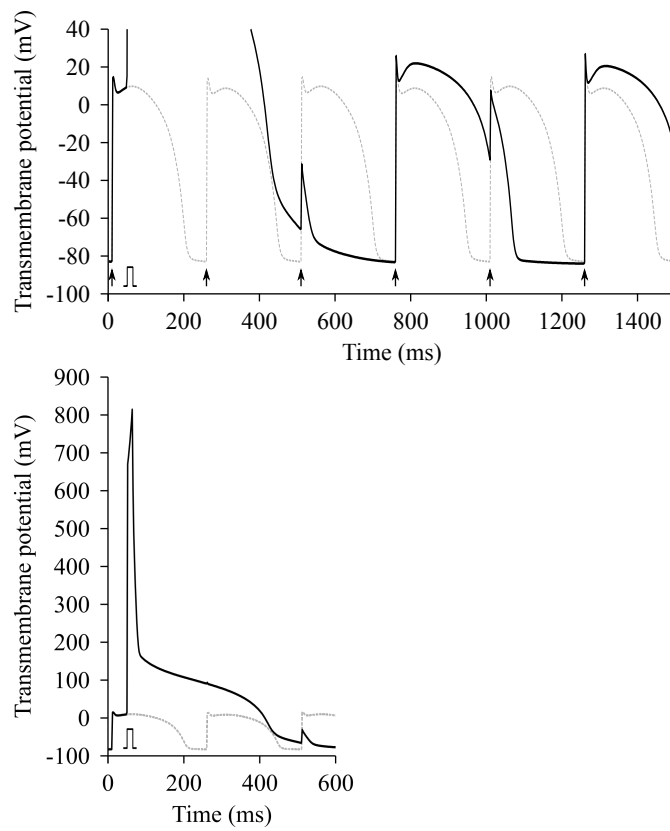
**Figure 3:** Energy Threshold Values of Refractoriness Extension Areas at a Depolarizing Pulse Duration of 15ms



**Figure 4:** Energy Threshold Values of Refractoriness Extension Areas at a Depolarizing Pulse Duration of 30ms



**Figure 5:** Energy Threshold Values of Refractoriness Extension Areas at a Depolarizing Pulse Duration of 45ms



**Figure 6:** Time Chart of the Transmembrane Potential under the Influence of a Rectangular Depolarizing Pulse Duration of 15ms in the Area of Effectiveness No 5