

DEPENDENCE OF VENTRICULAR ACTION POTENTIAL SHAPE ON FITZHUGH-NAGUMO MODEL PARAMETERS

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Abstract

In this article, an action potential shape of cardiac ventricular cells was evaluated for various values of FitzHugh-Nagumo model parameters. Simulation results revealed that the action potential duration is affected mainly by the e and c_1 parameters, while the action potential duration is proportional to the value of the c_1 parameter and is inversely proportional to the value of the e tissue parameter.

1 Introduction

Electrical activity of the cells in the cardiac tissue is generated in the form of electrical impulses that are called action potentials (APs).

Modeling of the cardiac electrical activity on the cellular level can be performed using local models of various types of atrial and ventricular cells [1]. On the tissue level, propagation of the electrical activity can be modeled using spatial models based on reaction - diffusion (RD) equations (monodomain or bidomain models) that incorporate the cell models [2], [3], [4] or using less time-consuming models based on cellular automaton [5].

The complexity of cell models is an important aspect of their suitability to be used in RD spatial models. Even though very complex models are capable to model the shape of AP in detail, such evaluation is enormously time consuming.

Simplified models, like the FitzHugh-Nagumo (FHN) model, provide solution in acceptable time but the details of the AP shape are not retained.

The influence of FHN model parameters on the generated AP shape was evaluated and compared in a MATLAB and COMSOL Multiphysics program for local and spatial model, respectively.

2 Description of the FitzHugh-Nagumo model

Time changes of the membrane potential V_m of cardiac ventricular cells can be described using the modified FitzHugh-Nagumo (FHN) equations (local model) [6], [4]:

$$\frac{\partial V_m}{\partial t} = -i_{ion} + i_s \quad (1)$$

$$\frac{dR}{dt} = k e \left(\frac{(V_m - B)}{A} - R \right) \quad (2)$$

where i_{ion} and i_s is the ionic transmembrane current density and the external stimulation current density, respectively, R is the recovery variable, A is the action potential amplitude, B is the resting membrane potential and e is related to the cell excitability

The ionic transmembrane current density i_{ion} can be modeled in the FHN model as:

$$i_{ion} = k c_1 (V_m - B) \left(-\frac{(V_m - B)}{A} + a \right) \left(-\frac{(V_m - B)}{A} + 1 \right) + k c_2 R (V_m - B) \quad (3)$$

where a is related to the excitation threshold and c_1 , c_2 and k are other membrane-specific parameters.

Time and spatial changes of the membrane potential V_m can be modeled by the RD equation (spatial model) together with the FitzHugh-Nagumo equations (2) - (3):

$$\frac{\partial V_m}{\partial t} = \nabla \cdot (D \nabla V_m) - i_{ion} + i_s \quad (4)$$

The tissue diffusivity D is determined as

$$D = \frac{\sigma}{\beta C_m} \quad (5)$$

where σ is the tissue conductivity, β is the membrane surface-to-volume ratio, and C_m is the membrane capacitance per unit area.

3 Parameters of the FitzHugh-Nagumo model

Following default values of the parameters of modified FHN equations [4] for the ventricular membrane of local and RD models were used: $a = 0.13$, $c_1 = 2.6$, $c_2 = 1$, $e = 0.006$, $k = 1000 \text{ s}^{-1}$, $A = 0.120 \text{ V}$, $B = -0.085 \text{ V}$. The default value of diffusivity was set to $D = 0.0005 \text{ m}^2/\text{s}$ and was related to tissue conductivity $\sigma = 0.5 \text{ S/m}$ while supposing $C_m = 1 \text{ }\mu\text{F}/\text{cm}^2$ and $\beta = 1000 \text{ cm}^{-1}$.

The stimulation current density of amplitude $i_{s0} = 100 \text{ A/F}$ was flowing during the stimulation interval $T_s = 0.005 \text{ s}$. Initial values of the membrane potential and the recovery variable were -0.085 V and 0 , respectively.

The local model was numerically solved in MATLAB and the spatial model was numerically solved in COMSOL Multiphysics program. Results of both models were evaluated in MATLAB.

One-dimensional propagation of the electrical activation was computed in a slab model of size $25 \times 2 \times 2 \text{ mm}$ (Fig. 1), representing the heart tissue.

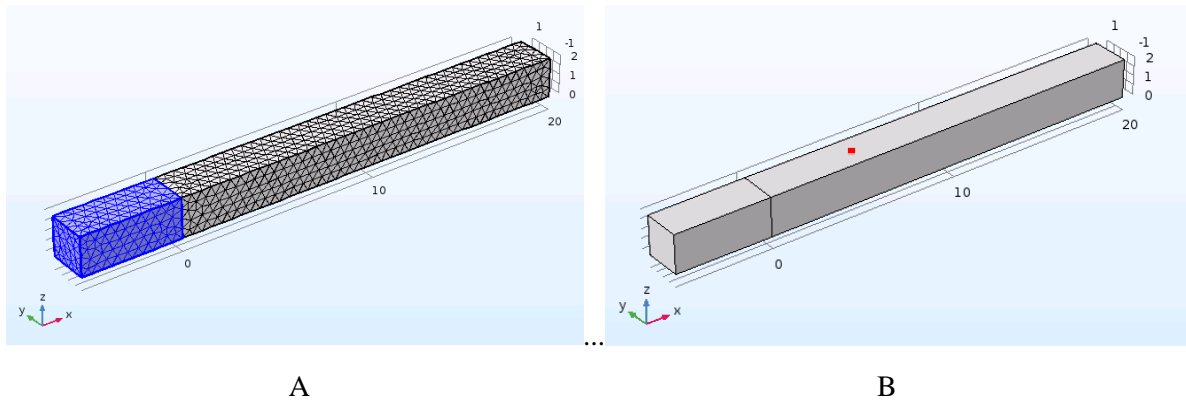


Figure 1: (A) The generated mesh of the slab model of the heart wall with the stimulated part (blue color) on the left side. (B) The position of the point (red dot) from which the data were taken. All dimensions are in mm.

4 Results

An example of the spatial distribution of membrane potential V_m in time $t = 10 \text{ ms}$ in the slab model obtained from a numerical solution in COMSOL Multiphysics for default values of FHN parameters is shown in Fig. 2.

The time courses of the membrane potential V_m and recovery variable R were solved numerically for various values of the e parameter in the local model in MATLAB (Fig. 3). Solution for the same values of the e parameter solved in spatial RD model (slab) is shown in Fig. 4.

As we can see from the results shown in Fig. 3 and Fig. 4, there are only very small differences of AP shape in the local and space model.

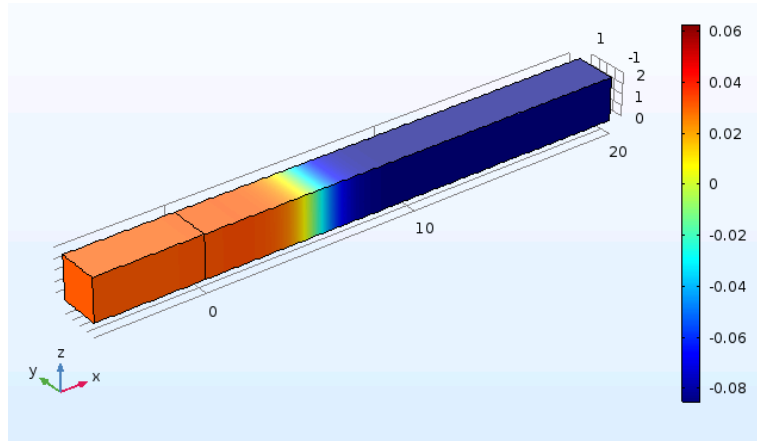


Figure 2: Spatial distribution of the membrane potential V_m in time $t = 10$ ms in the slab model. The membrane potentials are in volts.

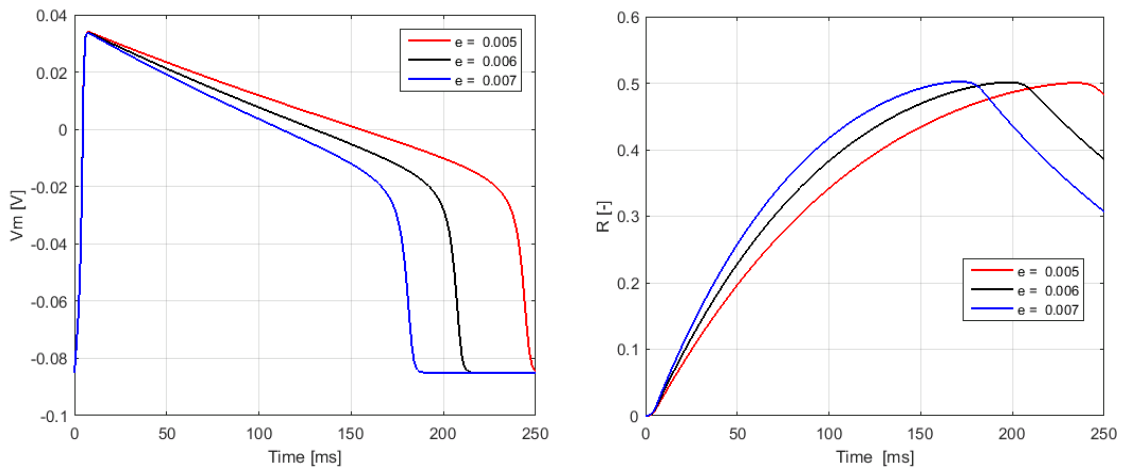


Figure 3: Time courses of the membrane potential V_m and recovery variable R for various values of the e parameter in the local model in MATLAB.

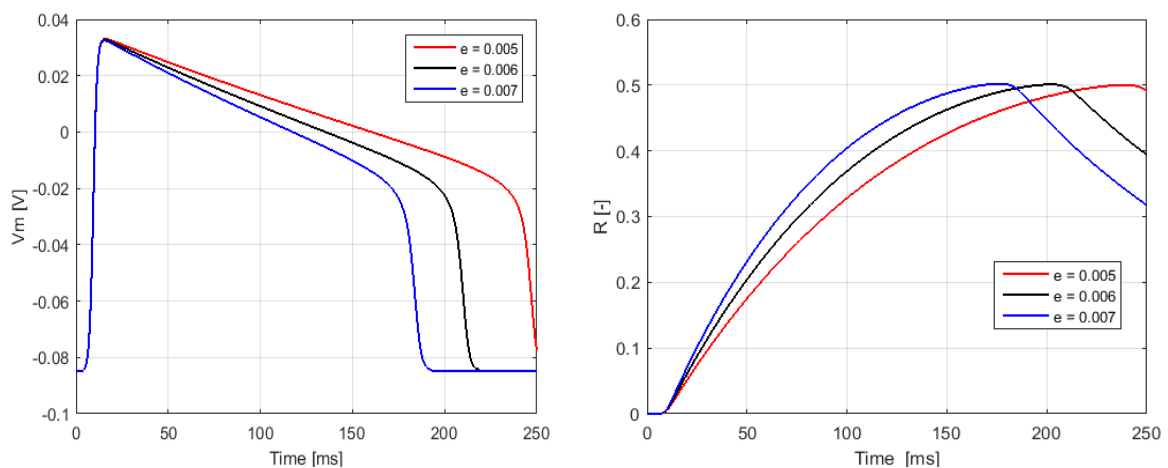


Figure 4: Time courses of the membrane potential V_m and recovery variable R for various values of the e parameter in the slab model.

Time courses of the membrane potential V_m and recovery variable R solved numerically in the local model in MATLAB for various values of the A and c_1 parameter are shown in Fig. 5 and Fig. 6, respectively.

The value of the A parameter determines the amplitude of AP, while it has no effect on the recovery variable R (Fig. 5). The increase of c_1 parameter has effect on the prolongation of AP, up to a certain value of $c_1 = 3$, from which the AP is not terminating (Fig. 6).

Changed values of tissue diffusivity D had nearly no effect on AP amplitude and AP duration in the spatial slab model (Fig. 7).

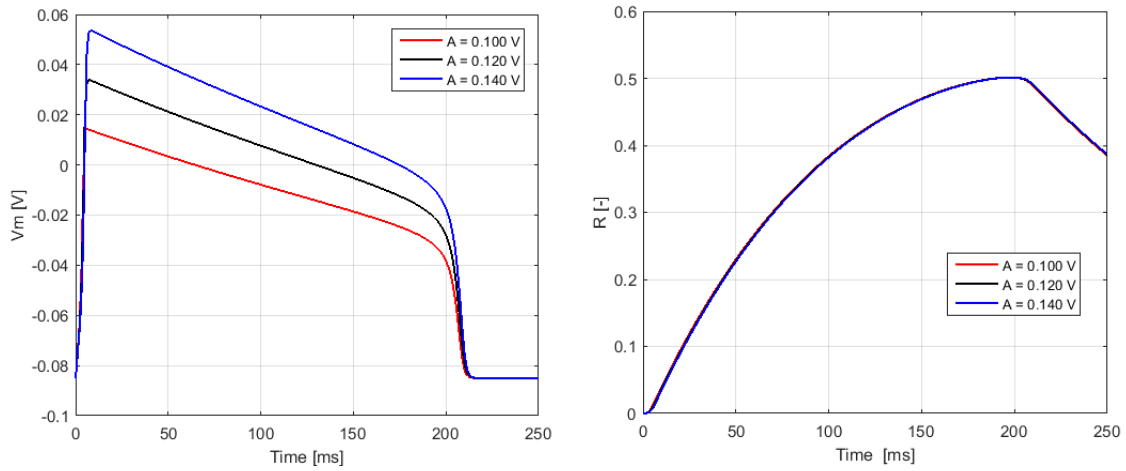


Figure 5: Time courses of the membrane potential V_m and recovery variable R for various values of the A parameter in the local model in MATLAB.

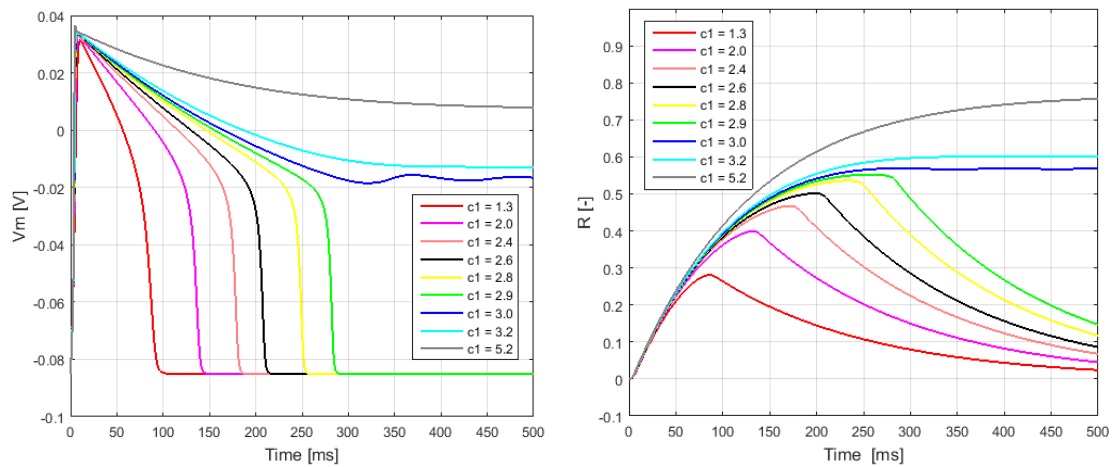


Figure 6: Time courses of the membrane potential V_m and recovery variable R for various values of the c_1 parameter in the local model in MATLAB.

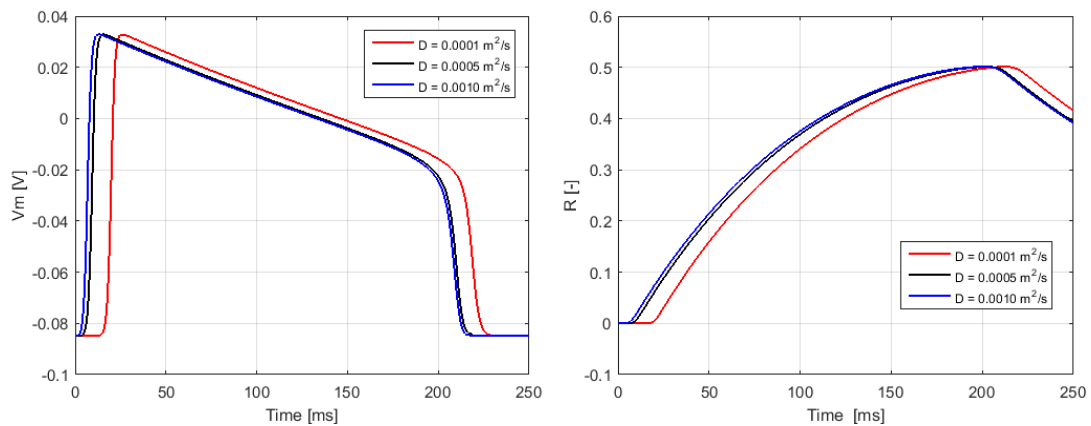


Figure 7: Time courses of the membrane potential V_m and recovery variable R for various values of the D parameter in a slab model.

5 Conclusion

The comparison of numerical results from MATLAB and COMSOL Multiphysics programs shows only small differences between the AP amplitudes and durations obtained from local and spatial models. The AP amplitude is mainly determined by the A parameter, while the AP duration is affected by the e and c_1 parameters.

For the default value of the e parameter ($e = 0.006$), a threshold value of the c_1 parameter ($c_1 = 3$) was found, above which the AP was not terminated.

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