ELECTROPHYSIOLOGICAL PROPERTIES OF ATRIAL CELLS SIMULATED IN MATLAB

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Abstract

Electrophysiological properties of atrial cells are modeled in this article. Generation of action potential (AP) and its characteristics are simulated and analyzed in MATLAB. The strength-duration curve of the Courtemanche-Ramirez-Nattel model of human atrial cell is evaluated. The action potential duration (APD) varies for different species, as well as for different part of the heart: atrial and ventricular cells. Furthermore, APD can be affected by various parameters. Therefore, the heart frequency as the major factor influencing the APD was examined.

1 Introduction

Electrophysiological activity of human atrial cell may be modeled using various models, e.g. the Nygren model [1], or the Courtemanche-Ramirez-Nattel model [2]. For simulations of time courses of action potential and evaluation of other variables, Courtemanche-Ramirez-Nattel (CRN) model was used in this article. This model is described by a set of 21 ordinary differential equations and tens of algebraic equations. This model was numerically solved using ode15s Matlab ODE solver.

The time change of the membrane potential V is given by:

$$\frac{dV}{dt} = \left[- I_{ionic} + I_{st} \right] / C_m \tag{1}$$

where I_{ionic} and I_{st} are the ionic current and stimulation current, C_{m} is the membrane capacity. The ionic current comprises the fast sodium current (I_{Na}) and eleven other membrane currents. Since calcium ions are crucial for contraction of myofibrils in myocytes, model contains different calcium buffers, calcium ion fluxes through the sarcolemmal (cell) membrane and through the membrane of the sarcoplasmic reticulum (SR) which is the main intracellular store of calcium ions.

2 Excitability of CRN model

Excitability is the property of excitable cells (like atrial and ventricular heart cells) enabling to respond on proper stimuli by generation of AP [3]. Excitability is evaluated usually by means of strength-duration curve and related terms: rheobase and chronaxy. We will use for stimulation of the excitable membrane of the atrial cell rectangular current stimulus with amplitude I_{st0} and duration T_{s}. The strength-duration curve represents the threshold values of I_{st0} in dependence on stimulus duration that are able to elicit the action potential. Typical phases of AP of an atrial cell are shown in Fig. 1.

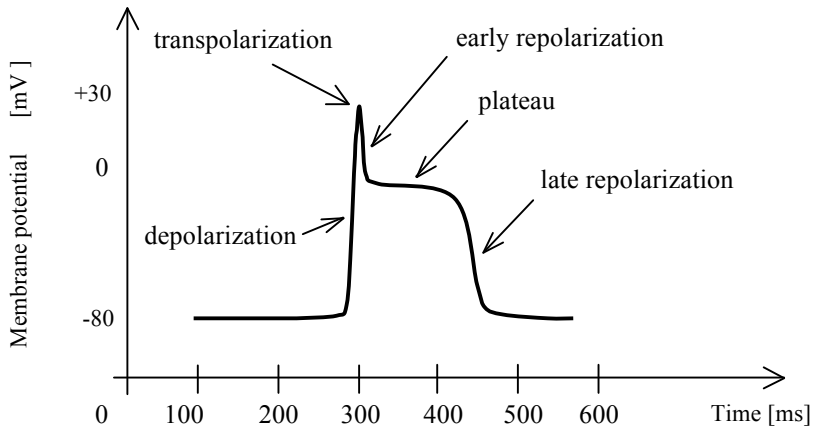

Figure 1: Phases of AP of an atrial cell

Stimuli of amplitudes approximately less than 1000 pA are subthreshold (Fig. 2), i.e. they are not able to elicit the APs, only membrane is charged and discharged through the membrane capacity. Stimulus with amplitude of about 1100 pA is threshold (I_{st0_thr}), i.e. it invokes AP but with remarkable time delay and without transpolarization. As it is shown in detail in Fig. 3, stimuli with amplitudes from about 1100 pA to 1300 pA produce APs with some delay, and above 1500 pA without remarkable delay (so these are suitable for stimulation). Stimulus with amplitude of about 3000 pA produces AP with distorted onset (up to time of 2 ms, marked in Fig. 3 by blue vertical dash-dotted line notifying the end of stimulus impulse T_s).

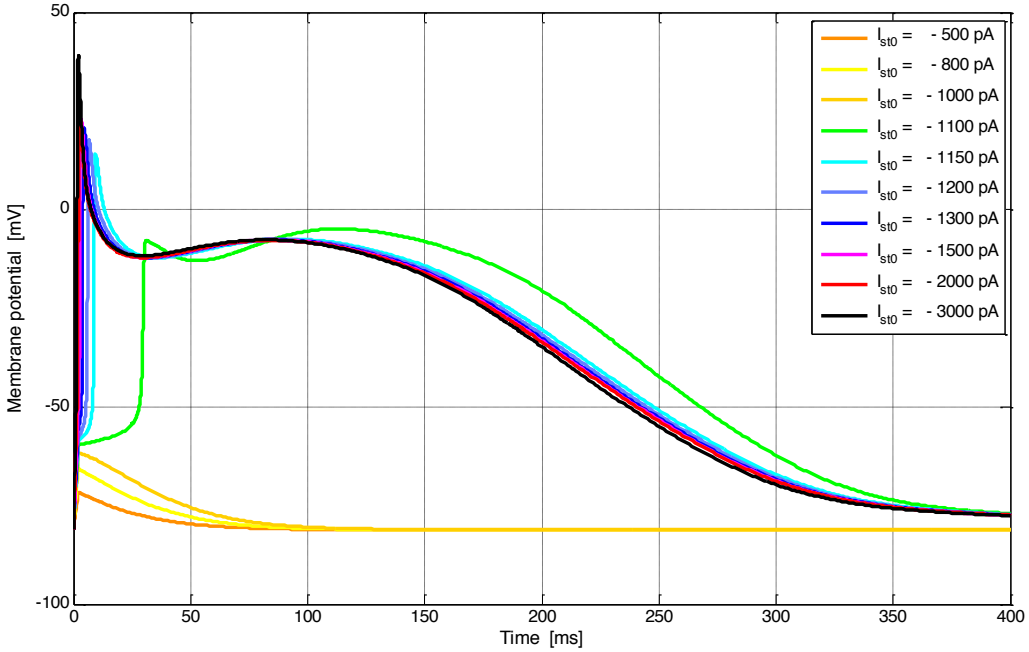

Figure 2: Time courses of membrane potential V for the CRN model of human atrial cell for stimulus duration T_s = 2 ms and various stimulation amplitudes

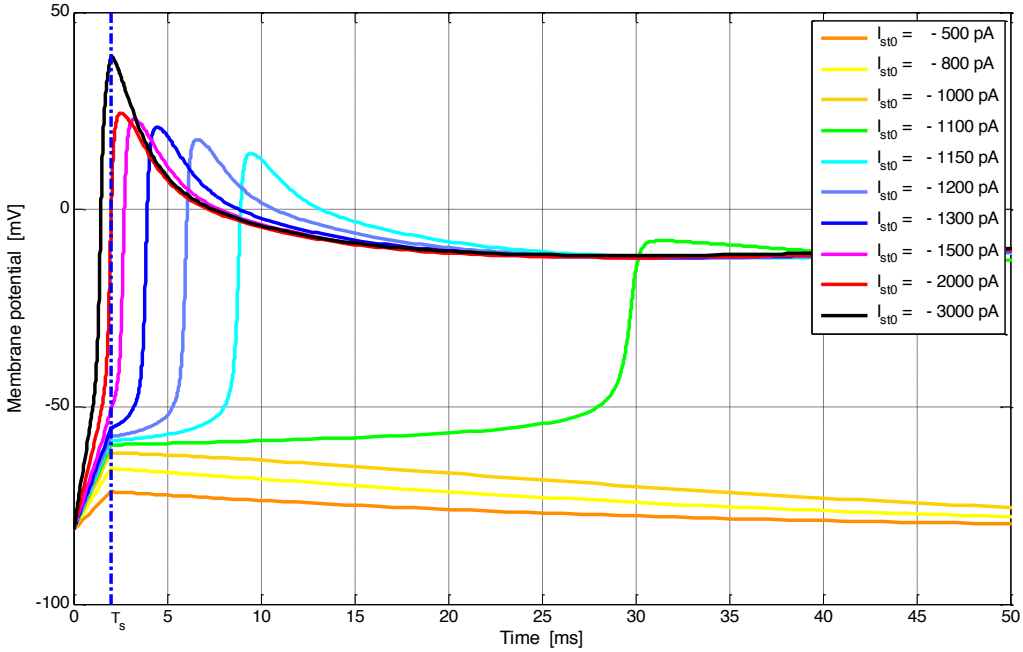

Figure 3: Time courses of V for the CRN model of human atrial cell for stimulus duration T_s = 2 ms and various stimulation amplitudes: detail of the depolarization and early repolarization phase

Threshold values (I_{st0_thr}) were examined by analyzing the initial part of V trace (first 50 ms may cover the depolarization and early repolarization phase of AP). In the initial 50 ms long part of V trace, the maximum value of membrane potential (V_{max}) and time of maximum (t_{Vmax}) are searched.

For example, for stimulus duration T_s = 2 ms and stimulus amplitude I_{st0} = 1100 pA (green line in Fig. 2 and Fig. 3), the maximum during the first 50 ms occurs in t_{Vmax} = 32.1 ms and has value V_{max} = - 8.4 mV (plotted with red circle markers in Fig. 4, Fig. 5).

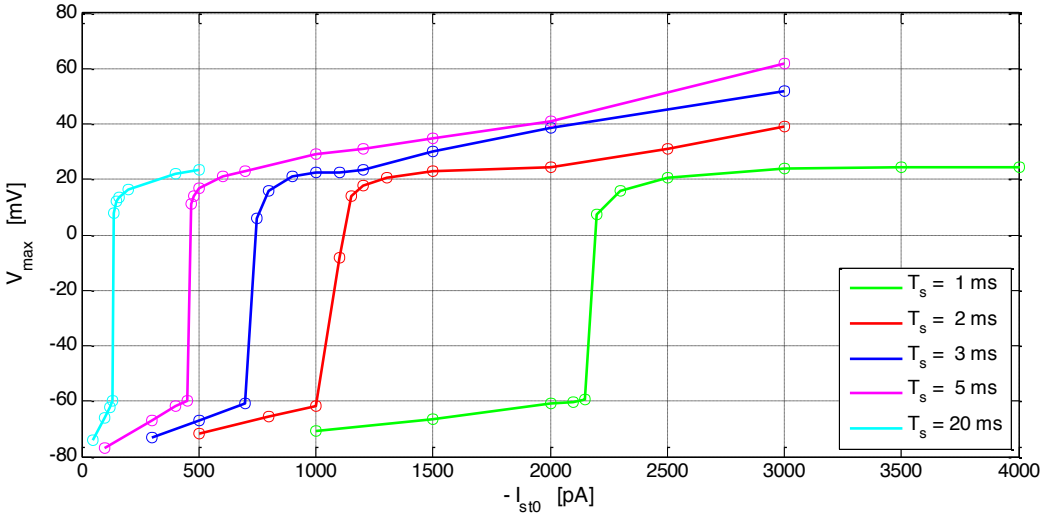

Figure 4: Dependences of V maxima for various stimulus durations T_s and amplitudes I_{st0}

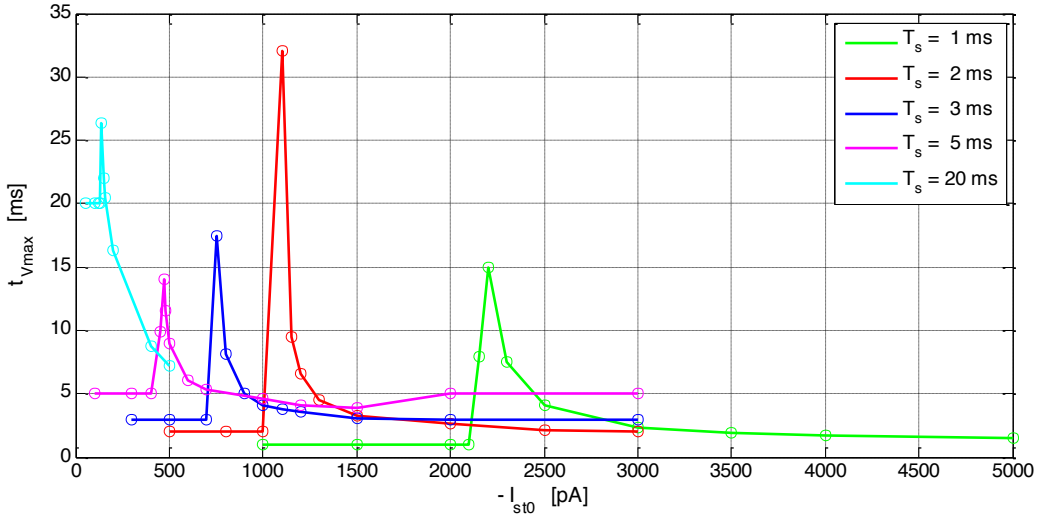

Figure 5: Dependences of time of V maxima for various stimulus durations T_s and amplitudes I_{st0}

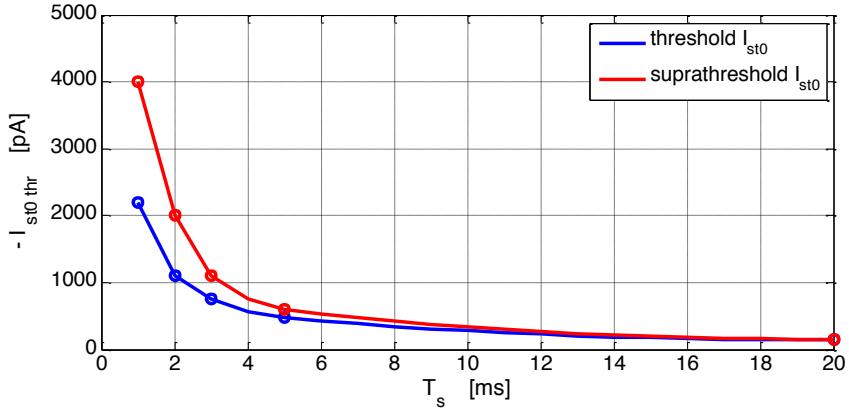

Figure 6: The strength-duration curve for the CRN model: threshold and suprathreshold stimuli

For given stimulus duration $T_s = 2$ ms, the action potentials are not generated for values of I_{st0} lower than 1100 pA. Therefore the value $I_{st0} = 1100$ pA is the threshold one (I_{st0_thr}) and is plotted in Fig. 6 with blue circle marker.

It is obvious that just the threshold value of I_{st0_thr} is not suitable for common stimulation, since the onset of AP has too big delay. Usually, the suprathreshold values are used. Suprathreshold values are shown in Fig. 6 with red markers and they are obtained as the lowest value of I_{st0} for which the AP rises smoothly from the initial increase of the membrane potential during the stimulation impulse.

3 Frequency changes of action potential duration

In this section, stimulation pulses with duration $T_s = 2$ ms and amplitude $I_{st0} = 2$ nA are used. Atrial cell model was stimulated with a constant value of the stimulation period (BCL, basic cycle length) for 10 s and steady-state AP was achieved.

Figure 7 shows the steady-state time courses of AP for three values of BCL. From Figure 7 is obvious that with increasing frequency of stimulation the APDs are shortened and the AP obtained more triangular shape.

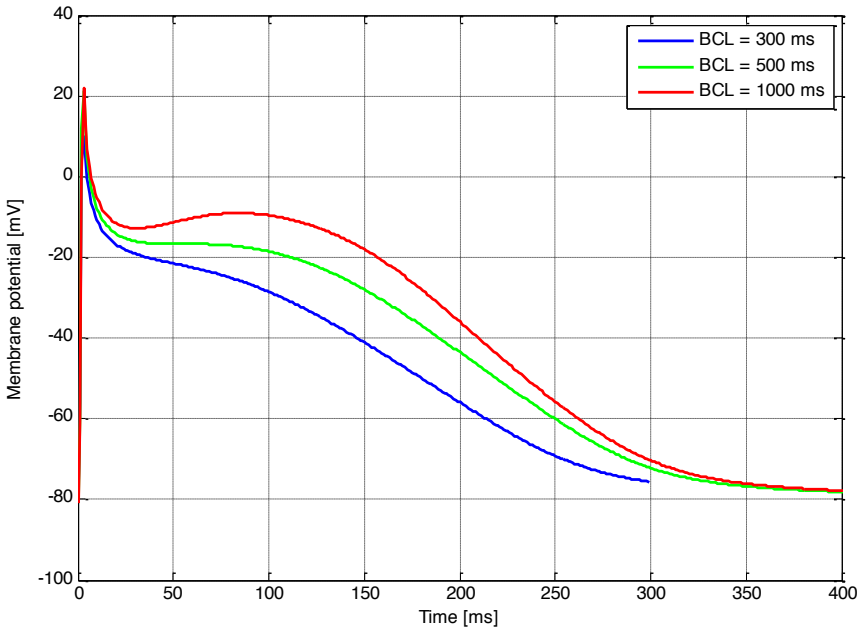

Figure 7: Time courses of AP for the Courtemanche - Ramirez - Nattel model of human atrial cell for three different stimulation frequencies

4 Conclusion

In this article, the Courtemanche-Ramirez-Nattel model of human atrial cell was implemented in MATLAB and cell excitability and other characteristics of the model were analyzed. The strength-duration curve as the principal representation of excitability was evaluated.

Furthermore, values of APD were evaluated for changes of stimulation impulses frequency. The shortening of action potential duration with increased frequency determines the heart adaptability to load.

Acknowledgement

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References

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