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A Study of the Myocardium Cell Membrane Using the Luo–Rudy Model

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The Cell Electrophysiology Simulation Environment (CESE) modeling medium was used to study parameters of the myocardium cell membrane. The parameters of the model were experimentally tested using rectangular electric pulses. The growth of the transmembrane potential with respect to the resting potential increased the specific resistance, specific capacitance, and time constant τ_m of the cell membrane. Comparative analysis revealed that the Weiss–Lapicque model provided most adequate description of reaction to rectangular defibrillation electric pulses.

The effect of defibrillation pulses is usually tested using laboratory animals or isolated animal hearts. Such tests are expensive and time-consuming. Modeling of the defibrillation effect reduces the cost of tests.

The Weiss–Lapicque model, the first such model, was elaborated in 1901-1909. This model was based on experimental research on frog nerve [1]. The Blair model was proposed in 1932. This model represents the cell membrane as a RC-chain [2]. It was used in charge burping theory [3] and the characteristic energy method [4].

Progress in computer technology and cell membrane research provided the basis for the Luo–Rudy model of the mammalian myocardial cell [5].

Materials and Methods

The Cell Electrophysiology Simulation Environment (CESE) OSS 1.4.7 [6] modeling medium was used. The software contains five basic models, including the Luo–Rudy Mammalian Ventricular Model II (dynamic) of guinea pig myocardium membrane (1994-2000). This model was used in experimental research on the effect of electric pulses on myocardial cell membrane. The CESE medium can simulate the effect of electric pulses of arbitrary shape and time.

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Results

Characteristics of the membrane model. The model reaction was tested using a 100-msec rectangular electric pulse. The duration of this pulse is much longer than the model transition time.

The threshold amplitude of current density I_{thr} was determined for the action potential shown in Fig. 1. Then, the reaction of the model to pulses with current density amplitude of 0.1-0.9 of I_{thr} was tested (Fig. 2).

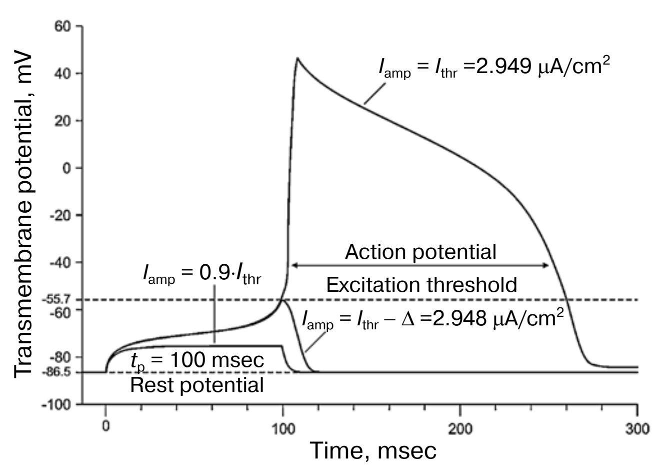

Fig. 1. Action potential.

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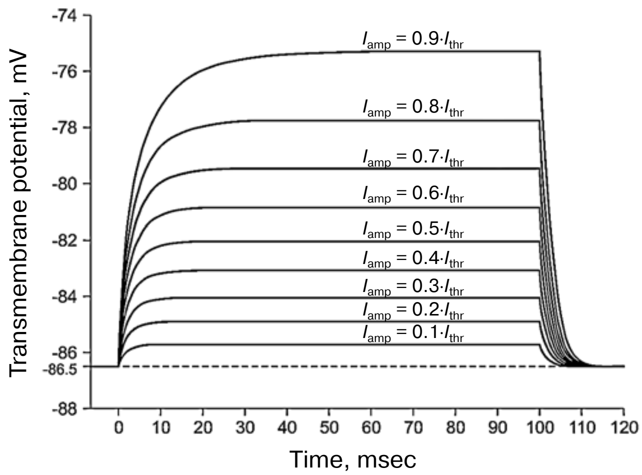

Fig. 2. Model reaction to pulses with various amplitudes.

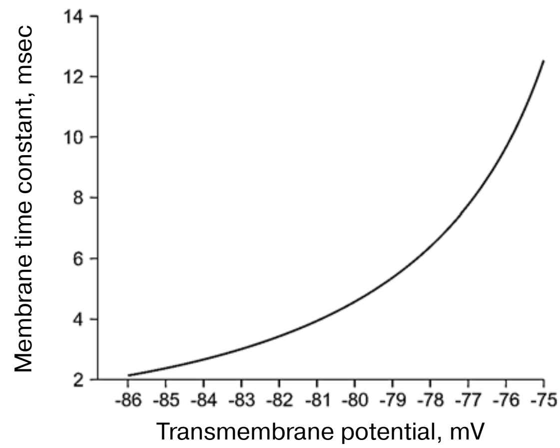

Fig. 4. Dependence of model time constant on transmembrane potential.

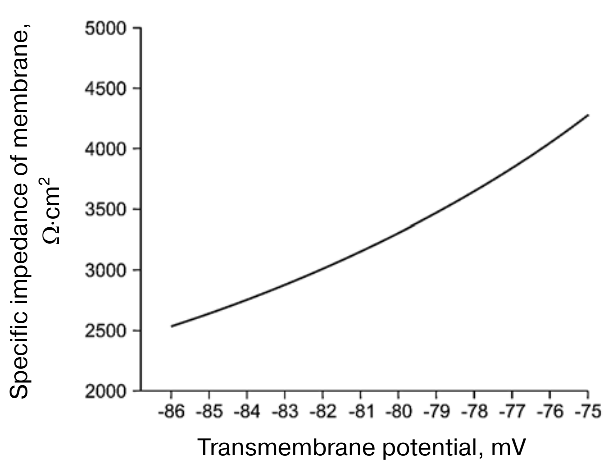

Fig. 3. Dependence of specific model impedance on transmembrane potential.

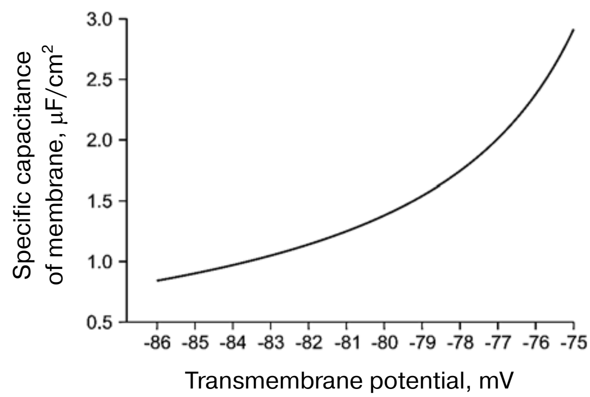

Fig. 5. Dependence of specific membrane capacitance on transmembrane potential.

The dependence of specific model impedance on transmembrane potential was tested within the range (–86)-(–75) mV. This curve is shown in Fig. 3.

The dependence of model time constant on transmembrane potential is shown in Fig. 4. This curve was measured using low-amplitude electric pulses with a plateau. The pulse time is 100 msec. This pulse generates membrane potential U_m. The 100-msec potential in static mode generates transmembrane potential U_m + 0.5 mV. The resulting curve is shown in Fig. 4.

The specific membrane capacitance was calculated from U_m, membrane time constant, and specific membrane impedance. The dependence of specific membrane capacitance on transmembrane potential is shown in Fig. 5.

Comparison between Weiss–Lapicque, Blair, and Luo–Rudy models. The models of Weiss–Lapicque, Blair, and Luo–Rudy were compared using the dependence of relative threshold energy on pulse time. For the Luo–Rudy model, the current density threshold I_{thr} at which the action potential appeared was calculated. Then the energy coefficient was calculated from the equation:

$$K_E(t_p) = I_{thr}^2 \cdot t_p.$$

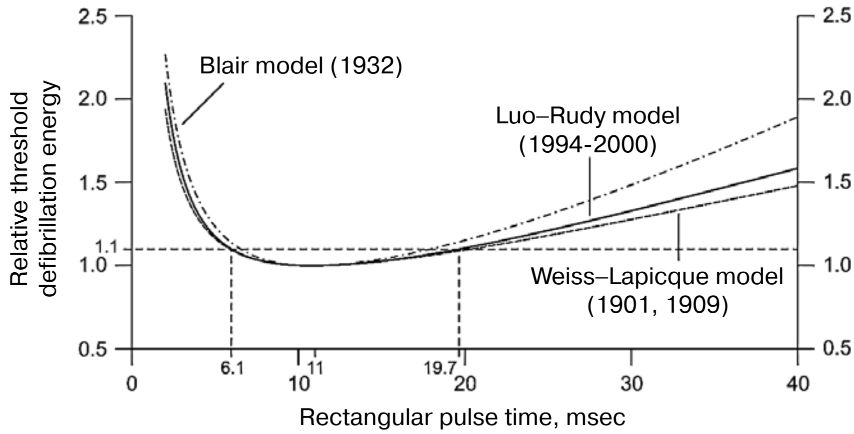

Fig. 6. Dependence of relative threshold energy of cell excitation on rectangular pulse time.

The optimal pulse time at minimal K_{Emin} = 264 μA^2·msec/cm^4 is 11 msec, which corresponds to τ_m = 8.8 msec (2-5 msec in humans [5]). Relative threshold energy is the quotient of energy coefficient $K_E(t_p)$ divided by K_{Emin}.

The relative threshold energy in the Weiss–Lapicque model was calculated as follows:

$$E_{rel}(t_p) = 0.0227 \cdot (1 + 11/t_p)2 \cdot t_p,$$

where t_p is measured in msec.

The relative threshold energy of membrane excitation in the Weiss–Lapicque model was calculated as follows:

$$E_{rel}(t_p) = 0.0463/[1 - \exp(-t_p/8.8)]^2 \cdot t_p,$$

where t_p is measured in msec.

The resulting curves are shown in Fig. 6. The relative threshold energy of membrane excitation in the Luo–Rudy model is 1.1 within rectangular pulse time range 6.1-19.7 msec. In the Blair model, this range is 6.6-18.0 msec.

Discussion

Representation of the myocardium cell membrane time constant τ_m as a static value (Blair model) is an empirical approximation for defibrillation. The defibrillation energy increases in the Blair model faster than in the Luo–Rudy and Weiss–Lapicque models (Fig. 6). In contrast to the Weiss–Lapicque model, the Blair model differentiates between triangular ascending and triangular descending pulses [7]. It is reasonable to perform further research into defibrillation pulses using the CESE software and myocardium cell models.

Conclusion

Specific impedance, specific capacitance, and time constant τ_m of myocardium cell membrane model are not static parameters and increase with increasing transmembrane potential with respect to the resting potential.

The time constant τ_m of the myocardium cell membrane model depends on the transmembrane potential from 2.5 msec (at –86 mV) to 12.5 msec (at –75 mV).

For the Luo–Rudy model, the rectangular pulse time for membrane excitation is 11 msec, which corresponds to τ_m = 8.8 msec (2-5 msec in humans).

The Weiss–Lapicque model provides more adequate description of myocardium cell membrane reaction to rectangular defibrillation pulses.

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