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A model of the guinea-pig ventricular cardiac myocyte incorporating a transverse-axial tubular system

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► To cite this version:

Michal Pásek, Jiri Simurda, Clive H. Orchard, Georges Christé. A model of the guinea-pig ventricular cardiac myocyte incorporating a transverse-axial tubular system. *Progress in Biophysics and Molecular Biology*, 2007, 96 (1-3), pp.258-280. 10.1016/j.pbiomolbio.2007.07.022 . inserm-00326040

HAL Id: inserm-00326040

<https://inserm.hal.science/inserm-00326040v1>

Submitted on 1 Oct 2008

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Appendix 2

Fig. 6A represents the simplified equivalent electrical circuit of the cardiac cell connected to the voltage source (V_c) through electrode resistance R_{el} , including the transverse-axial tubular system (TATS). It is applicable for small (sub-threshold) voltage variations around resting membrane voltage. C_s and C_t are the capacitance, and R_{ms} and R_{mt} the resistance, of the surface and tubular membranes, respectively. V_{ms} and V_{mt} are membrane voltages. R_{st} stands for luminal resistance in a single-compartment approximation.

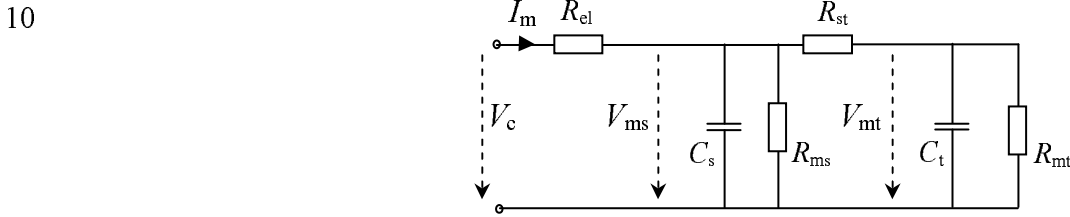


Fig. 6A

The circuit is described by a set of two differential equations

$$\frac{dV_{ms}}{dt} = a_{11} V_{ms} + a_{12} V_{mt} + \frac{V_c}{R_{el} C_s}, \quad \frac{dV_{mt}}{dt} = a_{21} V_{ms} + a_{22} V_{mt} \quad (1)$$

where

$$a_{11} = -\frac{1}{C_s} \left(\frac{1}{R_{el}} + \frac{1}{R_{st}} + \frac{1}{R_{ms}} \right), \quad a_{12} = \frac{1}{C_s R_{st}}, \quad a_{21} = \frac{1}{C_t R_{st}}, \quad a_{22} = -\frac{1}{C_t} \left(\frac{1}{R_{st}} + \frac{1}{R_{mt}} \right). \quad (2)$$

For measurement of membrane capacitance from the current responses to a small voltage step, membrane voltage V_c is constant and solution of equations (1) is expressed as a sum of two exponential functions and a constant

$$V_{ms} = V_{s1} e^{-\frac{t}{\tau_1}} + V_{s2} e^{-\frac{t}{\tau_2}} + V_{s0}, \quad V_{mt} = V_{t1} e^{-\frac{t}{\tau_1}} + V_{t2} e^{-\frac{t}{\tau_2}} + V_{t0}. \quad (3)$$

The time constants τ_1 and τ_2 are obtained from the roots (λ_1, λ_2) of characteristic equation

$$\lambda^2 - \lambda(a_{11} + a_{22}) + a_{11}a_{22} - a_{12}a_{21} = 0$$

as

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$$\begin{aligned} \tau_1 &= -\frac{1}{\lambda_1} = \frac{-2}{a_{11} + a_{22} + \sqrt{(a_{11} - a_{22})^2 + 4a_{12}a_{21}}}, \\ \tau_2 &= -\frac{1}{\lambda_2} = \frac{-2}{a_{11} + a_{22} - \sqrt{(a_{11} - a_{22})^2 + 4a_{12}a_{21}}}. \end{aligned} \quad (4)$$

The constants V_{s0} and V_{t0} depend only on the circuit resistances

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$$V_{s0} = V_c \frac{R_{ms}(R_{st} + R_{mt})}{R_{ms}(R_{st} + R_{mt}) + R_{cl}(R_{st} + R_{mt} + R_{ms})}, \quad V_{t0} = V_{s0} \frac{R_{mt}}{R_{mt} + R_{st}}. \quad (5)$$

Assuming initial conditions $V_{ms} = 0$, $V_{mt} = 0$ and taking into account (2), (4) and (5), the magnitudes of exponential components can be calculated as

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$$V_{s1} = \frac{1}{A} [V_{s0}a_{21}a_{12} + V_{t0}(a_{22}a_{12} - a_{12}\lambda_2)],$$

$$V_{s2} = \frac{1}{A} [V_{s0}a_{11}(\lambda_2 - a_{22}) + V_{s0}\lambda_1(a_{22} - \lambda_2) + V_{t0}a_{12}(\lambda_2 - a_{22})],$$

$$50 \quad V_{t1} = \frac{1}{A} [-V_{s0}a_{21}(a_{11} - \lambda_1) + V_{t0}(\lambda_2 - a_{22})(a_{11} - \lambda_1)], \quad (6)$$

$$V_{t2} = \frac{1}{A} [V_{s0}(a_{21}a_{11} - a_{21}\lambda_1) + V_{t0}a_{21}a_{12}].$$

where

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$$A = -a_{21}a_{12} + a_{22}a_{11} - a_{11}\lambda_2 - a_{22}\lambda_1 + \lambda_1\lambda_2.$$

The solution of equation (1) allows us to express the response of membrane current (I_m) to an imposed voltage step from resting voltage (regarded as zero voltage) to the level V_c considering the relation $I_m = (V_c - V_{ms})/R_{el}$.

$$I_m = I_1 e^{-\frac{t}{\tau_1}} + I_2 e^{-\frac{t}{\tau_2}} + I_0, \quad (7)$$

where $I_1 = -\frac{V_{s1}}{R_{el}}, \quad I_2 = -\frac{V_{s2}}{R_{el}}, \quad I_0 = \frac{V_c - V_{s0}}{R_{el}}.$

If numeric values of passive electrical parameters adopted for our model cardiac cell are inserted into (6) and (7), the second exponential terms of V_s , V_t , and I_m related to the short time constant ($\tau_2 \sim 1 \mu s$) become negligible (in contrast to the situation in skeletal muscle cells). The time constant τ_1 of the dominant component approaches the value corresponding to the limit conditions ($R_{st} \rightarrow 0, R_{ms} \rightarrow \infty, R_{st} \rightarrow \infty$) under which the cell would respond to small voltage steps by processes following single exponential course with time constant $\tau = R_{el}(C_s + C_t)$.