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

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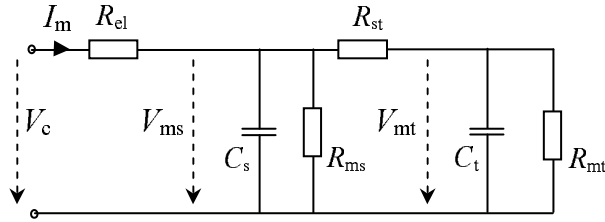
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## Appendix 2

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.

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Fig. 6A

The circuit is described by a set of two differential equations

$$20 \quad \frac{dV_{ms}}{dt} = a_{11} V_{ms} + a_{12} V_{mt} + \frac{V_c}{R_{el} C_s}, \quad \frac{dV_{mt}}{dt} = a_{21} V_{ms} + a_{22} V_{mt} \quad (1)$$

where

$$25 \quad a_{11} = -\frac{1}{C_s} \left( \frac{1}{R_{el}} + \frac{1}{R_{st}} + \frac{1}{R_{ms}} \right), \quad a_{12} = \frac{1}{C_s R_{st}}, \quad a_{21} = \frac{1}{C_t R_{st}}, \quad a_{22} = -\frac{1}{C_t} \left( \frac{1}{R_{st}} + \frac{1}{R_{mt}} \right). \quad (2)$$

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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

$$30 \quad V_{ms} = V_{s1} e^{-\frac{t}{\tau_1}} + V_{s2} e^{-\frac{t}{\tau_2}} + V_{s0}, \quad V_{mt} = V_{t1} e^{-\frac{t}{\tau_1}} + V_{t2} e^{-\frac{t}{\tau_2}} + V_{t0}. \quad (3)$$

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The time constants  $\tau_1$  and  $\tau_2$  are obtained from the roots ( $\lambda_1, \lambda_2$ ) 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  $\tau_1$  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  $\tau = R_{el}(C_s + C_t)$ .