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

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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.

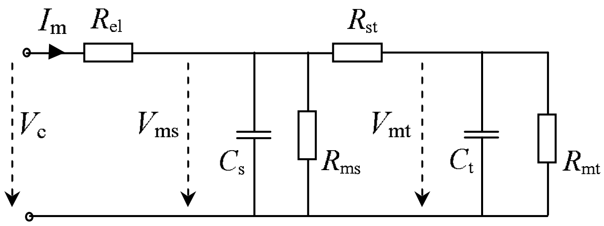

Fig. 6A

The circuit is described by a set of two differential equations

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

where

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

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

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

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

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

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

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

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

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

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

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

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

where

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

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 $I_m = (V_c - V_{ms})/R_{el}$.

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

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 ($\tau_2 \sim 1$ μs) 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 $\tau = R_{el} (C_s + C_t)$.