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 \(R_{cl}\), 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. \(R_\alpha\) stands for luminal resistance in a single-compartment approximation.

![Circuit Diagram](image)

The circuit is described by a set of two differential equations

\[
\frac{dV_{ms}}{dt} = a_{11} V_{ms} + a_{12} V_{mt} + \frac{V_c}{R_{cl} C_s}, \quad \frac{dV_{mt}}{dt} = a_{21} V_{ms} + a_{22} V_{mt}
\]

(1)

where

\[
a_{11} = -\frac{1}{C_s} \left( \frac{1}{R_{cl}} + \frac{1}{R_{st}} + \frac{1}{R_{ms}} \right), \quad a_{12} = \frac{1}{C_s R_{st}}, \quad a_{21} = \frac{1}{C_t R_{st}}, \quad a_{22} = -\frac{1}{C_t} \left( \frac{1}{R_{st}} + \frac{1}{R_{mt}} \right)
\]

(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

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

(3)

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

\[
\tau_1 = -\frac{1}{\lambda_1} = \frac{-2}{a_{11} + a_{22} + \sqrt{(a_{11} - a_{22})^2 + 4a_{12}a_{21}}},
\]

\[
\tau_2 = -\frac{1}{\lambda_2} = \frac{-2}{a_{11} + a_{22} - \sqrt{(a_{11} - a_{22})^2 + 4a_{12}a_{21}}}. \tag{4}
\]

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

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

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

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

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

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

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

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

\[
I_m = I_1 e^{-t/\tau_1} + I_2 e^{-t/\tau_2} + I_0,
\]

(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 \( \tau_2 \sim 1 \) ms 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 \( R_s \to 0, R_{ms} \to \infty, R_{st} \to \infty \) under which the cell would respond to small voltage steps by processes following single exponential course with time constant \( \tau = R_{el}(C_s + C_t). \).