Passive cable solutions and channel descriptions

The simulations required the following integral for $\Phi_0(X, T)$, representing the solution to the linear cable equation, to be evaluated:

$$\Phi_0(X, T) = \int_0^T \frac{I_A(0, s)}{U_{\text{peak}}} G(X, 0; T - s) dY ds,$$

where $I_A(0, T)$ represents the shape of the action potential, $H(T)$ is the Heaviside step function and $G(X, X_i; T)$ is the Green’s function given by the solution to the following initial value problem:

$$\frac{\partial G}{\partial T}(X, X_i; T) = \frac{\partial^2 G}{\partial X^2}(X, X_i; T) - G(X, X_i; T) + \delta(X - X_i)\delta(T)$$

$$G(X, X_i; T) = \begin{cases} I_A(0, T) & \text{for } X_i = 0 \\ 0 & \text{for } X_i \neq 0 \end{cases}$$

and corresponds to the response at time $T$ at position $X$ to a unit impulse at $X = X_i$ and $T = 0$. For a semi-infinite cable with the above nonhomogeneous boundary condition at $X = 0$ the Green’s functions $G(X, 0; T)$ for $X_i = 0$ and $G(X, X_i; T)$ for $X_i \neq 0$ are given by

$$G(X, 0; T) = \frac{e^{-T}}{\sqrt{4\pi T^3}} X \exp \left( -\frac{X^2}{4T} \right),$$

and

$$G(X, X_i; T) = \frac{e^{-T}}{\sqrt{4\pi T}} \left[ \exp \left( -\frac{(X - X_i)^2}{4T} \right) - \exp \left( -\frac{(X + X_i)^2}{4T} \right) \right],$$

respectively.

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The integral expression for $\Phi_0(X, T)$ can be solved analytically but requires the following integrals to be used,

$$
\Gamma(-n - v - 1; \frac{X^2}{4T}) = \int_{\frac{X^2}{4T}}^{\infty} z^{-v-2-n} \exp(-z) dz,
$$

$$
I = \int_{0}^{T} \zeta^v \exp \left( \zeta(\alpha - 1) - \frac{X^2}{4} \right) d\zeta,
$$

where $\Gamma$ is the incomplete Gamma function. Keeping only the first two terms of the series, and utilizing the following identities

$$
\Gamma \left( \frac{1}{2}; \frac{X^2}{4T} \right) = \sqrt{\pi} \operatorname{erfc} \left( \frac{X}{\sqrt{4T}} \right),
$$

$$
\Gamma \left( -\frac{1}{2}; \frac{X^2}{4T} \right) = \frac{4\sqrt{T}}{X} \exp \left( \frac{X^2}{4T} \right) - 2\sqrt{\pi} \operatorname{erfc} \left( \frac{X}{\sqrt{4T}} \right),
$$

leads to the following expression for $\Phi_0(X, T)$ used in the simulations, here the action potential has an after depolarizing tail and is generally given by the following expression,

$$
I_A(0, T) = U_0 \left( 10e^{-AT/7.5} \sin((2\pi/150)AT) + 67e^{-2AT} - 70e^{-4AT} + 3e^{-AT/24} \right) H(T),
$$

where $A = 15$ and $H(T)$ is the Heaviside step function. Then, the integral expression for $\Phi_0(X, T)$ can be evaluated analytically (keeping only leading order terms of the expansion) and is given by the following,

$$
\Phi_0(X, T) = \frac{10U_0}{U_{\text{peak}}\sqrt{\pi}} \left\{ \sin \left( \frac{2\pi AT}{150} \right) \left[ 1 - \left( \frac{X^2}{2} \right) \left( \frac{A}{7.5} - 1 \right) - \frac{2}{3} \left( \frac{2\pi A}{150} \right)^2 \left( \frac{X^2}{4} \right)^2 \right] + \frac{4}{15} \left( \frac{2\pi A}{150} \right)^2 \left( \frac{A}{7.5} - 1 \right) \left( \frac{X^2}{4} \right)^3 + \cos \left( \frac{2\pi AT}{150} \right) \left( \frac{2\pi A}{150} \right)^2 \left( \frac{X^2}{2} \right) \times \left[ 1 - \frac{2}{3} \left( \frac{A}{7.5} - 1 \right) \left( \frac{X^2}{4} \right)^2 - \frac{2}{45} \left( \frac{2\pi A}{150} \right)^2 \left( \frac{X^2}{4} \right)^2 \right] + \frac{4}{315} \left( \frac{2\pi A}{150} \right)^2 \left( \frac{A}{7.5} - 1 \right) \left( \frac{X^2}{4} \right)^3 \pi \operatorname{erfc} \left( \frac{X}{\sqrt{4T}} \right) e^{-AT/7.5} + \sin \left( \frac{2\pi AT}{150} \right) X\sqrt{T} \left[ \left( \frac{A}{7.5} - 1 \right) - \frac{1}{2} \left( \frac{2\pi AT}{150} \right)^2 \left( \frac{T}{3} - \frac{X^2}{6} \right) \right] \exp \left( -\frac{X^2}{4T} - \frac{AT}{7.5} \right) - \frac{1}{2} \left( \frac{2\pi AT}{150} \right)^2 \left( \frac{A}{7.5} - 1 \right) \left( \frac{T^2}{5} - \frac{X^2 T}{30} + \frac{X^4}{60} \right) \exp \left( -\frac{X^2}{4T} - \frac{AT}{7.5} \right) - \cos \left( \frac{2\pi AT}{150} \right) X\sqrt{T} \exp \left( -\frac{X^2}{4T} - \frac{AT}{7.5} \right) \left( \frac{2\pi A}{150} \right)^2 \left( \frac{T^2}{5} - \frac{X^2 T}{30} + \frac{X^4}{60} \right) - \frac{1}{6} \left( \frac{2\pi AT}{150} \right)^3 \left( \frac{A}{7.5} - 1 \right) \left( \frac{T^3}{7} - \frac{X^2 T^2}{70} + \frac{X^4 T}{420} - \frac{X^6}{840} \right) + \left[ 6.7 \left( 1 - \frac{X^2}{2} \left( 2A - 1 \right) \right) e^{-2AT} - 7 \left( 1 - \frac{X^2}{2} \left( 4A - 1 \right) \right) e^{-4AT} + 0.3 \left( 1 - \frac{X^2}{2} \left( 2A - 1 \right) \right) e^{-AT/24} \right] \sqrt{\pi \operatorname{erfc} \left( \frac{X}{\sqrt{4T}} \right)} + 4X\sqrt{T} \exp \left( -\frac{X^2}{4T} \right) \left[ 6.7 \left( \frac{2A - 1}{4} \right) e^{-2AT} - 7 \left( \frac{2A - 1}{4} \right) e^{-4AT} + 0.3 \left( \frac{A - 1}{4} \right) e^{-AT/24} \right] \right\},
$$

where $\operatorname{erfc}$ is the complementary error function.
The descriptions of the ionic currents used in the simulations

Sodium current $I_{Na}$

\[
I_{Na} = \varepsilon g_{Na} N_{Na} (X_i) m^3 h (\Phi_{Na} - \Phi)
\]

\[
\frac{1}{\tau_m} \frac{\partial m}{\partial T} = \alpha_m - (\alpha_m + \beta_m) m
\]

\[
\alpha_m = 0.182(\Phi U_{peak} + Er + 35)/(1 - \exp(-(\Phi U_{peak} + Er + 35)/9))
\]

\[
\beta_m = -0.124(\Phi U_{peak} + Er + 35)/(1 - \exp(\Phi U_{peak} + Er + 35)/9)
\]

\[
\frac{1}{\tau_h} \frac{\partial h}{\partial T} = (h_\infty - h)/\tau_h
\]

\[
\alpha_h = 0.02(\Phi U_{peak} + Er + 50)/(1 - \exp(-(\Phi U_{peak} + Er + 50)/5))
\]

\[
\beta_h = -0.009(\Phi U_{peak} + Er + 75)/(1 - \exp(\Phi U_{peak} + Er + 75)/5)
\]

\[
h_\infty = 1/(1 + \exp(\Phi U_{peak} + 65)/6.2)
\]

\[
\tau_h = 1/(\alpha_h + \beta_h)
\]

Potassium current $I_K$

\[
I_K = \varepsilon g_K N_K (X_i) n (\Phi_K - \Phi)
\]

\[
\frac{1}{\tau_m} \frac{\partial n}{\partial T} = \alpha_n - (\alpha_n + \beta_n) n
\]

\[
\alpha_n = 0.02(\Phi U_{peak} + Er - 20)/(1 - \exp(-(\Phi U_{peak} + Er - 20)/9))
\]

\[
\beta_n = -0.002(\Phi U_{peak} + Er - 20)/(1 - \exp(\Phi U_{peak} + Er - 20)/9)
\]

Transient Potassium A-current $I_{K(A)}$

\[
I_{K(A)} = \varepsilon g_{K(A)} N_{K(A)} (X_i) m^4 h (\Phi_{K(A)} - \Phi)
\]

\[
\frac{1}{\tau_m} \frac{\partial m}{\partial T} = (m_\infty - m)/\tau_{m_{K(A)}}
\]

\[
\frac{1}{\tau_m} \frac{\partial h}{\partial T} = (h_\infty - h)/\tau_{h_{K(A)}}
\]

\[
m_\infty = 1/(1 + \exp(-(\Phi U_{peak} + 60)/8.5))
\]

\[
h_\infty = 1/(1 + \exp((\Phi U_{peak} + 78)/6)
\]

\[
\tau_{m_{K(A)}} = 0.185 + 0.5/[\exp((\Phi U_{peak} + 35.8)/19.7) + \exp(-(\Phi U_{peak} + 79.7)/12.7)]
\]

\[
\tau_{h_{K(A)}} = 0.5/[\exp((\Phi U_{peak} + 46)/5)
\]

\[
+ \exp(-(\Phi U_{peak} + 238)/37.5)]
\]

\[
= 9.5
\]

for $\Phi U_{peak} \leq -63$

for $\Phi U_{peak} > -63$

High-Voltage-Activated (HVA) L-type calcium current $I_{Ca(HVA)}$

\[
I_{Ca(HVA)} = \varepsilon g_{Ca(HVA)} N_{Ca(HVA)} (X_i) m^2 (\Phi_{Ca(HVA)} - \Phi)
\]

\[
\frac{1}{\tau_m} \frac{\partial m}{\partial T} = \alpha_m - (\alpha_m + \beta_m) m
\]

\[
\alpha_m = 1.6/(1 - \exp(-0.072(\Phi U_{peak} + Er - 5))
\]

\[
\beta_m = -0.02(\Phi U_{peak} + Er + 8.9)/(1 - \exp(\Phi U_{peak} + Er + 8.9)/5)
\]
Low-Voltage-Activated T-type calcium current $I_{Ca(T)}$

$$I_{Ca(T)} = \varepsilon g_{Ca(T)} N_{Ca(T)}(X_i) m^2 h (\Phi_{Ca(T)} - \Phi)$$

$$\frac{1}{\tau_m} \frac{\partial m}{\partial T} = \frac{(m_\infty - m)}{\tau_{m_{Ca(T)}}}$$

$$\frac{1}{\tau_m} \frac{\partial h}{\partial T} = \frac{(h_\infty - h)}{\tau_{h_{Ca(T)}}}$$

Low-Voltage-Activated T-type calcium current $I_{Ca(T)}$

$$m_\infty = \frac{1}{(1 + \exp((-\Phi_{peak} + 56)/6.5))}$$

$$\tau_{m_{Ca(T)}} = 0.204 + \frac{0.333}{\exp((\Phi_{peak} - 15.8)/18.2) + \exp(- (\Phi_{peak} + 131)/16.7)}$$

$$h_\infty = \frac{1}{(1 + \exp((-\Phi_{peak} + 80)/4))}$$

$$\tau_{h_{Ca(T)}} = \begin{cases} 
0.333 \exp((\Phi_{peak} + 466)/66.6) & \Phi_{peak} \leq -81 \\
9.32 + 0.333 \exp(- (\Phi_{peak} + 21)/10.5) & \Phi_{peak} \geq -81 
\end{cases}$$

Single channel conductance used in the simulations were:

$$g_{Na} = 18 \text{ pS}$$

$$g_{K} = 20 \text{ pS}$$

$$g_{K(A)} = 6 \text{ pS}$$

$$g_{Ca(HVA)} = 25 \text{ pS}$$

$$g_{CaT} = 8 \text{ pS}$$

$$g_{NMDA} = 50 \text{ pS}$$

Simulations were conducted using 10 equally spaced hotspots between $X = 0$ to $X = 0.3$ dimensionless units ($x = 300 \mu m$) for all ion channels and a single hotspot of NMDA receptors.

The number of channels per hotspot was calculated by finding the total number of channels in a cable of length 300 $\mu m$ from the channel density $\overline{g}_\mu$ (units of pS/$\mu m^2$) and dividing this by the number of hotspots for the specific channel under consideration. The channel densities used were as follows:

$$\overline{g}_{Na} = 100 \text{ pS/} \mu m^2$$

$$\overline{g}_{K} = 80 \text{ pS/} \mu m^2$$

$$\overline{g}_{K(A)} = 50 \text{ pS/} \mu m^2$$

$$\overline{g}_{Ca(HVA)} = 40 \text{ pS/} \mu m^2$$

$$\overline{g}_{CaT} = 20 \text{ pS/} \mu m^2$$

Finally, the parameter values for the calculation of the internal accumulation and diffusion of calcium used for the chemical cable were given by the following:

$$[Ca]_{ref} = 2 \text{ mM}$$

$$D_{Ca} = 0.23 \text{ } \mu m^2/\text{msec}$$

$$D_{M} = 0.13 \text{ } \mu m^2/\text{msec}$$

$$P_{m} = 2 \text{ } \mu m/\text{msec}$$

$$\beta = 10.$$ 

A value of $\varepsilon = 0.095$ was used in all simulations.