Supplementary Information - A nonlinear cable framework for bidirectional synaptic plasticity

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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,

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

$$I = \int_0^T \zeta^v \exp\left(\zeta(\alpha - 1) - \frac{X^2}{4\zeta}\right) d\zeta,$$

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

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

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

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,

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

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,

$$\Phi_0(X, T) = \frac{10U_0}{U_{\text{peak}} \sqrt{\pi}} \left\{ \sin\left(\frac{2\pi AT}{150}\right) \left[ 1 - \left(\frac{X^2}{2}\right) \left(\frac{X^2}{7.5} - 1\right) - \frac{2}{3} \left(\frac{2\pi A}{150}\right)^2 \left(\frac{X^2}{4}\right)^2 \right] + \frac{4}{15} \left(\frac{2\pi A}{150}\right)^2 \left(\frac{A}{7.5} - 1\right) \left(\frac{X^2}{4}\right)^3 \right\} \text{erfc}\left(\frac{X}{\sqrt{4T}}\right) e^{-AT/7.5}$$

$$+ \sin\left(\frac{2\pi AT}{150}\right) X \sqrt{T} \left[ \left(\frac{A}{7.5} - 1\right) - \frac{1}{2} \left(\frac{2\pi AT}{150}\right)^2 \left(\frac{T}{3} - \frac{X^2}{6}\right) \right. - \frac{1}{2} \left(\frac{2\pi AT}{150}\right)^2 \left(\frac{AT}{7.5} - 1\right) \left(\frac{T^2}{5} - \frac{X^2 T}{30} + \frac{X^4}{60}\right) \left. \right] \exp\left(\frac{X^2}{4T} - AT/7.5\right)$$

$$- \cos\left(\frac{2\pi AT}{150}\right) X \sqrt{T} \exp\left(-\frac{X^2}{4T} - \frac{AT}{7.5}\right) \frac{2\pi A}{150}$$

$$+ \left(\frac{2\pi AT}{150}\right) \left(\frac{A}{7.5} - 1\right) \left(\frac{T^3}{3} - \frac{X^2 T}{6} - \frac{1}{6} \left(\frac{2\pi AT}{150}\right)^3 \left(\frac{T^2}{5} - \frac{X^2 T}{30} + \frac{X^4}{60}\right) \right)$$

$$- \frac{1}{6} \left(\frac{2\pi AT}{150}\right)^3 \left(\frac{A}{7.5} - 1\right) \left(\frac{T^3}{3} - \frac{X^2 T^2}{70} + \frac{X^4 T}{120} - \frac{X^6}{840}\right)$$

$$+ \left[6.7\left(1 - \left(\frac{X^2}{2}\right) (2A - 1)\right) e^{-2AT} - 7\left(1 - \left(\frac{X^2}{2}\right) (4A - 1)\right) e^{-4AT}\right.$$

$$+ 0.3\left(1 - \left(\frac{X^2}{2}\right) (4A - 1)\right) e^{-AT/24}\right] \sqrt{\pi} \text{erfc}\left(\frac{X}{\sqrt{4T}}\right)$$

$$+ 4X \sqrt{T} \exp\left(-\frac{X^2}{4T}\right) \left[6.7\left(\frac{2A - 1}{4}\right) e^{-2AT} - 7\left(\frac{2A - 1}{4}\right) e^{-4AT}\right.$$

$$+ 0.3\left(\frac{A}{24} - 1\right) e^{-AT/24}\right],$$

where erfc is the complementary error function.
The descriptions of the ionic currents used in the simulations

Sodium current \( I_{Na} \)

\[
\begin{align*}
I_{Na} &= \varepsilon g_{Na} N_{Na}(X_i)m^3h(\Phi_{Na} - \Phi) \\
\frac{1}{\tau_m} \frac{\partial m}{\partial T} &= \alpha_m - (\alpha_m + \beta_m)m \\
\alpha_m &= 0.182(\Phi U_{peak} + Er + 35)/(1 - \exp(-(\Phi U_{peak} + Er + 35)/9)) \\
\beta_m &= -0.124(\Phi U_{peak} + Er + 35)/(1 - \exp(\Phi U_{peak} + Er + 35)/9) \\
\frac{1}{\tau_h} \frac{\partial h}{\partial T} &= (h_{\infty} - h)/\tau_h \\
\alpha_h &= 0.024(\Phi U_{peak} + Er + 50)/(1 - \exp(-(\Phi U_{peak} + Er + 50)/5)) \\
\beta_h &= -0.0091(\Phi U_{peak} + Er + 75)/(1 - \exp(\Phi U_{peak} + Er + 75)/5) \\
h_{\infty} &= 1/(1 + \exp(\Phi U_{peak} + 65)/6.2) \\
\tau_h &= 1/(\alpha_h + \beta_h)
\end{align*}
\]

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 \( I_{K(A)} \)

\[
I_{K(A)} = \varepsilon g_{K(A)} N_{K(A)}(X_i)m^4h(\Phi_{K(A)} - \Phi) \\
\frac{1}{\tau_m} \frac{\partial m}{\partial T} = (m_{\infty} - m)/\tau_{m_{K(A)}} \\
\frac{1}{\tau_h} \frac{\partial h}{\partial T} = (h_{\infty} - h)/\tau_{h_{K(A)}} \\
m_{\infty} &= 1/(1 + \exp(-(\Phi U_{peak} + 60)/8.5)) \\
h_{\infty} &= 1/(1 + \exp((\Phi U_{peak} + 78)/6) \\
\tau_{m_{K(A)}} &= 0.185 + 0.5/[\exp((\Phi U_{peak} + 35.8)/19.7) + \exp(-(\Phi U_{peak} + 79.7)/12.7)] \\
\tau_{h_{K(A)}} &= 0.5/[\exp((\Phi U_{peak} + 46)/5) \\
&\quad + \exp(-(\Phi U_{peak} + 238)/37.5)] \\
&= 9.5 \\
&\text{for } \Phi U_{peak} \leq -63 \\
&\text{for } \Phi U_{peak} > -63
\]

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

\[
\begin{align*}
I_{Ca(HVA)} &= \varepsilon g_{Ca(HVA)} N_{Ca(HVA)}(X_i)m^2(\Phi_{Ca(HVA)} - \Phi) \\
\frac{1}{\tau_m} \frac{\partial m}{\partial T} &= \alpha_m - (\alpha_m + \beta_m)m \\
\alpha_m &= 1.6/(1 - \exp(-0.072(\Phi U_{peak} + Er - 5)) \\
\beta_m &= -0.02(\Phi U_{peak} + Er + 8.9)/(1 - \exp(\Phi U_{peak} + Er + 8.9)/5)
\end{align*}
\]
Low-Voltage-Activated T-type calcium current $I_{Ca(T)}$

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

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

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

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

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

$$\tau_{m_{Ca(T)}} = \frac{0.204 + 0.333 \exp(\left(\Phi_{peak} - 15.8\right)/18.2) + \exp(-\left(\Phi_{peak} + 131\right)/16.7)}{1/(1 + \exp(-\left(\Phi_{peak} + 80\right)/4))}$$

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

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

Single channel conductance used in the simulations were:

- $g_{Na} = 18 \text{ pS}$
- $g_{K} = 20 \text{ pS}$
- $g_{K(A)} = 6 \text{ pS}$
- $g_{Ca(HVA)} = 25 \text{ pS}$
- $g_{Ca(T)} = 8 \text{ pS}$
- $g_{NMDA} = 50 \text{ pS}$

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 $\overline{\gamma}_\mu$ (units of $\text{pS}/\mu m^2$) and dividing this by the number of hotspots for the specific channel under consideration. The channel densities used were as follows:

- $\overline{\gamma}_{Na} = 100 \text{ pS}/\mu m^2$
- $\overline{\gamma}_{K} = 80 \text{ pS}/\mu m^2$
- $\overline{\gamma}_{K(A)} = 50 \text{ pS}/\mu m^2$
- $\overline{\gamma}_{Ca(HVA)} = 40 \text{ pS}/\mu m^2$
- $\overline{\gamma}_{Ca(T)} = 20 \text{ pS}/\mu m^2$

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:

- $[Ca]_{ref} = 2 \text{ mM}$
- $D_{Ca} = 0.23 \mu m^2/msec$
- $D_M = 0.13 \mu m^2/msec$
- $P_m = 2 \mu m/msec$
- $\beta = 10$. 

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