Supplementary Information:

A mathematical model for the effects of amyloid beta on intracellular calcium

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S1 Appendix

Here we provide a summary of both the IP$\textsubscript{3}$ receptor model equations and those governing the membrane potential. We also give the model parameters used in the Hodgkin and Huxley formulation of the membrane potential.

The IP$\textsubscript{3}$ receptor has six states that can be reduced to the following five equations

\[
\begin{align*}
\frac{dR}{dt} &= \phi_{-2}O - \phi_{2p}R + k_{-1}I_1 - \phi_1 R, \\
\frac{dO}{dt} &= \phi_{2p}R - (\phi_{-2} + \phi_4 + \phi_3)O + \phi_{-4}A + k_{-3}S, \\
\frac{dA}{dt} &= \phi_4 O - \phi_{-4}A - \phi_5 A + k_{-1}I_2, \\
\frac{dI_1}{dt} &= \phi_1 R - k_{-1}I_1, \\
\frac{dI_2}{dt} &= \phi_5 A - k_{-1}I_2,
\end{align*}
\]

where $R + O + A + S + I_1 + I_2 = 1$, and where each rate function $\phi(c)$ between states is given below. The rate functions for the IP$\textsubscript{3}$ receptor model are taken from \cite{1} which are a simplification of the Sneyd and Dufour (2002) model. The rate functions are given by

\begin{align*}
\phi_1(c) &= \frac{\alpha_1 c}{\beta_1 + c}, \\
\phi_2(c) &= \frac{\alpha_2 + \beta_3 c}{\beta_1 + c}, \\
\phi_3(c) &= \frac{\alpha_3}{\beta_3 + c}, \\
\phi_4(c) &= \frac{\alpha_4 c}{\beta_3 + c}, \\
\phi_5(c) &= \frac{\alpha_5 c}{\beta_5 + c}, \\
\phi_{-2}(c) &= \frac{\alpha_{-2} + \beta_{-2} c}{\beta_3 + c}, \\
\phi_{-4}(c) &= \frac{\alpha_{-4}}{\beta_5 + c}
\end{align*}

The relevant parameters for the IP$\textsubscript{3}$ receptor model used in the simulations are provided in \cite{2}. This model was chosen since it does respond reasonably well to changes in Ca$^{2+}$ and IP$\textsubscript{3}$ \cite{3}.
The formulation of our Hodgkin and Huxley like membrane potential is given by

\[
C_m \frac{dV}{dt} = -I_{\text{Kir}}(V) - \bar{g}_n a m^3 h(V - V_{na}) - \bar{g}_l (V - V_l) - I_{\text{Ca}}(V) + I_{\text{app}},
\]

(13)

\[
\frac{dm}{dt} = \alpha_m(V)(1 - m) - \beta_m(V)m,
\]

(14)

\[
\frac{dh}{dt} = \alpha_h(V)(1 - h) - \beta_h(V)h,
\]

(15)

where \(C_m = 15 \mu \text{F/cm}^2\), \(\bar{g}_n a = 120 \text{mS/cm}^2\), \(\bar{g}_l = 0.1 \text{mS/cm}^2\), \(V_{na} = 50 \text{mV}\), \(V_l = -74 \text{mV}\), with the following gating functions

\[
\alpha_m(V) = \frac{0.1 (V + 40)}{1 - \exp(-(V + 40)/10)},
\]

(16)

\[
\beta_m(V) = 4 \exp(-(V + 65)/18),
\]

(17)

\[
\alpha_h(V) = 0.07 \exp(-(V + 65)/20),
\]

(18)

\[
\beta_h(V) = \frac{1}{1 + \exp(-(V + 35)/10)}.
\]

(19)

The calcium current in (13) takes the form

\[
I_{\text{Ca}}(V) = \bar{g}_{\text{Ca}} T m^2_{\text{Ca}} h_{\text{Ca}} T(V)(V - V_{\text{Ca}}),
\]

(20)

where the gating activation \(m_{\text{Ca}} T(V)\) and inactivation \(h_{\text{Ca}} T(V)\) have the form

\[
\frac{dm_{\text{Ca}} T}{dt} = \frac{m_{\text{Ca}} T, \infty(V) - m_{\text{Ca}} T}{\tau_{m_{\text{Ca}} T}(V)},
\]

(21)

and

\[
\frac{dh_{\text{Ca}} T}{dt} = \frac{h_{\text{Ca}} T, \infty(V) - h_{\text{Ca}} T}{\tau_{h_{\text{Ca}} T}(V)},
\]

(22)

with

\[
m_{\text{Ca}} T, \infty(V) = \frac{1}{1 + \exp(-(V + 56.1)/10)},
\]

(23)

\[
\tau_{m_{\text{Ca}} T}(V) = \frac{1}{1 + \exp((V + 86.4)/4.7)}.
\]

(24)

\[
h_{\text{Ca}} T, \infty(V) = \frac{7}{(\exp((V + 50)/9) + \exp(-(V + 50)/9))} + 0.8,
\]

(25)

\[
\tau_{h_{\text{Ca}} T}(V) = 22.
\]

(26)

The form and values of the gating variables were chosen to match those used by LeBeau et al. (2000) in their study using hypothalamic neurons [4]. Also note that in our simulations involving membrane potentials, we used a timescale

\[
\tilde{t} = C_m \left(1 + \exp \left(\frac{V - V_{ka} - V_{a2}}{V_{a3}}\right)\right) / (g_{\text{Kir}} \sqrt{K_0})
\]

(27)

as in [5] to account for the rectifier channel-mediated return to equilibrium of the astroglial membrane potential.

References


