

## S1 FILE. MODEL EQUATIONS

For each modeled channel  $x$ , equations for steady-state activation and inactivation curves, time constants and current are reported below. When necessary,  $m_x^f$ ,  $m_x^m$ ,  $m_x^s$  ( $h_x^f$ ,  $h_x^m$ ,  $h_x^s$ ) denote fast, medium and slow component, respectively, of activating (inactivating) variable associated to the  $x$  channel, while  $\tau_{m_x}^f$ ,  $\tau_{m_x}^m$ ,  $\tau_{m_x}^s$  ( $\tau_{h_x}^f$ ,  $\tau_{h_x}^m$ ,  $\tau_{h_x}^s$ ) denote the corresponding time constants. Data obtained from these equations are reported in the corresponding panels of Figs 1, 2, 3, and S1, S2, S3, S5 Figs. Fitted values of parameters are reported in S1 Table.

### A. VOLTAGE-GATED POTASSIUM CURRENTS

#### SHL1

$$(A1) \quad m_{\text{SHL1},\infty}(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(A2) \quad \tau_{m_{\text{SHL1}}}(V) = \frac{a}{e^{-\frac{(V-b)}{c}} + e^{\frac{(V-d)}{e}}} + f$$

$$(A3) \quad h_{\text{SHL1},\infty}^f(V) = h_{\text{SHL1},\infty}^s(V) = \frac{1}{1 + e^{\frac{(V-V_{0.5})}{k_i}}}$$

$$(A4) \quad \tau_{h_{\text{SHL1}}}^f(V) = \tau_{h_{\text{SHL1}}}^s(V) = \frac{a}{1 + e^{\frac{(V-b)}{c}}} + d$$

$$(A5) \quad I_{\text{SHL1}} = \bar{g}_{\text{SHL1}} \cdot m_{\text{SHL1}}^3 \cdot (0.7 h_{\text{SHL1}}^f + 0.3 h_{\text{SHL1}}^s) \cdot (V - V_K)$$

#### KVS1

$$(A6) \quad m_{\text{KVS1},\infty}(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(A7) \quad h_{\text{KVS1},\infty}(V) = \frac{1}{1 + e^{\frac{(V-V_{0.5})}{k_i}}}$$

$$(A8) \quad \tau_{m_{\text{KVS1}}}(V) = \tau_{h_{\text{KVS1}}}(V) = \frac{a}{1 + e^{\frac{(V-b)}{c}}} + d$$

$$(A9) \quad I_{\text{KVS1}} = \bar{g}_{\text{KVS1}} \cdot m_{\text{KVS1}} \cdot h_{\text{KVS1}} \cdot (V - V_K)$$

#### SHK1

$$(A10) \quad m_{\text{SHK1},\infty}(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(A11) \quad \tau_{m_{\text{SHK1}}}(V) = \frac{a}{e^{-\frac{(V-b)}{c}} + e^{\frac{(V-d)}{e}}} + f$$

$$(A12) \quad h_{\text{SHK1},\infty}(V) = \frac{1}{1 + e^{\frac{(V-V_{0.5})}{k_i}}}$$

$$(A13) \quad \tau_{h_{\text{SHK1}}} = a$$

$$(A14) \quad I_{\text{SHK1}} = \bar{g}_{\text{SHK1}} \cdot m_{\text{SHK1}} \cdot h_{\text{SHK1}} \cdot (V - V_K)$$

**KQT3**

$$(A15) \quad m_{\text{KQT3},\infty}^f(V) = m_{\text{KQT3},\infty}^s(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(A16) \quad \tau_{m_{\text{KQT3}}}^f(V) = \frac{a}{1 + \left(\frac{V+b}{c}\right)^2}$$

$$(A17) \quad \tau_{m_{\text{KQT3}}}^s(V) = a + \frac{b}{1 + 10^{-c(d-V)}} + \frac{e}{1 + 10^{-f(g+V)}}$$

$$(A18) \quad w_{\text{KQT3},\infty}(V) = s_{\text{KQT3},\infty}(V) = a + \frac{b}{1 + e^{-\frac{V-V_{0.5}}{k_i}}}$$

$$(A19) \quad \tau_{w_{\text{KQT3}}}(V) = a + \frac{b}{1 + \left(\frac{V-c}{d}\right)^2}$$

$$(A20) \quad \tau_{s_{\text{KQT3}}} = a$$

$$(A21) \quad I_{\text{KQT3}} = \bar{g}_{\text{KQT3}} \cdot (0.7 m_{\text{KQT3}}^f + 0.3 m_{\text{KQT3}}^s) \cdot w_{\text{KQT3}} \cdot s_{\text{KQT3}} \cdot (V - V_K)$$

**EGL2**

$$(A22) \quad m_{\text{EGL2},\infty}(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(A23) \quad \tau_{m_{\text{EGL2}}}(V) = \frac{a}{1 + e^{-\frac{(V-b)}{c}}} + d$$

$$(A24) \quad I_{\text{EGL2}} = \bar{g}_{\text{EGL2}} \cdot m_{\text{EGL2}} \cdot (V - V_K)$$

**EGL36**

$$(A25) \quad m_{\text{EGL36},\infty}^f(V) = m_{\text{EGL36},\infty}^m(V) = m_{\text{EGL36},\infty}^s(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(A26) \quad \tau_{m_{\text{EGL36}}}^f = \tau_{m_{\text{EGL36}}}^m = \tau_{m_{\text{EGL36}}}^s = a$$

$$(A27) \quad I_{\text{EGL36}} = \bar{g}_{\text{EGL36}} \cdot (0.33 m_{\text{EGL36}}^f + 0.36 m_{\text{EGL36}}^m + 0.39 m_{\text{EGL36}}^s) \cdot (V - V_K)$$

**IRK**

$$(A28) \quad m_{\text{IRK},\infty}(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(A29) \quad \tau_{m_{\text{IRK}}}(V) = \frac{a}{e^{-\frac{(V-b)}{c}} + e^{-\frac{(V-d)}{e}}} + f$$

$$(A30) \quad I_{\text{IRK}} = \bar{g}_{\text{IRK}} \cdot m_{\text{IRK}} \cdot (V - V_K)$$

## B. VOLTAGE-GATED CALCIUM CURRENTS

**EGL19**

$$(B1) \quad m_{\text{EGL19},\infty}(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(B2) \quad \tau_{m_{\text{EGL19}}}(V) = \left[ a e^{-\left(\frac{V-b}{c}\right)^2} \right] + \left[ d e^{-\left(\frac{V-e}{f}\right)^2} \right] + g$$

$$(B3) \quad h_{\text{EGL19},\infty}(V) = \left[ \frac{a}{1 + e^{-\frac{(V-V_{0.5})}{k_i}}} + b \right] + \left[ \frac{c}{1 + e^{-\frac{(V-V_{0.5})}{k_i^b}}} + d \right]$$

$$(B4) \quad \tau_{h_{\text{EGL19}}}(V) = a \left[ \frac{b}{1 + e^{-\frac{V-c}{d}}} + \frac{e}{1 + e^{-\frac{V-f}{g}}} + h \right]$$

$$(B5) \quad I_{\text{EGL19}} = \bar{g}_{\text{EGL19}} \cdot m_{\text{EGL19}} \cdot h_{\text{EGL19}} \cdot (V - V_{Ca})$$

**UNC2**

$$(B6) \quad m_{\text{UNC2},\infty}(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(B7) \quad \tau_{m_{\text{UNC2}}}(V) = \frac{a}{e^{-\frac{(V-b)}{c}} + e^{-\frac{(V-b)}{d}}} + e$$

$$(B8) \quad h_{\text{UNC2},\infty}(V) = \frac{1}{1 + e^{-\frac{(V-V_{0.5})}{k_i}}}$$

$$(B9) \quad \tau_{h_{\text{UNC2}}}(V) = \frac{a}{1 + e^{-\frac{(V-b)}{c}}} + \frac{d}{1 + e^{-\frac{(V-e)}{f}}}$$

$$(B10) \quad I_{\text{UNC2}} = \bar{g}_{\text{UNC2}} \cdot m_{\text{UNC2}} \cdot h_{\text{UNC2}} \cdot (V - V_{Ca})$$

**CCA1**

$$(B11) \quad m_{\text{CCA1},\infty}(V) = \frac{1}{1 - e^{-\frac{(V-V_{0.5})}{k_a}}}$$

$$(B12) \quad h_{\text{CCA1},\infty}(V) = \frac{1}{1 + e^{-\frac{(V-V_{0.5})}{k_i}}}$$

$$(B13) \quad \tau_{m_{\text{CCA1}}}(V) = \tau_{h_{\text{CCA1}}}(V) = \frac{a}{1 + e^{-\frac{(V-b)}{c}}} + d$$

$$(B14) \quad I_{\text{CCA1}} = \bar{g}_{\text{CCA1}} \cdot m_{\text{CCA1}}^2 \cdot h_{\text{CCA1}} \cdot (V - V_{Ca})$$

## C. CALCIUM-REGULATED POTASSIUM CURRENTS

**SLO1-SLO2**

CaV=EGL19, UNC2

$$(C1) \quad m_{\text{BK},\infty}(V, Ca) = \frac{m_{\text{CaV}} k_o^+ (\alpha + \beta + k_c^-)}{(k_o^+ + k_o^-)(k_c^- + \alpha) + \beta k_c^-}$$

$$(C2) \quad \tau_{m_{\text{BK}}}(V, Ca) = \frac{\alpha + \beta + k_c^-}{(k_o^+ + k_o^-)(k_c^- + \alpha) + \beta k_c^-}$$

$$(C3) \quad \alpha = \frac{m_{\text{CaV},\infty}}{\tau_{m_{\text{CaV}}}}$$

$$(C4) \quad \beta = \tau_{m_{\text{CaV}}}^{-1} - \alpha$$

$$(C5) \quad I_{\text{BK}} = \bar{g}_{\text{BK}} \cdot m_{\text{BK}} \cdot h_{\text{CaV}} \cdot (V - V_K)$$

For  $k_o^+$ ,  $k_o^-$ ,  $k_c^-$  see Methods.  $Ca$  stands for the nano-scale calcium concentration close to CaV channels, i.e.  $[\text{Ca}^{2+}]_{o,i}^n$  and  $[\text{Ca}^{2+}]_{c,i}^n$  for  $k_o^{+/-}$  and  $k_c^{+/-}$ , respectively.

**KCNL**

$$(C6) \quad m_{\text{KCNL},\infty}(Ca) = \frac{Ca}{K_{Ca} + Ca}$$

$$(C7) \quad \tau_{m_{\text{KCNL}}} = a$$

$$(C8) \quad I_{\text{KCNL}} = \bar{g}_{\text{KCNL}} \cdot m_{\text{KCNL}} \cdot (V - V_K)$$

For intracellular calcium calculation see Methods.  $Ca$  stands for the micro-scale calcium concentration, i.e. the intracellular calcium  $[\text{Ca}^{2+}]_i^m$ .

**NCA**

$$(C9) \quad I_{\text{NCA}} = \bar{g}_{\text{NCA}} \cdot (V - V_{Na})$$

**LEAK**

$$(C10) \quad I_{\text{LEAK}} = \bar{g}_{\text{LEAK}} \cdot (V - V_L)$$