

S1 Appendix: Equations used in the model simulations.

L-type Calcium current – I_{CaL}

$$I_{CaL} = \overline{g_{CaL}} n^2 h v h c (V - E_{CaL})$$

$$n_{\infty} = \frac{1}{1 + \exp\left(\frac{-(V+9)}{8}\right)}$$

$$h v_{\infty} = \frac{1}{1 + \exp\left(\frac{(V+30)}{13}\right)}$$

$$h c_{\infty} = \frac{ki}{ki + Cai}$$

$$\tau_n = \frac{0.001}{1 + \exp\left(\frac{-(V+22)}{308}\right)}$$

$$\tau_{hv} = 90 * \left(1 - \frac{1}{(1 + \exp\left(\frac{(V+14)}{45}\right)) (1 + \exp\left(\frac{-(V+9.8)}{3.39}\right))}\right)$$

$$\tau_{hc} = 20$$

T-type Calcium current – I_{CaT}

$$I_{CaT} = \overline{g_{CaT}} b^2 c (V - E_{CaT})$$

$$b_{\infty} = \frac{1}{1 + \exp\left(\frac{-(V+32.1)}{6.9}\right)}$$

$$c_{\infty} = \frac{1}{1 + \exp\left(\frac{(V+63.8)}{5.3}\right)}$$

$$\tau_b = 0.45 + \frac{3.9}{1 + \left(\frac{(V+66)}{26}\right)^2}$$

$$\tau_c = \left(150 - \frac{150}{(1 + \exp\left(\frac{(V-417.43)}{203.18}\right)) (1 + \exp\left(\frac{-(V+61.11)}{8.07}\right))}\right)$$

Voltage gated Potassium current – I_{Kv7} (KCNQ)

$$I_{KCNQ} = \overline{g_{KCNQ}} x^2 z^1 (V - E_K)$$

$$x_{\infty} = \frac{1}{1 + \exp\left(\frac{-(V+7.1)}{15}\right)}$$

$$z_{\infty} = \frac{0.55}{1 + \exp\left(\frac{(V + 55)}{9}\right)} + 0.45$$

$$\tau_x = \left(\frac{1}{1 + \exp\left(\frac{(V+15)}{20}\right)}\right)$$

$$\tau_z = 10 * \left(200 + \frac{10}{1 + 2 * \left(\frac{(V+56)}{120}\right)^5}\right)$$

Voltage gated Potassium current – I_{Kv}

$$I_{Kv1} = \overline{g_{Kv1}} p^1 q (V - E_K)$$

$$p_{\infty} = \frac{1}{1 + \exp\left(\frac{-(V+1.1)}{11}\right)}$$

$$q_{\infty} = \frac{1}{1 + \exp\left(\frac{(V+58)}{15}\right)}$$

$$\tau_p = \left(\frac{1}{1 + \exp\left(\frac{(V+15)}{20}\right)}\right)$$

$$\tau_q = 400 * \left(200 + \frac{10}{1 + 2 * \left(\frac{(V+54.18)}{120}\right)^5}\right)$$

Calcium dependent large potassium current – I_{BK}

$$I_{BK} = \overline{g_{BK}} * O * (V - E_K)$$

Common rate equations:

$$a = \exp\left(\frac{(38*v)}{380}\right), \quad b = \exp\left(\frac{(17*v)}{330}\right)$$

$$K_{on} = 345, \quad K_{coff} = 25, \quad K_{off} = 25$$

$$O = O1 + O2 + O3 + O4$$

Rate equations for voltage dependent transitions:

$$K_{C00} = 0.02162 * a, \quad K_{C101} = 0.000869 * a, \quad K_{C202} = 0.0000281 * a, \quad K_{C303} = 0.000781 * a, \quad K_{C404} = 0.044324 * a,$$

$$K_{O0C0} = 318.1084 * b, \quad K_{O1C1} = 144.1736 * b, \quad K_{O2C2} = 32.6594 * b, \quad K_{O3C3} = 0.095312 * b, \quad K_{O4C4} = 0.000106 * b * cai$$

Rate equations for calcium dependent transitions:

$$K_{C0C1} = 4 * K_{on} * cai, \quad K_{C1C2} = 3 * K_{on} * cai, \quad K_{C2C3} = 2 * K_{on} * cai, \quad K_{C3C4} = K_{on} * cai$$

$$K_{C4C3} = 4 * K_{coff} * cai, \quad K_{C3C2} = 3 * K_{coff} * cai, \quad K_{C2C1} = 2 * K_{coff} * cai, \quad K_{C1C0} = K_{coff} * cai$$

$$K_{0001} = 4 * K_{on} * cai, K_{0102} = 3 * K_{on} * cai, K_{0203} = 2 * K_{on} * cai, K_{0304} = K_{on} * cai$$

$$K_{0403} = 4 * K_{off} * cai, K_{0302} = 3 * K_{off} * cai, K_{0201} = 2 * K_{off} * cai, K_{0100} = K_{off} * cai$$

Calcium dependent intermediate potassium current – I_{IK}

$$I_{IK} = \overline{g_{IK}} * l^2 * k * (V - E_K)$$

$$l_{\infty} = \frac{0.27}{1 + \exp\left(\frac{(li - v)}{15}\right)}$$

$$li = -190 + (37 * \exp^{(ci*50)}) + (96 * \exp^{(-27*ci)})$$

$$\tau_l = 15 * \left(\frac{20}{1 + \exp\left(\frac{(V+20.52)}{35}\right)}\right)$$

$$k_{\infty} = \frac{0.32}{1 + \exp\left(\frac{(66 + v)}{8}\right)}$$

$$\tau_k = 45 * \left(1 - \frac{1}{\left(1 + \exp\left(\frac{(v + 13.9629)}{45.3782}\right)\right) * \left(1 + \exp\left(\frac{-(v + 9.49866)}{3.3945}\right)\right)}\right)$$

Calcium dependent small potassium current – I_{SK}

$$I_{SK} = \overline{g_{SK}} r^2 * (V - E_K)$$

$$r_{\infty} = 1.3 \exp 4 * \left(\frac{cai}{1.1}\right)^4 / (1.3 \exp 4 * \left(\frac{cai}{1.1}\right)^4 + 0.06^1)$$

$$\tau_r = \frac{0.2}{1.3 \exp 4 * \left(\frac{cai}{1.1}\right)^4 + 0.06^1}$$

Inwardly-rectifying channel - I_h

$$I_h = \overline{g_h} s^2 (V - E_h)$$

$$s_{\infty} = \frac{1}{1 + \exp\left(\frac{(V-85)}{16}\right)}$$

$$\tau_s = 5 * \left(\frac{15}{\left(1 + \exp\left(\frac{(49.042-V)}{10}\right)\right)}\right)$$

ATP-sensitive K⁺ channel (K_{ATP})

$$I_{katp} = \overline{g_{KATP}} * t * (V_m - E_{rev})$$

$$t_{\infty} = \frac{1}{1 + \left(\frac{ATPh}{ATPi}\right)^n}$$

$$\tau_t = 1 + \frac{1}{(1.37 + (atpi * \exp(\frac{1}{187})))}$$