Supplementary Material

S1 Mathematical Model

Global variables used are listed in tables S1.

Table S1: Global variables used in the model.

Variable	Value		Variable	Value	
vessel length	2000	μm	diameter	40	μm
F	96485	$\frac{C}{mol}$	R	8341.0	$\frac{mJ}{K \cdot mol}$
T	293.0	K			
Ca_{ext}	1.5	mM	Na_{ext}	140.0	mM
K_{ext}	5.0	mM	Cl_{ext}	146.0	mM
SMC specific parameters			EC specific parameters		
Dimensions	$63 \times 6.3 \times 5$	μm^3	Dimensions	$100 \times 7.8 \times 1$	μm^3
F_{scl}	3/8		F_{scl}	2/16	
A_m	$20 \cdot 10^{-6}$	cm^2	A_m	$14 \cdot 10^{-6}$	cm^2
C_m	20	pF	C_m	14	pF
vol_i	1.0	pL	vol_i	1.173	pL
vol_S	0.077	pL	vol_S	0.335	pL
vol_{Ca}	0.7	pL	vol_{Ca}	0.911	pL

All electrophysiological models were adapted from [2, 1], i.e. (only) the maximal activity parameters were adjusted to fit IV-curves from cerebral arterioles.

Table S2: Diffusional parameters used in the model.

	D_{Ca}	D_{Na}	D_K	D_{Cl}
D_c $[\frac{m^2}{s}]$	$2.5 \cdot 10^{-10}$	$6.0 \cdot 10^{-10}$	$15.0 \cdot 10^{-10}$	$10.0 \cdot 10^{-10}$

S1.1 Diffusion Models

Grid specific directional diffusion constants are calculated via $D_X = K \cdot D_c$, where $K = \frac{A}{V \cdot l}$ is the grid specific constant (A: Diffusional area, V: grid volume, and l: length of grid volume in the diffusional direction). In the longitudinal directions $K = 26.0 \cdot 10^9 \frac{1}{m^2}$ and in the circumferential directions $K = 16.6 \cdot 10^9 \frac{1}{m^2}$.

At each grid point in the discretization, the diffusional contribution to electrolyte concentrations, X equal to Ca^{2+}, Na^+, Cl^- or K^+ are calculated by:

$$\partial_t X_{diff} = \sum^{N} D_X \left(y_{X,j} - y_{X,i} \right)$$

where subscript i refer to the current grid and j to the neighboring grid (N neighbors in total).

S1.2 Gap Junctional Current Models

The models of gap junctions are equivalent for homo- and heterocellular gap junctions and apply to both ECs and VSMCs.

y^* denotes the relevant variable in the neighboring cell. Permeability parameters, P_{GJ} are either:

$P_{GJhet} = 3.53 \cdot 10^{-7} nL/s$,
$P_{EC,GJhom} = 4.6 \cdot 10^{-5} nL/s$,
$P_{VSMC,GJhom} = 3.13 \cdot 10^{-6} nL/s$

$$GJ_X = \frac{P_{GJ} F^2 z_X^2 \left(y_{V_m} - y_{Vm}^* \right) \left(y_X - y_X^* e^{-\frac{F z_X \left(y_{V_m} - y_{Vm}^* \right)}{RT}} \right)}{RT \left(1 - e^{-\frac{F z_X \left(y_{V_m} - y_{Vm}^* \right)}{RT}} \right)}$$

S1.3 EC Ion Channel Current Models

The current models described in the following are used in the calculation of differential equations. Thus, names of individual ion channel models are reused in the differential equation section below. This also applies to VSMC Ion Channel Current Models.

Calcium-activated Chloride Channel, CaCC:

Parameters:

$$\begin{aligned} n_{CaCC} &= 1.89 \\ K_{mCaCC} &= 2.87 \cdot 10^{-4} \quad \text{mM} \\ g_{CaCC} &= 2.95 \quad \tfrac{\text{nS}}{\text{pF}} \end{aligned}$$

$$CaCC = \frac{C_m F_{scl} g_{CaCC} y_{PoCaCC} y_{Ca}^{n_{CaCC}} \left(y_{V_m} - \frac{RT \log\left(\frac{y_{D_{Cl}}}{y_{Cl}}\right)}{F z_{Cl}} \right)}{K_{mCaCC}^{n_{CaCC}} + y_{Ca}^{n_{CaCC}}}$$

Calcium-activated Potassium Currents, SK_{Ca} + IK_{Ca}:

Parameters:

$$\begin{aligned} K_{hIKCa} &= 7.4 \cdot 10^{-4} \quad \text{mM} \\ K_{hSKCa} &= 2.371 \cdot 10^{-4} \quad \text{mM} \\ n_{SKCa} &= 5.0 \\ n_{IKCa} &= 4.0 \\ g_{SKCa} &= 0.45 \quad \text{nS} \\ g_{IKCa} &= 1.4 \quad \text{nS} \end{aligned}$$

$$KCa = F_{scl} \left(\frac{g_{IKCa} y_{Ca}^{n_{IKCa}} \left(y_{V_m} - \frac{RT \log\left(\frac{y_{D_K} y_{D_{Ca}}}{y_K}\right)}{F z_K} \right)}{K_{hIKCa}^{n_{IKCa}} + y_{Ca}^{n_{IKCa}}} + \frac{g_{SKCa} y_{Ca}^{n_{SKCa}} \left(y_{V_m} - \frac{RT \log\left(\frac{y_{D_K}}{y_K}\right)}{F z_K} \right)}{K_{hSKCa}^{n_{SKCa}} + y_{Ca}^{n_{SKCa}}} \right)$$

Inward Rectifier Current, K_{ir}:

Parameters:

$$\begin{aligned} n_{Kir} &= 0.50 \\ k_{Kir} &= 7.084 \quad \text{mV} \\ d_{Vkir} &= 39.42 \quad \text{mV} \\ g_{Kir} &= 0.13 \quad \frac{\text{nS}}{\sqrt{\text{mM}}} \end{aligned}$$

$Kir =$

$$\frac{F_{scl} g_{Kir} y_{D_K}^{n_{Kir}} \left(y_{V_m} - \frac{RT \log\left(\frac{y_{D_K}}{y_K}\right)}{F z_K} \right)}{1 + e^{\frac{y_{V_m} - d_{Vkir} - \frac{RT \log\left(\frac{y_{D_K}}{y_K}\right)}{F z_K}}{k_{Kir}}}}$$

Sodium-Calcium Exchanger Current, NCX:

Parameters:

$$\begin{aligned} K_{mNCX} &= 0.5016 \quad \text{mM} \\ p_{NCX} &= 0.4834 \\ g_{NCX} &= 1.99 \quad \text{nS} \\ n_{NCX} &= 1.50 \\ d_{NCX} &= 3.043 \cdot 10^{-4} \end{aligned}$$

$NCX =$

$$\frac{F_{scl} g_{NCX} \left(y_{D_{Ca}} y_{Na}^3 e^{\frac{F p_{NCX} y_{V_m}}{RT}} - y_{Ca} y_{D_{Na}}^3 e^{-\frac{F y_{V_m} (1 - p_{NCX})}{RT}} \right)}{\left(1 + \left(\frac{K_{mNCX}}{y_{Ca}}\right)^{n_{NCX}}\right) \left(1 + d_{NCX} \left(y_{D_{Ca}} y_{Na}^3 + y_{Ca} y_{D_{Na}}^3\right)\right)}$$

Non Selective Cation Channel (Ca^{2+}), NSC_{Ca}:

Parameters:

$$P_{NSCCa} = 2.4 \cdot 10^{-8} \quad \text{cm/s}$$

$NSC_{Ca} =$

$$P_f \frac{A_m F_{scl} P_{NSCCa} y_{V_m} F^2 z_{Ca}^2 \left(y_{Ca} - y_{D_{Ca}} e^{-\frac{F y_{V_m} z_{Ca}}{RT}} \right)}{RT \left(1 - e^{-\frac{F y_{V_m} z_{Ca}}{RT}} \right)}$$

Non Selective Cation Channel (K^+), NSC$_K$:

Parameters:

$$P_{NSCK} \quad = \quad 4.3 \cdot 10^{-8} \quad \text{cm/s}$$

$NSC_K =$

$$P_f \frac{A_m F_{scl} P_{NSCK} y_{V_m} F^2 z_K^2 \left(y_K - y_{D_K} e^{-\frac{F y_{V_m} z_K}{RT}} \right)}{RT \left(1 - e^{-\frac{F y_{V_m} z_K}{RT}} \right)}$$

Non Selective Cation Channel (Na^+), NSC$_{Na}$:

Parameters:

$$\begin{array}{lcll} K_{dNSC} & = & 1.1 & \text{mM} \\ P_{NSCNa} & = & 5.34 \cdot 10^{-8} & \text{cm/s} \\ n_{NSC} & = & 1.6 & \end{array}$$

$NSC_{Na} =$

$$P_f \frac{A_m F_{scl} P_{NSCNa} y_{V_m} F^2 z_{Na}^2 \left(y_{Na} - y_{D_{Na}} e^{-\frac{F y_{V_m} z_{Na}}{RT}} \right)}{RT \left(1 + \left(\frac{y_{D_{Ca}}}{K_{dNSC}} \right)^{n_{NSC}} \right) \left(1 - e^{-\frac{F y_{V_m} z_{Na}}{RT}} \right)}$$

Na/K ATPase pump, NKA:

Parameters:

$$\begin{array}{lcll} K_{mK} & = & 1.32 & \text{mM} \\ A_{NKA} & = & 135.1 & \text{mV} \\ B_{NKA} & = & 300 & \text{mV} \\ K_{mNa} & = & 14.52 & \text{mM} \\ I_{NKAb} & = & 20.2 & \text{pA} \end{array}$$

$NKA =$

$$\frac{F_{scl} I_{NKAb} y_{D_K} y_{Na}^{1.5} \left(A_{NKA} + y_{V_m}\right)}{\left(B_{NKA} + y_{V_m}\right)\left(K_{mK} + y_{D_K}\right)\left(K_{mNa}^{1.5} + y_{Na}^{1.5}\right)}$$

Na/K/2Cl cotransport, NKCC:

Parameters:

$$L_{NKCC} \quad = \quad 3.2 \cdot 10^{-9} \quad \frac{\text{mmol}^2}{J \cdot s \cdot cm^2}$$

$NKCC =$

$$-1000.0 A_m F F_{scl} L_{NKCC} R T z_{Cl} \log\left(\frac{y_{D_K} y_{D_{Na}} y_{D_{Cl}}^2}{y_K y_{Na} y_{Cl}^2}\right)$$

Plama Membrane Calcium ATPase current, PMCA:

Parameters:

$$\begin{array}{lcll} K_{mPMCA} & = & 2.6 \cdot 10^{-4} & \text{mM} \\ I_{PMCA} & = & 2.67 & \text{pA} \\ n_{PMCA} & = & 1.40 & \end{array}$$

$PMCA =$

$$\frac{F_{scl} I_{PMCA} y_{Ca}^{n_{PMCA}}}{K_{mPMCA}^{n_{PMCA}} + y_{Ca}^{n_{PMCA}}}$$

Store Operated Cation current (Ca^{2+}), SOC_{Ca}:

Parameters:

$$P_{SOC_{Ca}} = 1.15 \cdot 10^{-7} \quad \text{cm/s}$$

$$SOC_{Ca} = P_f \frac{A_m F_{scl} P_{SOC_{Ca}} y_{V_m} y_{PoSOC} F^2 z_{Ca}^2 \left(y_{Ca} - y_{D_{Ca}} e^{-\frac{F y_{V_m} z_{Ca}}{RT}} \right)}{RT \left(1 - e^{-\frac{F y_{V_m} z_{Ca}}{RT}} \right)}$$

Store Operated Cation current (Na^{+}), SOC_{Na}:

Parameters:

$$\begin{aligned} P_{SOC_{Na}} &= 3.946 \cdot 10^{-7} \quad \text{cm/s} \\ K_{dSOC} &= 2.0 \cdot 10^{-4} \quad \text{mM} \\ n_{SOC} &= 6.22 \cdot 10^{-1} \end{aligned}$$

$$SOC_{Na} = P_f \frac{A_m F_{scl} P_{SOC_{Na}} y_{V_m} y_{PoSOC} F^2 z_{Na}^2 \left(y_{Na} - y_{D_{Na}} e^{-\frac{F y_{V_m} z_{Na}}{RT}} \right)}{RT \left(1 + \left(\frac{y_{D_{Ca}}}{K_{dSOC}} \right)^{n_{SOC}} \right) \left(1 - e^{-\frac{F y_{V_m} z_{Na}}{RT}} \right)}$$

Volume-Regulated Anion Channel, VRAC:

Parameters:

$$g_{VRAC} = 0.105 \quad \text{nS}$$

$$VRAC = F_{scl} g_{VRAC} \left(y_{V_m} - \frac{RT \log \left(\frac{y_{D_{Cl}}}{y_{Cl}} \right)}{F z_{Cl}} \right)$$

ER leakage current, $\mathbf{ER}_{leak}$:

Parameters:

$$k_{ER_{leak}} = 1.76 \cdot 10^{-2} \quad \frac{1}{\text{mM}\cdot\text{ms}}$$

$$ER_{leak} =$$

$$F_{scl} k_{ER_{leak}} \left(y_{ERCa} - y_{Ca}\right)^2$$

SR Ca-ATPase pump, SERCA:

Parameters:

$$\begin{aligned} I_{SERCA} &= 8.8 \cdot 10^{-1} \quad \text{pA} \\ K_{SERCA} &= 1.5 \cdot 10^{-4} \quad \text{mM} \end{aligned}$$

$$SERCA =$$

$$\frac{F_{scl} I_{SERCA} y_{Ca}^2}{\left(K_{SERCA} + y_{Ca}\right)^2}$$

S1.4 Differential equations, EC

[$\mathbf{Ca}^{2+}$]:

Parameters:

$$\begin{aligned} B_T &= 1.2 \cdot 10^{-1} \quad \text{mM} \\ K_B &= 3.0 \cdot 10^{-3} \quad \text{mM} \end{aligned}$$

$$\frac{dy_{Ca}}{dt} =$$

$$\frac{\partial_t Ca_{diff}}{1 + \frac{B_T K_B}{(K_B + y_{Ca})^2}} - \frac{GJ_{Ca} - NSC_{Ca} + PMCA + SERCA + SOC_{Ca} - ER_{leak} - 2NCX}{Fvol_{Ca} z_{Ca} \left(1 + \frac{B_T K_B}{(K_B + y_{Ca})^2}\right)}$$

[Na⁺]:

$\frac{dy_{Na}}{dt} =$

$$\partial_t Na_{diff} + \frac{-NSC_{Na} - SOC_{Na} - 3NCX - 3NKA + 0.5NKCC - GJ_{Na}}{Fvol_I z_{Na}}$$

[K⁺]:

$\frac{dy_k}{dt} =$

$$\partial_t K_{diff} + \frac{-KCa - Kir - NSC_K + 2NKA + 0.5NKCC - GJ_K}{Fvol_I z_K}$$

[Cl⁻]:

$\frac{dy_{Cl}}{dt} =$

$$\partial_t Cl_{diff} + \frac{-CaCC - NKCC - VRAC - GJ_{Cl}}{Fvol_I z_{Cl}}$$

[ERCa²⁺]:

Parameters:

$$\begin{aligned} CSQN &= 15 \quad \text{mM} \\ K_{CSQN} &= 0.8 \quad \text{mM} \end{aligned}$$

$\frac{dy_{ERCa}}{dt} =$

$$\frac{SERCA - ER_{leak}}{Fvol_S z_{Ca}\left(1 + \frac{CSQN K_{CSQN}}{\left(K_{CSQN} + y_{ERCa}\right)^2}\right)}$$

SOC Open Probability, PoSOC:

Parameters:

$$\begin{aligned} t_{SOC} &= 100 \quad \text{ms} \\ a_{SOCact} &= 0.083 \\ n_{SOCact} &= 3.2 \\ K_{SOCact} &= 0.47 \quad \text{mM} \end{aligned}$$

$\frac{dy_{PoSOC}}{dt} =$

$$\frac{1}{t_{SOC}} \left(a_{SOCact} - y_{PoSOC} + 0.25 \frac{1}{1 + \left(\frac{y_{ERCa}}{K_{SOCact}} \right)^{n_{SOCact}}} \right)$$

CaCC Open Probability, PoCaCC:

Parameters:

$$\begin{array}{lcll} t_{CaCC} & = & 386.2 & \text{ms} \\ s_{CaCC} & = & 132 & \text{mV} \\ E_{CaCC} & = & 662 & \text{mV} \\ V_{CaCC} & = & 19.9 & \text{mV} \\ d_{CaCC} & = & 88.9 & \text{mV} \end{array}$$

$\frac{dy_{PoCaCC}}{dt} =$

$$\frac{1}{t_{CaCC}} \left(-y_{PoCaCC} + \frac{1}{1 + e^{\frac{E_{CaCC} - y_{V_m}}{s_{CaCC}}}} \right) e^{\frac{\left(y_{V_m} - V_{CaCC} \right)^2}{d^2_{CaCC}}}$$

S1.5 VSMC Ion Channel Current Models

Large-Conductance Ca^{2+} Channel, CaL:

Parameters:

$$P_{CaL} = 1.65 \cdot 10^{-5} \quad \text{cm/s}$$

$$CaL =$$

$$P_f \frac{A_m F_{scl} P_{CaL} y_{V_m} y_{dL} y_{fL} F^2 z_{Ca}^2 \left(y_{U_{Ca}} - y_{Ca} e^{\frac{F y_{V_m} z_{Ca}}{RT}} \right)}{RT \left(1 - e^{\frac{F y_{V_m} z_{Ca}}{RT}} \right)}$$

Calcium-activated Chloride current, ICl:

Parameters:

$$\begin{array}{lcll} K_{ClCa} & = & 3.65 \cdot 10^{-4} & \text{mM} \\ g_{Cl} & = & 0.91 & \text{nS} \end{array}$$

$$ICl =$$

$$C_m F_{scl} g_{Cl} \left(y_{V_m} - \frac{RT \log \left(\frac{y_{U_{Cl}}}{y_{Cl}} \right)}{F z_{Cl}} \right) \cdot \left(\frac{0.0132 y_{Ca}^2}{K_{ClCa}^2 + y_{Ca}^2} \right)$$

K^+ Inward Rectifier, K_{IR}:

Parameters:

$$\begin{array}{lcll} g_{Kir} & = & 0.09 & \frac{\text{nS}}{\sqrt{\text{mM}}} \\ V_{Kir} & = & 28.89 & \text{mV} \\ n_{Kir} & = & 0.5 & \\ a_{Kir} & = & -0.04 & \frac{1}{\text{mV}} \\ x_{Kir} & = & -45.0 & \text{mV} \end{array}$$

$$Kir =$$

$$\frac{F_{scl} g_{Kir} y_{U_K}^{n_{Kir}} \left(y_{V_m} - \frac{RT \log\left(\frac{y_{U_K}}{y_K}\right)}{F z_K}\right)}{1 + e^{\frac{y_{V_m} - \frac{RT \log\left(\frac{y_{U_K}}{y_K}\right)}{F z_K}}{V_{Kir}}}} \cdot \frac{1}{e^{-a_{Kir}(y_{V_m} - x_{Kir})} + 1.0}$$

K$^+$ leak channel current, Kleak:

Parameters:

$$g_{Kleak} \quad = \quad 2.0 \cdot 10^{-4} \quad \text{nS}$$

$$Kleak =$$

$$F_{scl} g_{Kleak} \left(y_{V_m} - \frac{RT \log\left(\frac{y_{U_K}}{y_K}\right)}{F z_K}\right)$$

Large Conductance Calcium-activated K$^+$ Channels, BKCa:

Parameters:

$$\begin{aligned} N_{BKCa} &= 6.6 \cdot 10^{6} \quad 1/\text{cm}^2 \\ P_{BKCa} &= 2.0 \cdot 10^{-13} \quad \text{cm}^3/\text{s} \end{aligned}$$

$$BKCa =$$

$$P_f \frac{A_m F_{scl} N_{BKCa} P_{BKCa} y_{V_m} F^2 \left(0.17 y_{pf} + 0.83 y_{ps}\right) \left(y_{U_K} - y_K e^{\frac{F y_{V_m}}{RT}}\right)}{RT \left(1 - e^{\frac{F y_{V_m}}{RT}}\right)}$$

Voltage-gated K$^+$ Channels, Kv:

Parameters:

$$g_{Kv} \quad = \quad 0.32 \quad \text{nS}$$

$Kv =$

$$F_{scl} g_K y_{pK} \left(0.55 y_{q2} + 0.45 y_{q1}\right) \left(y_{V_m} - \frac{RT \log\left(\frac{y_{U_K}}{y_K}\right)}{F z_K} \right)$$

Plasma membrane Na-Ca exchanger, NCX:

Parameters:

$$\begin{array}{lcll} p_{NCX} & = & 4.5 \cdot 10^{-1} & \\ g_{NCX} & = & 9.0 \cdot 10^{-3} & \text{nS} \\ d_{NCX} & = & 5.0 \cdot 10^{-4} & \end{array}$$

$NCX =$

$$\frac{F_{scl} g_{NCX} \left(y_{U_{Ca}} y_{Na}^3 e^{\frac{F p_{NCX} y_{V_m}}{RT}} - y_{Ca} y_{U_{Na}}^3 e^{-\frac{F y_{V_m}(1-p_{NCX})}{RT}} \right)}{1 + d_{NCX}\left(y_{U_{Ca}} y_{Na}^3 + y_{Ca} y_{U_{Na}}^3 \right)}$$

Non Selective Cation Channel (Ca^{2+}), NSC_{Ca}:

Parameters:

$$\begin{array}{lcll} P_{CaNSC} & = & 2.7 \cdot 10^{-6} & \text{cm/s} \\ P_{min_{NSC}} & = & 0.4344 & \\ p_{fNSC} & = & 24.24 & \\ p_{VNSC} & = & 47.1 & \\ d_{min_{NSC}} & = & 2.44 \cdot 10^{-2} & \end{array}$$

$NSC_{Ca} =$

$$P_f \frac{A_m F_{scl} P_{CaNSC} d_{min_{NSC}} y_{V_m} F^2 z_{Ca}^2 \left(y_{U_{Ca}} - y_{Ca} e^{\frac{F y_{V_m} z_{Ca}}{RT}} \right) \left(P_{min_{NSC}} + \frac{1-P_{min_{NSC}}}{1+e^{\frac{p_{V_{NSC}} - y_{V_m}}{p_{f_{NSC}}}}} \right)}{RT\left(1 - e^{\frac{F y_{V_m} z_{Ca}}{RT}}\right)}$$

Non Selective Cation Channel (K^+), NSC_K:

Parameters:

$$P_{KNSC} = 3.5 \cdot 10^{-7} \quad \text{cm/s}$$

$$NSC_K =$$

$$P_f \frac{A_m F_{scl} P_{KNSC} y_{V_m} F^2 \left(d_{min_{NSC}} +\right) \left(P_{min_{NSC}} + \frac{1 - P_{min_{NSC}}}{1 + e^{\frac{p_{V_{NSC}} - y_{V_m}}{p_{f_{NSC}}}}}\right) \left(y_{U_K} - y_K e^{\frac{F y_{V_m}}{RT}}\right)}{RT \left(1 - e^{\frac{F y_{V_m}}{RT}}\right)}$$

Non Selective Cation Channel (Na^+), NSC_{Na}:

Parameters:

$$\begin{aligned} K_{NSC} &= 3.0 \cdot 10^{-4} \quad \text{mM} \\ P_{NaNSC} &= 7.65 \cdot 10^{-7} \quad \text{cm/s} \end{aligned}$$

$$NSC_{Na} =$$

$$P_f \frac{A_m F_{scl} P_{NaNSC} y_{V_m} F^2 \left(y_{U_{Na}} - y_{Na} e^{\frac{F y_{V_m}}{RT}}\right) \left(d_{min_{NSC}} +\right) \left(P_{min_{NSC}} + \frac{1 - P_{min_{NSC}}}{1 + e^{\frac{p_{V_{NSC}} - y_{V_m}}{p_{f_{NSC}}}}}\right)}{RT \left(1 - e^{\frac{F y_{V_m}}{RT}}\right)}$$

Na/K ATPase pump, NKA:

Parameters:

$$\begin{aligned} K_{mK} &= 1.6 \quad \text{mM} \\ Q10_{NKA} &= 1.87 \\ K_{mNa} &= 22.0 \quad \text{mM} \\ I_{NKAb} &= 2.0 \quad \text{pA/pF} \end{aligned}$$

$NKA =$

$$\frac{C_m F_{scl} I_{NKA} Q_{NKA10}^{-30.915+\frac{1}{10}T} y_{U_K}^{1.1} y_{Na}^{1.7} \left(150 + y_{V_m}\right)}{\left(200 + y_{V_m}\right)\left(K_{mNa}^{1.7} + y_{Na}^{1.7}\right)\left(K_{mK}^{1.1} + y_{U_K}^{1.1}\right)}$$

Na/K/2Cl cotransport, NKCC:

Parameters:

$$L_{NKCC} = 1.79 \cdot 10^{-8} \quad \frac{n\mathrm{mol}^2}{\mathrm{J \cdot s \cdot cm^2}}$$

$NKCC =$

$$-A_m F F_{scl} L_{NKCC} R T z_{Cl} \log\left(\frac{y_{U_K} y_{U_{Na}} y_{U_{Cl}}^2}{y_K y_{Na} y_{Cl}^2}\right)$$

Plama Membrane Calcium ATPase current, PMCA:

Parameters:

$$\begin{aligned} K_{mPMCA} &= 1.7 \cdot 10^{-4} \quad \mathrm{mM} \\ I_{PMCA} &= 3.0 \quad \mathrm{pA} \end{aligned}$$

$PMCA =$

$$\frac{F_{scl} I_{PMCA} y_{Ca}}{K_{mPMCA} + y_{Ca}}$$

Store Operated Cation current (Ca^{2+}), SOC_{Ca}:

Parameters:

$$g_{SOC_{Ca}} = 8.3 \cdot 10^{-3} \quad \mathrm{nS}$$

$SOC_{Ca} =$

$$F_{scl} g_{SOC_{Ca}} y_{PoSOC} \left(y_{V_m} - \frac{RT \log\left(\frac{y_{U_{Ca}}}{y_{Ca}}\right)}{F z_{Ca}}\right)$$

Store Operated Cation current (Na^+), SOC_{Na}:

Parameters:

$$g_{SOC_{Na}} = 6.0 \cdot 10^{-2} \quad \text{nS}$$

$$SOC_{Na} =$$

$$F_{scl} g_{SOC_{Na}} y_{PoSOC} \left(y_{V_m} - \frac{RT \log\left(\frac{y_{U_{Na}}}{y_{Na}}\right)}{F z_{Na}} \right)$$

SR Ca-ATPase pump, SERCA:

Parameters:

$$\begin{array}{lcll} I_{SERCAb} & = & 6.68 & \text{pA} \\ K_{mup} & = & 1.0 \cdot 10^{-3} & \text{mM} \end{array}$$

$$SERCA =$$

$$\frac{F_{scl} I_{SERCAb} y_{Ca}}{K_{mup} + y_{Ca}}$$

SR leakage current, SR_{leak}:

Parameters:

$$\begin{array}{lcll} SR_{leak} & = & 1.07 \cdot 10^{-5} & \text{mM} \\ \tau & = & 3.33 \cdot 10^{-2} & \text{ms} \end{array}$$

$$SR_{leak} =$$

$$\frac{F F_{scl} SR_{leak} vol_S z_{Ca} \left(y_{ERCa} - y_{Ca} \right)}{\tau}$$

S1.6 Differential equations, VSMC

[Ca^{2+}]:

Parameters:

$$
\begin{array}{lcll}
S_{CM} & = & 1.0 \cdot 10^{-1} & \text{mM} \\
K_{dB} & = & 5.3 \cdot 10^{-4} & \text{mM} \\
K_{d} & = & 2.6 \cdot 10^{-4} & \text{mM} \\
B_{F} & = & 1.0 \cdot 10^{-1} & \text{mM}
\end{array}
$$

$$
\frac{dy_{Ca}}{dt} = - \frac{CaL + NSC_{Ca} + PMCA + SERCA + SOC_{Ca} - SR_{leak} - 2NCX - GJ_{Ca}}{Fvol_{Ca} z_{Ca} \left(1 + \frac{B_F K_{dB}}{(K_{dB}+y_{Ca})^2} + \frac{K_d S_{CM}}{(K_d+y_{Ca})^2}\right)} + \frac{\partial_t Ca_{diff}}{1 + \frac{B_F K_{dB}}{(K_{dB}+y_{Ca})^2} + \frac{K_d S_{CM}}{(K_d+y_{Ca})^2}}
$$

[Na^{+}]:

$$
\frac{dy_{Na}}{dt} = \partial_t Na_{diff} + \frac{-NSC_{Na} - SOC_{Na} - 3NCX - 3NKA + 0.5NKCC - GJ_{Na}}{Fvol_I z_{Na}}
$$

[K^{+}]:

$$
\frac{dy_{k}}{dt} = \partial_t K_{diff} + \frac{-Kleak - Kir - KCa - Kv - NSC_K + 2NKA + 0.5NKCC - GJ_K}{Fvol_I z_K}
$$

[Cl^{-}]:

$$
\frac{dy_{Cl}}{dt} = \partial_t Cl_{diff} + \frac{-ICl - NKCC - GJ_{Cl}}{Fvol_I z_{Cl}}
$$

[ERCa^{2+}]:

Parameters:

$$
\begin{array}{lcll}
K_{CSQN} & = & 8.0 \cdot 10^{-1} & \text{mM} \\
CSQN & = & 15 & \text{mM}
\end{array}
$$

$\frac{dy_{ERCa}}{dt} =$

$$\frac{SERCA - SR_{leak}}{Fvol_S z_{Ca}\left(1 + \frac{CSQN K_{CSQN}}{\left(K_{CSQN}+y_{ERCa}\right)^2}\right)}$$

SOC Open Probability, PoSOC:

Parameters:

$$\begin{array}{lll} K_{SOC} & = & 1.0 \cdot 10^{-4} \quad \text{mM} \\ t_{SOC} & = & 1.0 \cdot 10^{2} \quad \text{ms} \end{array}$$

$\frac{dy_{PoSOC}}{dt} =$

$$\frac{1}{t_{SOC}}\left(-y_{PoSOC} + \frac{1}{1 + \frac{y_{ERCa}}{K_{SOC}}}\right)$$

q1:

Parameters:

$$\begin{array}{lll} t_{q1} & = & 3.71 \cdot 10^{2} \quad \text{ms} \\ p_q & = & 40 \quad \text{mV} \end{array}$$

$\frac{dy_{q1}}{dt} =$

$$\frac{1}{t_{q1}}\left(-y_{q1} + \frac{1}{1 + e^{0.071 p_q + 0.071 y_{V_m}}}\right)$$

q2:

Parameters:

$$t_{q2} = 2.884 \cdot 10^{3} \quad \text{ms}$$

$\frac{dy_{q2}}{dt} =$

$$\frac{1}{t_{q2}}\left(-y_{q2} + \frac{1}{1 + e^{\frac{1}{14} p_q + \frac{1}{14} y_{V_m}}}\right)$$

pK:

Parameters:

$$\begin{array}{lcll} p_{KV} & = & -2.68 \cdot 10^{-2} & \\ k_{pK} & = & 15 & \text{mV} \\ p_{Kk} & = & 61.49 & \\ V_{hf} & = & 11 & \text{mV} \end{array}$$

$\frac{dy_{pK}}{dt} =$

$$\frac{1}{p_{Kk}} \left(-y_{pK} + \frac{1}{1 + e^{\frac{-V_{hf} - y_{V_m}}{k_{pK}}}} \right) e^{-p_{K_V} y_{V_m}}$$

dL:

Parameters:

$$\begin{array}{lcll} d_{Lp1} & = & 8.3 & \text{mV} \\ d_{Lp2} & = & 30 & \text{mV} \end{array}$$

$\frac{dy_{dL}}{dt} =$

$$\frac{-y_{dL} + \left(1 + e^{-\frac{y_{V_m}}{d_{Lp1}}}\right)^{-1}}{1.15 + 2.5 e^{-\frac{\left(40 + y_{V_m}\right)^2}{d_{Lp2}^2}}}$$

fL:

Parameters:

$$\begin{array}{lcll} f_{Lp1} & = & 9.1 & \text{mV} \\ f_{Lp2} & = & 25 & \text{mV} \end{array}$$

$\frac{dy_{fL}}{dt} =$

$$\frac{-y_{fL} + \left(1 + e^{\frac{42.0 + y_{V_m}}{f_{Lp1}}}\right)^{-1}}{45 + 65e^{-\frac{\left(35 + y_{V_m}\right)^2}{f_{Lp2}^2}}}$$

pf:

Parameters:

$$\begin{array}{lcll} p_{KCa1} & = & -41.7 & \text{mV} \\ p_{KCa2} & = & 128.2 & \text{mV} \\ p_{KCa3} & = & 18.25 & \text{mV} \\ t_{pf} & = & 0.84 & \text{ms} \end{array}$$

$\frac{dy_{pf}}{dt} =$

$$\frac{1}{t_{pf}}\left(-y_{pf} + \left(1 + e^{\frac{-p_{KCa2} - y_{V_m} + p_{KCa1}\log(y_{Ca})}{p_{KCa3}}}\right)^{-1}\right)$$

ps:

Parameters:

$$t_{ps} = 35.9 \quad \text{ms}$$

$\frac{dy_{ps}}{dt} =$

$$\frac{1}{t_{ps}}\left(-y_{ps} + \left(1 + e^{\frac{-p_{KCa2} - y_{V_m} + p_{KCa1}\log(y_{Ca})}{p_{KCa3}}}\right)^{-1}\right)$$

References

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[2] Haroldo S Silva, Adam Kapela, and Nikolaos M Tsoukias. A mathematical model of plasma membrane electrophysiology and calcium dynamics in vascular endothelial cells. *Am J Physiol Cell Physiol*, 293(1):C277–C293, Jul 2007.