A mathematical modeling toolbox for ion channels and transporters across cell membranes

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Supplementary material This manuscript's supplementary material contains an overview of all equations related to Ion channels, Pumps, Cotransporters, and Symporters, organized in a table form.

1. Ion channels

1.1. Potassium Channels

1.1.1. Inward-Rectifier Potassium K Channels (IRKC, Kir)

Inward-Rectifier Potassium (K) Channels (IRKC, Kir)	**Ref**
$$\boxed{i_{K,kir}^{M-N} = g_{kir} f_o^{k,kir}(V_m^{M,N} - V_{K,rev}^{M-N})} \quad (1)$$ $$g_{kir} = g_{kir}^{max}\left(\frac{[K]_e}{[K]_{ref}}\right)^{n_{kir}} \quad (2)$$ $$f_o^{k,kir} = \frac{1}{1 + exp\left(\frac{V_m^{M-N} - V_{1/2,kir}}{k_{kir}}\right)} \quad (3)$$ $$V_{1/2,kir} = A\log[K]_i + B \quad (4)$$	[1–4]

Table 1: The corresponding equations describing the ionic current transported via Inward-Rectifier Potassium K Channels (IRKC, Kir) across the cell membrane

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1.1.2. *Calcium-Activated Potassium (K) channels (CaKC)*

Calcium-Activated Potassium (K) channels (CaKC)	**Ref**
$\boxed{I''^{M-N}_{K,X_{CaKC}} = n''^{M-N}_{X_{CaKC}}\, g_{X_{CaKC}}\, f_o^{K,X_{CaKC}}\, A\left(V_m^{M-N} - V_{K,rev}^{M-N}\right)} \quad (5)$ where X denotes SK or IK or BK $f_o^{K,CaKC} = \dfrac{1}{1+\left(\frac{K_{Ca}^{CaKC}}{[Ca]_{i(c)}}\right)^{\eta_{CaKC}}} \quad (6)$	[5–7]
$\boxed{I''^{M,N}_{K,X_{CaKC}} = n''_{X_{CaKC}} P^{M-N}_{K,X_{CaKC}} \dfrac{z_K^2 F^2 V_m^{M-N}}{RT} \dfrac{[K]_M - [K]_N exp\frac{-z_K F V_m^{M-N}}{RT}}{1 - exp\frac{-z_K F V_m^{M-N}}{RT}}} \quad (7)$ where X denotes IK or BK.	[8]
$\boxed{i^{M-N}_{K,BK_{CaKC}} = g_{BK_{CaKC}} f_o^{BK_{CaKC}}\left(V_m^{M-N} - V_{K,rev}^{M-N}\right)} \quad (8)$ $f_o^{BK_{CaKC}} = C_f f_f^{BK_{CaKC}} + C_s f_s^{BK_{CaKC}} \quad (9)$ $\dfrac{df_f^{BK_{CaKC}}}{dt} = \dfrac{\bar{f}_f^{BK_{CaKC}} - f_f^{BK_{CaKC}}}{\tau_{f_f}^{BK_{CaKC}}} \quad (10)$ $\dfrac{df_s^{BK_{CaKC}}}{dt} = \dfrac{\bar{f}_s^{BK_{CaKC}} - f_s^{BK_{CaKC}}}{\tau_{f_s}^{BK_{CaKC}}} \quad (11)$ $\bar{f}^{BK_{CaKC}} = \dfrac{1.0}{1.0 + exp[\frac{-(V_m^{M-N} - V_{1/2,BK_{CaKC}}^{M-N})}{k_{CaKC}}]} \quad (12)$ $\bar{f}_f^{BK_{CaKC}} = \bar{f}_s^{BK_{CaKC}} - \bar{f}^{BK_{CaKC}} \quad (13)$ $V_{1/2,BK_{CaKC}} = A\log[Ca]_i + B \quad (14)$	[4]

Table 2: The corresponding equations describing the ionic current transported via Calcium-Activated Potassium (K) channels (CaKC) across the cell membrane

1.1.3. Voltage Gated Potassium Channel (VGPC, k_v)

Voltage Gated Potassium Channel (VGPC, k_v)	**Ref**
$$\boxed{i_{K,K_v} = g_{K_v}(f_o^{Kv})^2\left(V_m^{M-N} - V_{K,rev}^{M-N}\right)} \tag{15}$$ where: $$f_o^{Kv} = C_f f_f^{Kv} + C_s f_s^{Kv} \tag{16}$$ $$\frac{df_f^{Kv}}{dt} = \frac{\bar{f}_o^{Kv} - f_f^{Kv}}{\tau_{f_f}^{Kv}} \tag{17}$$ $$\frac{df_s^{Kv}}{dt} = \frac{\bar{f}_o^{Kv} - f_s^{Kv}}{\tau_{f_s}^{Kv}} \tag{18}$$ $$\tau_{f_f}^{Kv} = A_{\tau_{f_f}^{Kv}}\ exp\left[\left(\frac{-(V_m^{M-N} + V_{\tau_{f_f}^{Kv}})}{k_{\tau_{f_f}^{Kv}}}\right)^2\right] - B_{\tau_{f_f}^{Kv}} \tag{19}$$ $$\tau_{f_s}^{Kv} = A_{\tau_{f_s}^{Kv}}\ exp\left[\left(\frac{-(V_m^{M-N} + V_{\tau_{f_s}^{Kv}})}{k_{\tau_{f_s}^{Kv}}}\right)^2\right] + B_{\tau_{f_s}^{Kv}} \tag{20}$$ $$\bar{f}_o^{Kv} = \frac{1.0}{1.0 + exp\left(\frac{-(V_m^{M-N} - V_{1/2,Kv}^{M-N})}{k_{Kv}}\right)} \tag{21}$$ $$V_{1/2,Kv} = A \tag{22}$$	[4]
$$\boxed{i_{K,Kv} = g_{K_v}\left(V_m - V_{K,rev}\right)} \tag{23}$$ where: $$g_{K_v} = g^{\circ}_{Kv} n^4 \tag{24}$$ $$\frac{dn}{dt} = \alpha_n\ \left(1 - n(t)\right) - \beta_n\ \ n(t) \tag{25}$$	[9]

Table 2: The corresponding equations describing the ionic current transported via Voltage Gated Potassium Channel (VGPC, k_v) across the cell membrane

9 *1.1.4. ATP-sensitive Potassium (K) Channel (KATP)*

ATP-sensitive Potassium (K) Channel (KATP)	**Ref**
$$\boxed{I_{K,K_{ATP}} = g_{K_{ATP}} f_o^{K_{ATP}} \left(V_m^{M-N} - V_{K,rev}^{M-N}\right)} \quad (26)$$ where $$g_{KATP} = g_{KATP}^{max} \left(\frac{[K]_o}{[K]_{ref}}\right)^{n_{KATP}} \quad (27)$$ $$f_o^{KATP} = \frac{1}{1 + \left(\frac{[ATP]_i}{k_{0.5}}\right)^{\eta_{KATP}}} \quad (28)$$	[2, 10]

Table 2: The corresponding equations describing the ionic current transported via ATP-sensitive potassium (K) channel (KATP) across the cell membrane

10 *1.1.5. Two pore domain potassium channels*

Two-Pore-domain potassium channels	**Ref**
$$\boxed{I''^{M,N}_{K,leak\ channels} = P_{K,K2P}^{M-N} \frac{z_K^2 F^2 V_m^{M-N}}{RT} \frac{[K]_M - [K]_N exp\frac{-z_K F V_m^{M-N}}{RT}}{1 - exp\frac{-z_K F V_m^{M-N}}{RT}}} \quad (29)$$	[11]
$$V_{K,rev}^{M-N} = \frac{RT}{z_K F} ln\left(\frac{[K]_{M(out)}}{[K]_{N(in)}}\right) \quad (30)$$	

Table 2: The corresponding equations describing the current transported via Two pore domain potassium channels across the cell membrane

*1.2. Sodium Channels (**NaC**)*

1.2.1. Epithelial Sodium (Na) Channels ($ENaC$)

Epithelial Sodium (Na) Channels ($ENaC$)	**Ref**
$\boxed{I_{ENaC} = n''_{ENaC}\ g_{ENaC}\left(V_m^{M-N} - V_{Na,rev}^{M-N}\right)}$ (31)	[5, 6]
$\boxed{I_{Na,ENaC}^{M,N} = P_{Na,ENaC}^{M-N}\ \frac{z_{Na}^2 F^2 V_m^{M-N}}{RT} \frac{[Na]_M - [Na]_N exp\frac{-z_{Na} F V_m^{M-N}}{RT}}{1 - exp\frac{-z_{Na} F V_m^{M-N}}{RT}}}$ (32)	[8, 12]

Table 3: The corresponding equations describing the current transported via epithelial sodium (Na) channels ($ENaC$s) across the cell membrane

1.2.2. Voltage Gated Sodium Channel ($VGSC$, Na_v, $VONa$)

Voltage Gated Sodium Channel ($VGSC$, Na_v, $VONa$)	**Ref**
$\boxed{I_{Na,Na_v} = g_{Na_v}^{max} m_{Na_v}^3\ \ h_{Na_v}\ \left(V_m - V_{Na,rev}^{M-N}\right)}$ (33) $\frac{dm_{Na_v}}{dt} = \frac{\bar{m}_{Na_v} - m_{Na_v}}{\tau_m}$ (34) $\frac{dh_{Na_v}}{dt} = \frac{\bar{h}_{Na_v} - h_{Na_v}}{\tau_h}$ (35) $\bar{m}_{Na_v} = \frac{1}{1 + exp\left(\frac{-(V_m^{M-N} + V_{1/2,m\ Na_v}^{M-N})}{k_{m\ Na_v}}\right)}$ (36) $\bar{h}_{Na_v} = \frac{1}{1 + exp\left(\frac{(V_m^{M-N} + V_{1/2,h\ Na_v}^{M-N})}{k_{h\ Na_v}}\right)}$ (37)	[2, 13]

Table 3: The corresponding equations describing the ionic current transported via voltage gated sodium channels ($VGSC$s, Na_vs, $VONa$s) across the cell membrane (part 1/3 continued from previous page)

Voltage Gated Sodium Channel ($VGSC$, Na_v, $VONa$)	**Ref**
$$\boxed{I_{Na,Na_v} = g^{max}_{Na_v} m^3_{Na_v} h_{Na_v} j_{Na_v} \Big(V_m - V^{M-N}_{Na,rev}\Big)} \quad (38)$$ $$\frac{dm_{Na_v}}{dt} = \frac{\bar{m}_{Na_v} - m_{Na_v}}{\tau_m} \quad (39)$$ $$\frac{dh_{Na_v}}{dt} = \frac{\bar{h}_{Na_v} - h_{Na_v}}{\tau_h} \quad (40)$$ $$\frac{dj_{Na_v}}{dt} = \frac{\bar{j}_{Na_v} - j_{Na_v}}{\tau_j} \quad (41)$$ $$\bar{m}_{Na_v} = \frac{1}{\left(1 + exp\left(\frac{-(V^{M-N}_m - V^{M-N}_{1/2,m\ Na_v})}{k_{m\ Na_v}}\right)\right)^2} \quad (42)$$ $$\bar{h}_{Na_v} = \frac{1}{\left(1 + exp\left(\frac{(V^{M-N}_m + V^{M-N}_{1/2,h\ Na_v})}{k_{h\ Na_v}}\right)\right)^2} \quad (43)$$ $$\bar{j}_{Na_v} = \frac{1}{\left(1 + exp\left(\frac{(V^{M-N}_m + V^{M-N}_{1/2,j\ Na_v})}{k_{j\ Na_v}}\right)\right)^2} \quad (44)$$ $$\tau_m = \alpha_m\, \beta_m \quad (45)$$ $$\tau_h = \frac{1}{\alpha_h + \beta_h} \quad (46)$$ $$\tau_j = \frac{1}{\alpha_j + \beta_j} \quad (47)$$	[14–16]

Table 3: The corresponding equations describing the ionic current transported via voltage gated sodium channels ($VGSC$s, Na_vs, $VONa$s) across the cell membrane (part 2/3 continued from previous page)

Voltage Gated Sodium Channel ($VGSC$, Na_v, $VONa$)	Ref
$$For\ all\ range\ of\ V_m: \begin{cases} \alpha_m = \frac{1}{1+exp\left(\frac{-(V_m^{M-N}+V_{1\alpha m})}{k_{\alpha m}}\right)} \\ \beta_m = \frac{A_{\beta m}}{1+exp\left(\frac{(V_m^{M-N}+V_{1\beta m})}{k_{\beta m}}\right)} + \frac{B_{\beta m}}{1+exp\left(\frac{(V_m^{M-N}-V_{2\beta m})}{k_{2\beta m}}\right)} \end{cases} \quad (48)$$ $$For\ \ V_m \geq -40: \begin{cases} \alpha_h = 0 \\ \beta_h = \frac{A_{\beta_h}}{1+exp\left(\frac{-(V_m^{M-N}+V_{1\beta_h})}{k_{\beta_h}}\right)} \end{cases} \quad (49)$$ $$For\ \ V_m < -40: \begin{cases} \alpha_h = A_{\alpha_h} exp\left(\frac{-(V_m+V_{\alpha_h}^{Na_v})}{k_{\alpha_h}^{Na_v}}\right) \\ \beta_h = A_{\beta_h}\ exp(a_{\beta_h}\ V_m) + B_{\beta_h} exp(b_{\beta_h} V_m) \end{cases} \quad (50)$$ $$For\ \ V_m \geq -40: \begin{cases} \alpha_j = 0 \\ \beta_j = \dfrac{A_{\beta_j} exp(-a_{\beta_j}\ V_m)}{1+exp\left(\frac{-(V_m^{M-N}+V_{2\beta_j})}{k_{\beta_j}}\right)} \end{cases} \quad (51)$$ $$For\ \ V_m < -40: \begin{cases} \alpha_j = \dfrac{\left(A_{\alpha_j} exp(a_{\alpha_j} V_m) - B_{\alpha_j} exp(b_{\alpha_j} V_m)\right)(V_m + V_{1\alpha_j})}{1+exp(\frac{V+V_{2\alpha_j}}{k_{\alpha_j}})} \\ \beta_j = \dfrac{A_{\beta_j} exp(a_{\beta_j}\ V_m)}{1+exp\left(\frac{-(V_m^{M-N}+V_{2\beta_j})}{k_{\beta_j}}\right)} \end{cases} \quad (52)$$	
$$V_{Na,rev}^{M-N(a)} = \frac{RT}{z_{Na}F} ln\Big(\frac{[Na]_{M(l)}}{[Na]_{N(i)}}\Big) \quad (53)$$	[14–16]

Table 3: The corresponding equations describing the ionic current transported via voltage gated sodium channels ($VGSC$s, Na_vs, $VONa$s) across the cell membrane (part 3/3 continued from previous page)

1.3. Calcium Channels

1.3.1. L-type Voltage-Gated Calcium Channels

L-type Voltage-Gated Calcium Channels	Ref
$\boxed{I_i^{Ca_l,M-N} = P_i^M \dfrac{z_i^2 F^2 V_m^{M-N}}{RT} \dfrac{\gamma_i^N C_i^N - \gamma_i^M C_i^M exp\frac{-z_i FV_m^{M-N}}{RT}}{1 - exp\frac{-z_i FV_m^{M-N}}{RT}}}$ (54) $\boxed{I_{total}^{Ca_l,M-N} = I_{Na}^{Ca_l} + I_{Ca}^{Ca_l} + I_K^{Ca_l}}$ (55)	[12, 12, 17, 18]
$\boxed{I_{Ca,L} = g_{Ca_L}^{max} f_o^{Ca_l} f_d^{Ca_l} (V_m^{M-N} - V_{Ca,rev}^{M-N})}$ (56) $f_o^{Ca_l} = C_f f_f^{Ca_l} + C_s$ (57) $\dfrac{df_d^{Ca_l}}{dt} = \dfrac{\bar{f}_d^{Ca_l} - f_d^{Ca_l}}{\tau_{f_d}^{Ca_l}}$ (58) $\dfrac{df_f^{Ca_l}}{dt} = \dfrac{\bar{f}_o^{Ca_l} - f_f^{Ca_l}}{\tau_{f_f}^{Ca_l}}$ (59) $\bar{f}_d^{Ca_l} = \dfrac{1.0}{1.0 + exp\left(\frac{-(V_m^{M-N} + V_{1/2,f_d}^{Ca_l,M-N})}{k_{f_d}^{Ca_l}}\right)}$ (60) $\bar{f}_o^{Ca_l} = \dfrac{1.0}{1.0 + exp\left(\frac{(V_m^{M-N} + V_{1/2,f_o}^{Ca_l,M-N})}{k_{f_o}^{Ca_l}}\right)}$ (61) $\tau_{f_d}^{Ca_l} = A_{\tau_{f_d}^{Ca_l}}\ exp\left[\left(\dfrac{-(V_m + V_{\tau_{f_d}^{Ca_l}})}{k_{\tau_{f_d}^{Ca_l}}}\right)^2\right] + B_{\tau_{f_d}^{Ca_l}}$ (62) $\tau_{f_f}^{Ca_l} = A_{\tau_{f_f}^{Ca_l}}\ exp\left[\left(\dfrac{-(V_m - V_{\tau_{f_f}^{Ca_l}})}{k_{\tau_{f_f}^{Ca_l}}}\right)^2\right] + B_{\tau_{f_l}^{Ca_l}}$ (63) where $V_{1/2,f_d}^{Ca_l,M-N} = A_{f_d}^{Ca_l}$ and $V_{1/2,f_o}^{Ca_l,M-N} = A_{f_o}^{Ca_l}$.	[2, 4]

Table 4: The corresponding equations describing the flux and current transported via L-type voltage- gated calcium channels across the cell membrane

1.3.2. T-type voltage- gated calcium channels

T-type Voltage- Gated Calcium Channels	**Ref**
$\boxed{I^{M-N}_{Ca,Ca_t} = \overline{P}^{M-N}_{Ca,CaL} m^3_{Ca_t} h_{Ca_t} \frac{z^2_{Ca}F^2V^{M-N}_m}{RT} \frac{[Ca]_i - [Ca]_o exp\left(\frac{-z_{Ca}FV^{M-N}_m}{RT}\right)}{1 - exp\left(\frac{-z_{Ca}FV^{M-N}_m}{RT}\right)}} \quad (64)$ where: $\frac{dm_{Ca_t}}{dt} = \frac{\bar{m}_{Ca_t} - m_{Ca_t}}{\tau^{Ca_t}_m} \quad (65)$ $\frac{dh}{dt} = \frac{\bar{h} - h}{\tau_h} \quad (66)$ $\bar{m}_{Ca_t} = \frac{1}{1 + exp\left(\frac{-(V^{M-N}_m + V^{M-N}_{1/2,m\ Ca_v})}{k_{m\ Ca_v}}\right)} \quad (67)$ $\bar{h}_{Ca_t} = \frac{1}{1 + exp\left(\frac{(V^{M-N}_m + V^{M-N}_{1/2,h\ Ca_t})}{k_{h\ Ca_t}}\right)} \quad (68)$ $For\ all\ range\ of\ V_m : \begin{cases} \tau^{Ca_t}_m = \frac{A_{\tau^{Ca_t}_m}}{exp\left(\frac{-(V^{M-N}_m + V_{1\tau_m})}{k_{1\tau_m}}\right) + exp\left(\frac{(V^{M-N}_m + V_{2\tau_m})}{k_{2\tau_m}}\right)} + B_{\tau^{Ca_t}_m} \end{cases} \quad (69)$ $For\ \ V_m \geq -80mV : \begin{cases} \tau^{Ca_t}_h = A_{\tau^{Ca_t}_h}\ exp\left[\frac{-(V_m + V_{\tau^{Ca_t}_h})}{k_{\tau^{Ca_t}_h}}\right] + B_{\tau^{Ca_t}_h} \end{cases} \quad (70)$ $For\ \ V_m < -80mV : \begin{cases} \tau^{Ca_t}_h = A_{\tau^{Ca_t}_h}\ exp\frac{(V_m + V_{\tau^{Ca_t}_h})}{k_{\tau^{Ca_t}_h}} \end{cases}$	[19–22]

Table 5: The corresponding equations describing the flux and current transported via T-type voltage- gated calcium channels across the cell membrane

1.3.3. Store Operated Channels (SOC)

<table>
<tr><th>Store Operated Channels (SOC)</th><th>Ref</th></tr>
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$$\boxed{I^{M-N}_{Ca,SOC} = g^{max}_{Ca,SOC} f^{SOC}_o \left(V^{M-N}_m - V^{M-N}_{Ca,rev}\right)} \tag{71}$$

$$\boxed{I^{M-N}_{Na,SOC} = I^{M-N}_{Ca,SOC}\left(\frac{z^2_{Na}P^{SOC}_{Na}}{z^2_{Ca}P^{SOC}_{Ca}}\right)\times\left(\frac{[Na]_i-[Na]_o exp\left(\frac{-z_{Na}FV^{M-N}_m}{RT}\right)}{[Ca]_i-[Ca]_o exp\left(\frac{-z_{Ca}FV^{M-N}_m}{RT}\right)}\right)\left(\frac{1-exp\left(\frac{-z_{Ca}FV^{M-N}_m}{RT}\right)}{1-exp\left(\frac{-z_{Na}FV^{M-N}_m}{RT}\right)}\right)} \tag{72}$$

where

$$f^{SOC}_o = \frac{1}{1+\frac{[Ca]_{sr}^{\eta_{SOC}}}{K_{SOC}^{\eta_{SOC}}}} \tag{73}$$

</td><td>[2, 23]</td></tr>
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$$\boxed{I^{M,N}_{Ca,SOC} = A^{M-N}_m P_{Ca,SOC}\ \frac{z^2_{Ca}\ F^2V^{M-N}_m}{RT}\ \frac{[Ca]_i-[Ca]_o exp\frac{-z_{Ca}FV^{M-N}_m}{RT}}{1-exp\frac{-z_{Ca}FV^{M-N}_m}{RT}}} \tag{74}$$

$$\boxed{I^{M,N}_{Na,SOC} = A^{M-N}_m P_{Na,SOC}\ \frac{z^2_{Na}\ F^2V^{M-N}_m}{RT}\ \frac{[Na]_i-[Na]_o exp\frac{-z_{Na}FV^{M-N}_m}{RT}}{1-exp\frac{-z_{Na}FV^{M-N}_m}{RT}}} \tag{75}$$

$$\boxed{I^{M,N}_{SOC,total} = f^{SOC}_o\left(I^{M,N}_{Ca,SOC} + I^{M,N}_{Na,SOC}\right)} \tag{76}$$

(77)

where

$$P^{M-N}_{Na,SOC} = \frac{P^{max}_{SOC}}{1+\left(\frac{[Ca]_o}{K_{SOC,Ca_o}}\right)^{\eta_{SOC,Na}}} \tag{78}$$

$$f^{SOC}_o = a\left(\frac{1}{1+(\frac{[Ca]_{sr}}{K_{SOC}})^{\eta_{SOC}}}\right)+b \tag{79}$$

</td><td>[3]</td></tr>
<tr><td>

$$V^{M-N}_{Ca,rev} = \frac{RT}{z_{Ca}F} ln\left(\frac{[Ca]_o}{[Ca]_i}\right) \tag{80}$$

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Table 6: The corresponding equations describing the flux and current transported via store operated calcium channels (SOCs) across the cell membrane.

1.4. Chloride channels

1.4.1. Calcium dependent Chloride Channels (CaCC)

Calcium dependent Chloride Channels (CaCC)	Ref
$\boxed{I''^{M-N}_{Cl,CaCC} = n''^{M-N}_{CaCC}\, g^{M-N}_{Cl}\, f_o^{Cl,CaCC}(V_m^{M-N} - V_{Cl}^{M-N(a)})} \quad (81)$ `where:`	
1. Hill model: $f_o^{Cl,\,CaCC} = \frac{1}{1+\left(\frac{K_{CaCC}}{[Ca]_i}\right)^{\eta_{CaCC}}} \quad (82)$	[5]
2. High positive voltage (HPV) enhanced calcium activation CaCC model: $f_o^{Cl,\,CaCC} = f_o^{CaCC,\,HPV}\,\frac{1}{1+(\frac{K_{CaCC}}{[Ca]_i})^{\eta_1}} \quad (83)$ $\frac{\mathrm{d}f_o^{CaCC,\,HPV}}{\mathrm{d}t} = \frac{\bar{f}_o^{CaCC,HPV} - f_o^{CaCC,\,HPV}}{\tau_{CaCC}} \quad (84)$ $\bar{f}_o^{CaCC,HPV} = \frac{1}{1+exp\frac{-\left(V_m - V^{CaCC}_{half\ max}\right)}{V_{CaCC}}} \quad (85)$ $V^{CaCC}_{half\ max} = \sigma\sqrt{2ln2}+\mu \quad (86)$ $\tau_{CaCC}(V_m) = \frac{1}{\sigma\sqrt{2\pi}}exp\left(-\left(\frac{V_m-\mu}{\sqrt{2}\sigma}\right)^2\right) \quad (87)$	[3]
3. Steady state Arreola model: $f_o^{Cl,\,CaCC} = \frac{1}{1+K_2\left(\frac{K_1^2}{[Ca]_i^2}+\frac{K_1}{[Ca]_i}+1\right)} \quad (88)$ $K_1 = 234\ exp\left(\frac{-0.13FV_m^{M-N}}{RT}\right),\ K_2 = 0.58exp\left(\frac{-0.24FV_m^{M-N}}{RT}\right)$	[7, 24, 25]
$V_{Cl}^{M-N(a)} = \frac{RT}{z_{Cl}F}ln\left(\frac{[Cl]_{N(l)}}{[Cl]_{M(i)}}\right) \quad (89)$	

Table 7: The corresponding equations describing the flux and current transported via calcium dependent chloride channels (CaCC) across the cell membrane

1.4.2. Cystic Fibrosis Transmembrane conductance Regulator (CFTR)

Cystic Fibrosis Transmembrane conductance Regulator (CFTR)	Ref
$\boxed{I''^{M,N(a)}_{Cl,CFTR} = n''^{M-N(a)}_{CFTR} P^{M(a)}_{Cl,CFTR} \frac{z_{Cl}^2 F^2 V_m^{M-N(a)}}{RT} \frac{[Cl]_N - [Cl]_M exp\frac{z_{Cl} F V_m^{M-N(a)}}{RT}}{1 - exp\frac{z_{Cl} F V_m^{M-N(a)}}{RT}}}$ (90)	[26]
$\boxed{I''^{M-N(a)}_{Cl,CFTR} = n''^{M-N(a)}_{CFTR} g^{M-N}_{CFTR} f_o^{Cl,CFTR} (V_m^{M-N(a)} - V^{M-N(a)}_{Cl,rev})}$ (91)	[5, 8, 27]
$\boxed{I''^{M-N(a)}_{Cl,CFTR} = n''^{M-N}_{CFTR}\, g_{CFTR} \left(V_m^{M-N} - V^{M-N}_{Cl,rev}\right)}$ (92) $\boxed{I''^{M-N(a)}_{HCO3,CFTR} = n''^{M-N}_{CFTR}\, \beta\, g_{CFTR} \left(V_m^{M-N} - V^{M-N}_{HCO3,rev}\right)}$ (93) where: $\beta = \frac{g_{CFTR,HCO_3}}{g_{CFTR,Cl}}$ (94)	[6]
$\boxed{I''^{M-N}_{Cl,CFTR} = n''^{M-N}_{CFTR} (\overline{g}^{M-N}_{Cl}\ g^{CFTR}_{Cl}) \left(V_m^{M-N(a)} - V^{M-N}_{Cl,rev}\right)}$ (95) $\boxed{I''^{M-N}_{HCO_3,CFTR} = n''^{M-N}_{CFTR} (\overline{g}^{M-N}_{HCO_3}\ g^{CFTR}_{HCO3}) \left(V_m^{M-N(a)} - V^{M-N}_{HCO_3,rev}\right)}$ (96) Where $g_x^{M-N}([x]_M, [x]_N) = [x]_M [x]_N \frac{ln\left(\frac{[x]_M}{[x]_N}\right)}{[x]_M - [x]_N}$ (97) $V^{M-N(a)}_{Cl,rev} = \frac{RT}{z_{Cl} F} ln\left(\frac{[Cl]_{N(l)}}{[Cl]_{M(i)}}\right)$ (98) $V^{M-N}_{HCO_3,rev} = \frac{RT}{z_{HCO_3} F} ln\left(\frac{[HCO_3]_N}{[HCO_3]_M}\right)$ (99)	[28]

Table 8: The corresponding equations describing the ionic current transported via cystic fibrosis transmembrane conductance regulator (CFTR) channels across the cell membrane (part 1/2 continued on the next page).

2. ATPase model

2.1. Sodium Potassium ATPase pump (Na-K ATPase)

Sodium Potassium ATPase pump (Na-K ATPase)	**Ref**
$$\mathrm{ATP} + 3\,\mathrm{Na_M}^{+} + 2\,\mathrm{K_N}^{+} \rightleftarrows \mathrm{ADP} + \mathrm{Pi} + 3\,\mathrm{Na_N}^{+} + 2\,\mathrm{K_M}^{+} \quad (100)$$ $$\boxed{J_{Na^+}^{NakATpase} = J_{Na^+}^{NakATpase,max}\Big(\frac{[Na]_{M(i)}}{[Na]_{M(i)} + K_{Na_M}}\Big)^3\Big(\frac{[K]_{N(e)}}{[K]_{N(e)} + K_{K_N}}\Big)^2} \quad (101)$$ $$\boxed{J_{K^+}^{NakATpase} = (\frac{-2}{3})J_{Na^+}^{NakATpase}} \quad (102)$$	[29–34]
`where:` $$K_{Nai} = K_{Na}^{NaK}(1 + \frac{[K]_i}{a_{NaK}}) \quad (103)$$ $$K_{Ki} = K_{K}^{NaK}(1 + \frac{[Na]_e}{b_{NaK}}) \quad (104)$$	[31]
$$\boxed{J_{Na}^{Pump} = J_{Na}^{NaKATPase,max}\left(\frac{[Na]_c}{[Na]_c + K_{Na}}\right)^3\left(\frac{[K]_{bl}}{[K]_{bl} + K_K}\right)^2} \quad (105)$$ $$\boxed{J_K^{pump} + J_{NH4}^{pump} = -\frac{2}{3}J_{Na}^{pump}} \quad (106)$$ $$\boxed{\frac{J_{NH4}^{pump}}{J_K^{pump}} = \frac{[NH4]_e}{K_{NH4}} \cdot \frac{K_K}{[K]_e}} \quad (107)$$	[35, 36]

Table 9: The corresponding equations describing the flux and current transported via sodium potassium ATPase pumps across the cell membrane

Sodium Potassium ATPase pump (Na-K ATPase)	Ref
$$\boxed{I_{NaK}^{M-N} = I_{NaK}^{max}\psi_{NaK}^{cyt}\Big(\frac{[Na]_{cyt}^{1.5}}{[Na]_{cyt}^{1.5} + K_{m,Na,\alpha 1}^{1.5}}\Big)\Big(\frac{[K]_{out}}{[K]_{out} + K_{m,K}}\Big)} \quad (108)$$ $$\psi_{NaK}^{cyt} = \frac{1}{1 + 0.1245exp\left(-0.1\frac{V_m^{M-N}F}{RT}\right) + 0.365\ \sigma\ exp\left(\frac{-V_m^{M-N}F}{RT}\right)} \quad (109a)$$ $$\sigma = \frac{1}{7}\left(\frac{[Na]_{out}}{67.3} - 1\right) \quad (109b)$$	[2, 37]
$$\boxed{J_{pump} = P_{pump}\left(\frac{[Na]_c}{[Na]_c + K_{Na}}\right)^3\left(\frac{[K]_{bl}}{[K]_{bl} + K_K}\right)^2 (a \times V_m^b + b)} \quad (110)$$	[8, 38]
$$\boxed{J_{NaKATPase} = P_{pump}\left(\frac{[Na]_i}{[Na]_i + K_{Na}^{NaK}}\right)^3\left(\frac{[K]_{bl}}{[K]_{bl} + K_K^{NaK}}\right)^2 (V_m^{i-bl} - V_{rev})} \quad (111)$$	[38]

Table 10: The corresponding equations describing the flux and current transported via Sodium Potassium ATPase pumps across the cell membrane

23 *2.2. Proton-ATPase (H-ATPase)*

Proton-ATPase ($H - ATPase$)	Ref
$$\boxed{J_{H,HATPase}^{M-N(a)} = -J_{H,HATPase}^{max}\frac{1}{1 + exp\left(\zeta(v_H^{M-N(a)} - v_{1/2,H-ATPase}^{M-N(a)})\right)}} \quad (112)$$ $$\boxed{J_{H,HATPase}^{M-N(b)} = J_{H,HATPase}^{max}\frac{1}{1 + exp\left(-\zeta(v_H^{M-N(b)} - v_{1/2,H-ATPase}^{M-N(b)})\right)}} \quad (113)$$	[32]
$$\boxed{J_{H,H-ATPase}^{M(i)-N(e)} = J_{H,HATPase}^{max}\frac{[H^+]_{M(cell)}}{K_{H,H-ATPase}^{M(cell)} + [H^+]_{M(cell)}}} \quad (114)$$	[29]

Table 11: The corresponding equations describing the flux and current transported via proton-ATPase (H-ATPase) pumps across the cell membrane

2.3. Hydrogen-Potassium ATPase (H/KATPase)

Hydrogen-Potassium ATPase (H/KATPase)	**Ref**
$$\boxed{J^{net}_{Na,HK-ATPase} = k^{lc}_{Na}[P_iNa]_l - k^{cl}_{Na}[P_iNa]_c} \quad (115)$$ $$\boxed{J^{net}_{K,HK-ATPase} = k^{lc}_{K}[K]_l - k^{cl}_{K}[K]_c} \quad (116)$$ $$\boxed{J^{net}_{H,HK-ATPase} = k^{lc}_{H}[P_iH]_l - k^{cl}_{H}[P_iH]_c} \quad (117)$$ $$\boxed{J^{net}_{NH4,HK-ATPase} = k^{lc}_{NH4}[NH4]_l - k^{cl}_{NH4}[NH4]_c} \quad (118)$$	[39]

Table 12: The corresponding equations describing the flux and current transported via Hydrogen-Potassium ATPase (H/KATPase) pumps across the cell membrane

2.4. Calcium ATPase pumps ($Ca - ATPase$):

2.4.1. Plasma membrane calcium ATPase (PMCA)

Plasma Membrane Calcium ATPase (PMCA)	**Ref**
$$\boxed{I_{PMCA} = I^{max}_{PMCA} \frac{1}{1 + \left(\frac{K_{PMCA,Ca_i}}{[Ca]_{M(i)}}\right)^{\eta_{PMCA}}}} \quad (119)$$	[3, 7, 17, 24, 40, 41]

Table 13: The corresponding equations describing the flux and current transported via Plasma membrane calcium ATPase (PMCA) pumps across the cell membrane

2.4.2. *Sacro Endoplasmic Reticulum Calcium ATPase (SERCA)*

Sacro Endoplasmic Reticulum Calcium ATPase (SERCA)	**Ref**
$$\boxed{I_{SERCA} = I_{SERCA}^{max} \frac{1}{1 + \left(\frac{K_{SERCA}}{[Ca]_{M(cyt)}}\right)^{\eta_{SERCA}}}} \qquad (120)$$	[3, 4, 7, 24, 37, 42, 43]
$$\boxed{J_{SERCA} = J_{SERCA}^{max} \frac{(1)}{1 + (\frac{[Ca]_i}{K_{SERCA}})^{\eta_{serca}}} \quad \frac{1}{[Ca]_{er}}} \qquad (121)$$	[43, 44]
$$\boxed{J_{SERCA} = \frac{V_{maxf}\left(\frac{[Ca]_i}{K_{mf}}\right)^{\eta_f} - V_{maxr}\left(\frac{[Ca]_{sr}}{K_{mr}}\right)^{\eta_r}}{1 + \left(\frac{[Ca]_i}{K_{mf}}\right)^{\eta_f} + \left(\frac{[Ca]_{sr}}{K_{mr}}\right)^{\eta_r}} + K([Ca]_{sr} - [Ca]_i)} \qquad (122)$$	[45]
$$\boxed{I_{SERCA} = I_{SERCA}^{max} \frac{\left(\frac{[Ca]_i}{K_{mf}}\right)^{\eta_{serca}} - \left(\frac{[Ca]_{sr}}{K_{mr}}\right)^{\eta_{serca}}}{1 + \left(\frac{[Ca]_i}{K_{mf}}\right)^{\eta_{serca}} + \left(\frac{[Ca]_{sr}}{K_{mr}}\right)^{\eta_{serca}}}} \qquad (123)$$	[2, 18]

Table 14: The corresponding equations describing the flux and current transported via sacro endoplasmic reticulum calcium ATPase (SERCA) pumps across the cell membrane

3. Symporter model

3.1. Sodium Potassium Chloride Symporter (NKCC):

Sodium Potassium Chloride Symporter (NKCC)	**Ref**
NKCC1 $$J^{M,N(net)}_{Cl,NKCC} = [E]_{NKCC}\left(\frac{R_{NN}\left(g^{M}_{ECl}Cl^{M} + g^{M}_{EClNa}Cl^{M}Na^{M} + g^{M}_{EClNaCl}Cl^{M}Na^{M}Cl''^{M}\right.}{R_{M}R_{NN} + R_{N}R_{MM}} \frac{\left.+g^{M}_{EClNaClK}Cl^{M}Na^{M}Cl''^{M}K^{M}\right)}{R_{M}R_{NN} + R_{N}R_{MM}}\right) - [E]_{NKCC}\left(\frac{R_{MM}\left(g^{N}_{ECl}Cl^{N} + g^{N}_{EClNa}Cl^{N}Na^{N} + g^{N}_{EClNaCl}Cl^{N}Na^{N}Cl''^{N}\right.}{R_{M}R_{NN} + R_{N}R_{MM}} \frac{\left.+g^{N}_{EClNaClK}Cl^{N}Na^{N}Cl''^{N}K^{N}\right)}{R_{M}R_{NN} + R_{N}R_{MM}}\right) \tag{124a}$$ $$J^{M,N(net)}_{Na,NKCC} = [E]_{NKCC}\left(\frac{R_{NN}\left(g^{M}_{EClNa}Cl^{M}Na^{M} + g^{M}_{EClNaCl}Cl^{M}Na^{M}Cl''^{M} + g^{M}_{EClNaClK}Cl^{M}Na^{M}Cl''^{M}K^{M}\right)}{R_{M}R_{NN} + R_{N}R_{MM}} - \frac{R_{MM}\left(g^{N}_{EClNa}Cl^{N}Na^{N} + g^{N}_{EClNaCl}Cl^{N}Na^{N}Cl''^{N} + g^{N}_{EClNaClK}Cl^{N}Na^{N}Cl''^{N}K^{M}\right)}{R_{M}R_{NN} + R_{N}R_{MM}}\right) \tag{124b}$$ $$J^{M,N(net)}_{K,NKCC} = [E]_{NKCC}\left(\frac{R_{NN}(g^{M}_{EClNaClK}Cl^{M}Na^{M}Cl''^{M}K^{M}) - R_{MM}(g^{N}_{EClNaClK}Cl^{N}Na^{N}Cl''^{N}K^{N})}{R_{M}R_{NN} + R_{N}R_{MM}}\right) \tag{124c}$$	[34, 46–48]

Table 15: The corresponding equations describing the flux transported via sodium potassium chloride symporter (NKCC) across the cell membrane (part 1/2 continued on the next page)

Sodium Potassium Chloride Symporter (NKCC)	Ref
NKCC1-Continued from previous page Where $[E]_t = [E]_M + [ECl]_M + [EClNa]_M + [EClNaCl]_M + [EClNaClK]_M + [EClNaClK]_N + [EClNaCl]_N + [EClNa]_N + [ECl]_N + [E]_N$ $Cl^M = \frac{[Cl]_M}{K^M_{Cl}}$, $Na^M = \frac{[Na]_M}{K^M_{ClNa}}$, $Cl'^M = \frac{[Cl]_M}{K^M_{ClNaCl}}$, $K^M = \frac{[K]_M}{K^M_{ClNaClK}}$ $Cl^N = \frac{[A]_N}{K^N_A}$, $Na^N = \frac{[B]_N}{K^N_{ClNa}}$, $Cl'^N = \frac{[A]_N}{K^N_{ABA}}$, $K^N = \frac{[C]_N}{K^N_{ClNaClK}}$ $R_M = 1 + Cl^M + Cl^M Na^M + Cl^M Na^M Cl'^M + Cl^M Na^M Cl'^M K^M$ $R_N = 1 + Cl^N + Cl^N Na^N + Cl^N Na^N Cl'^N + Cl^N Na^N Cl'^N K^N$ $R_{MM} = g^M_E + g^M_{ECl} Cl^M + g^M_{EClNa} Cl^M Na^M + g^M_{EABA} Cl^M Na^M Cl'^M + g^M_{EClNaClK} Cl^M Na^M Cl'^M K^M$ $R_{NN} = g^N_E + g^N_{ECl} Cl^N + g^N_{EClNa} Cl^N Na^N + g^N_{EClNaCl} Cl^N Na^N Cl'^N + g^N_{EClNaClK} Cl^N Na^N Cl'^N K^N$	[34, 46–48]

Table 16: The corresponding equations describing the flux transported via sodium potassium chloride symporter (NKCC) across the cell membrane (part 2/2 continued from the previous page)

Sodium Potassium Chloride Symporter (NKCC)	Ref
$$\boxed{J^{M,N(net)}_{symporter} = [E]_t\left(\frac{\left(g^M_{ENaClKCl}Na^M Cl^M K^M Cl''^M\right) g^N_E - \left(g^N_{ENaClKCl}Na^N Cl^N K^N Cl''^N\right) g^M_E}{R_M R_{NN} + R_N R_{MM}}\right)} \quad (125a)$$ $$\boxed{J^{M,N(net)}_{Na,symporter} = J^{M,N(net)}_{symporter}} \quad (125b)$$ $$\boxed{J^{M,N(net)}_{Cl,symporter} = 2J^{M,N(net)}_{symporter}} \quad (125c)$$ $$\boxed{J^{M,N(net)}_{K,symporter} = J^{M,N(net)}_{symporter}} \quad (125d)$$ Where $[E]_t = [E]_M + [ENa]_M + [ENaCl]_M + [ENaClK]_M + [ENaClKCl]_M + [ENaClKCl]_N + [ENaClK]_N + [ENaCl]_N + [ENa]_N + [E]_N$. $Na^M = \frac{[Na]_M}{K^M_{Na}},\ Cl^M = \frac{[Cl]_M}{K^M_{NaCl}}, K^M = \frac{[K]_M}{K^M_{NaClK}}, Cl''^M = \frac{[Cl]_M}{K^M_{NaClKCl}},$ $Na^N = \frac{[Na]_N}{K^N_{NaClKCl}},\ \ Cl^N = \frac{[Cl]_N}{K^N_{BCB}}\ \ K^N = \frac{[K]_N}{K^N_{ABC}}, Na''^N = \frac{[Cl]_N}{K^N_{NaClKCl}}.$ $R_M = 1 + Na^M + Na^M Cl^M + Na^M Cl^M K^M + Na^M Cl^M K^M Cl''^M$ $R_N = 1 + Cl''^N + K^N Cl''^N + Cl^N K^N Cl''^N + Na^N Cl^N K^N Cl''^N$ $R_{MM} = g^M_E + g^M_{ENaClKCl}Na^M Cl^M K^M Cl''^M$ $R_{NN} = g^N_E + g^N_{ENaClKCl}Na^N Cl^N K^N Cl''^N$	[34, 49]
$$\boxed{J^{M,N(net)}_{Na,NKCC} = [E]_t\left(\frac{g^N_E R_{MM} - g^M_E R_{NN}}{R_M R_{NN} + R_N R_{MM}}\right)} \quad (126a)$$ $$\boxed{J^{M,N(net)}_{K,NKCC} = [E]_t\left(\frac{\left(g^M_{ENKCC}Na^M K^M (Cl^M)^2\right) R_{NN} - \left(g^N_{ENKCC}Na^N K^N (Cl^N)^2\right) R_{MM}}{R_M R_{NN} + R_N R_{MM}}\right)} \quad (126b)$$ Where $[E]_t = R_M[E]_M + R_N[E]_N$ $Na^M = \frac{[Na]_M}{K_{Na}}\ , K^M = \frac{[K]_M}{K_K}, Cl^M = \frac{[Cl]_M}{K_{Cl}}, NH_4{}^M = \frac{[NH_4]_M}{K_{NH_4}}$ $Na^N = \frac{[Na]_N}{K_{Na}}\ , K^N = \frac{[K]_N}{K_K}, Cl^N = \frac{[Cl]_N}{K_{Cl}}, NH_4{}^N = \frac{[NH_4]_N}{K_{NH_4}}$ $R_M = 1 + Na^M + Na^M Cl^M + Na^M K^M Cl^M + Na^M K^M (Cl^M)^2 + Na^M NH_4{}^M Cl^M + Na^M NH^M_4 (Cl^M)^2$ $R_N = 1 + Cl^N + K^N Cl^N + K^N (Cl^N)^2 + Na^N K^N (Cl^N)^2 + NH^N_4 Cl^N + NH_4{}^N (Cl^N)^2 + Na^N NH^N_4 + (Cl^N)^2$ $R_{MM} = g^M_E + g^M_{ENKCC}Na^M K^M (Cl^M)^2 + g^M_{ENNH_4CC}Na^M NH_4{}^M (Cl^M)^2$ $R_{NN} = g^N_E + g^N_{ENKCC}Na^N K^N (Cl^N)^2 + g^N_{ENNH_4CC}Na^N NH_4{}^N (Cl^N)^2$	[50]

Table 17: The corresponding equations describing the flux transported via sodium potassium chloride symporter (NKCC) across the cell membrane

Sodium Potassium Chloride Symporter (NKCC)	**Ref**
$$\boxed{J^{M-N}_{NKCC2} = P^{symporter}_{NKCC2} \frac{[Na]_{M(e)}[K]_{M(e)}[Cl]^2_{M(e)} - [Na]_{N(i)}[K]_{N(i)}[Cl]^2_{N(i)}}{\left[\frac{[Na]_{N(i)}}{K_{Na}} + 1\right]\left[\frac{[K]_{N(i)}}{K_K} + 1\right]\left[\frac{[Cl]_{N(i)}}{K_{Cl}} + 1\right]^2}} \quad (127)$$ $$\boxed{J^{M,N(net)}_{Na,NKCC2} = J^{M,N(net)}_{NKCC2}} \quad (128)$$ $$\boxed{J^{M,N(net)}_{K,NKCC2} = J^{M,N(net)}_{NKCC2}} \quad (129)$$ $$\boxed{J^{M,N(net)}_{Cl,NKCC2} = 2J^{M,N}_{NKCC2}} \quad (130)$$	[8, 51]
$$\boxed{J_{NKCC} = [E]_{NKCC}\left(r_{NKCC}\frac{1 - \alpha_1[Na]_i[K]_i[Cl]_i^2}{K_{NKCC} + \alpha_2[Na]_i[K]_i{[Cl]_i}^2}\right)} \quad (131)$$	[7, 52]

Table 18: The corresponding equations describing the flux transported via sodium potassium chloride symporter (NKCC) across the cell membrane

3.2. *Potassium chloride cotransporter*

Potassium Chloride Cotransporter	**Ref**
Competitor Ammonium $$\boxed{J^{M,N(net)}_{K,KCl} = [E]_t \frac{\left(g^M_{EClK} Cl^M K^M\right) R_{NN} - \left(g^N_{EClK} Cl^N K^N\right) R_{MM}}{R_M R_{NN} + R_N R_{MM}}} \quad (132a)$$ $$\boxed{J^{M,N(net)}_{NH_4,KCl} = [E]_t \frac{\left(g^M_{EClNH_4} Cl^M NH^M_4\right) R_{NN} - \left(g^N_{EClNH_4} Cl^N NH^N_4\right) R_{MM}}{R_M R_{NN} + R_N R_{MM}}} \quad (132b)$$ $$\boxed{J^{M,N(net)}_{Cl,KCl} = [E]_t \frac{\left(g^M_{EClK} Cl^M K^M + g^M_{EClNH_4} Cl^M NH^M_4\right) R_{NN} - \left(g^N_{EClK} Cl^N K^N + g^N_{EClNH_4} Cl^N NH^N_4\right) R_{MM}}{R_M R_{NN} + R_N R_{MM}}} \quad (132c)$$ where $[E]_t = [E]_M + [ECl]_M + [EClK]_M + [EClNH_4]_M + [EClNH_4]_N + [EClK]_N + [ECl]_N + [E]_N$. $Cl^M = \frac{[Cl]_M}{K^M_{Cl}},\ K^M = \frac{[K]_M}{K^M_K},\ NH^M_4 = \frac{[NH4]_M}{K^M_C} \mid Cl^N = \frac{[A]_N}{K^N_{Cl}},\ K^N = \frac{[K]_N}{K^N_B},\ NH^N_4 = \frac{[NH_4]_N}{K^N_{NH_4}}$ $R_M = 1 + Cl^M + Cl^M K^M + Cl^M NH^M_4 \mid R_N = 1 + Cl^N + Cl^N K^N + Cl^N NH^N_4$ $R_{MM} = g^M_E + g^M_{EClK} Cl^M K^M + g^M_{EClNH_4} Cl^M NH^M_4 \mid R_{NN} = g^N_E + g^N_{EClK} Cl^N K^N + g^N_{EClNH_4} Cl^N NH^N_4$	[34, 53]

Table 19: The corresponding equations describing the flux transported via potassium chloride symporters across the cell membrane

Potassium Chloride Cotransporter	Ref
Competitor Ammonium $$\boxed{J^{M,N(net)}_{K,KCC} = [E]_t \left(\frac{\left(g^M_{EKCl} K^M Cl^M\right) R_{NN} - \left(g^N_{EKCl} K^N Cl^N\right) R_{MM}}{R_M R_{NN} + R_N R_{MM}} \right)} \quad (133a)$$ $$\boxed{J^{M,N(net)}_{NH_4,KCl} = [E]_t \frac{\left(g^M_{ENH_4Cl} NH_4^M Cl^M\right) R_{NN} - \left(g^N_{ENH_4Cl} NH_4^N Cl^N\right) R_{MM}}{R_M R_{NN} + R_N R_{MM}}} \quad (133b)$$ $$\boxed{\begin{gathered} J^{M,N(net)}_{Cl,KCl} = [E]_t \\ \frac{\left(g^M_{EKCl} K^M Cl^M + g^M_{ENH_4Cl} NH_4^M Cl^M\right) R_{NN} - \left(g^N_{EKCl} K^N Cl^N + g^N_{ENH_4Cl} NH_4^N Cl^N\right) R_{MM}}{R_M R_{NN} + R_N R_{MM}} \end{gathered}} \quad (133c)$$ Where $[E]_t = R_M[E]_M + R_N[E]_N$ $K^M = \frac{[K]_M}{K^M_K}, \; Cl^M = \frac{[Cl]_M}{K^M_{Cl}}, \; NH_4^M = \frac{[NH4]_M}{K^M_C} \mid K^N = \frac{[K]_N}{K^N_B}, \; Cl^N = \frac{[A]_N}{K^N_{Cl}}, \; NH_4^N = \frac{[NH_4]_N}{K^N_{NH_4}}$ $R_M = 1 + K^M + K^M Cl^M + NH_4^M Cl^M \mid R_N = 1 + Cl^N + K^N Cl^N + NH_4^N Cl^N$ $R_{MM} = g^M_E + g^M_{EKCl} K^M Cl^M + g^M_{ENH_4Cl} NH_4^M Cl^M \mid R_{NN} = g^N_E + g^N_{EKCl} K^N Cl^N + g^N_{ENH_4Cl} NH_4^N Cl^N$	[36]

Table 20: The corresponding equations describing the flux transported via potassium chloride symporters across the cell membrane

3.3. Sodium chloride cotransporter

Sodium chloride cotransporter	Ref
$$\boxed{J_{Na,NCC}^{M,N(net)} = [E]_t \left(\frac{(g_{ENaCl}^{M} Na'^{M} Cl^{M})(g_E^N) - (g_{ENaCl}^{N} Na'^{N} Cl^{N})(g_E^M)}{R_M R_{NN} + R_N R_{MM}} \right)} \quad (134a)$$ $$\boxed{J_{Cl,NCC}^{M,N(net)} = [E]_t \left(\frac{(g_{ENaCl}^{M} Na'^{M} Cl^{M})(g_E^N) - (g_{ENaCl}^{N} Na'^{N} Cl^{N})(g_E^M)}{R_M R_{NN} + R_N R_{MM}} \right)} \quad (134b)$$ Where $[E]_t = [E]_M + [ECl]_M + [ENa]_M + [ENaCl]_M + [ENaCl]_N + [ENa]_N + [ECl]_N + [E]_N$ $Na^M = \frac{[Na]_M}{K_{Na}^M}$ $Na'^M = \frac{[Na]_M}{K_{ClNa}^M}$ $Cl^M = \frac{[Cl]_M}{K_{Cl}^M}$ | $Na^N = \frac{[Na]_N}{K_{Na}^N}$ $Na'^N = \frac{[Na]_N}{K_{ClNa}^N}$ $Cl^N = \frac{[Cl]_N}{K_{Cl}^N}$ $R_M = (1 + Na^M + Cl^M + Na'^M Cl^M)$ | $R_N = (1 + Na^N + Cl^N + Na'^N Cl^N)$ $R_{MM} = g_E^M + g_{ENaCl}^M Na'^M Cl^M$ | $R_{NN} = g_E^N + g_{ENaCl}^N Na'^N Cl^N$	[34, 54]

Table 21: The corresponding equations describing the flux transported via sodium chloride symporters across the cell membrane

3.4. Sodium Bicarbonate Symporter (NBC)

Sodium Bicarbonate Symporter (NBC)	Ref
$$\boxed{\begin{gathered} J_{NBCe} = P_{NBCe} \times \\ \frac{\left(\frac{[Na]_{bl}[HCO3]_{bl}^n}{K_{Na} K_{HCO3}^n} \times \phi_1 - \frac{[Na]_c [HCO3]_c^n}{K_{Na} K_{HCO3}^n} \times \phi_2 \right)}{\left(\phi_2 + g' \left(\frac{[Na]_{bl}[HCO3]_{bl}^n}{K_{Na} K_{HCO3}^n} \right) \right) \left(1 + \frac{[Na]_c}{K_{Na}} + \frac{[Na]_c [HCO3]_c^n}{K_{Na} K_{HCO3}^n} \right)} \\ - \left(\phi_1 + g' \left(\frac{[Na]_c [HCO3]_c^n}{K_{Na} K_{HCO3}^n} \right) \right) \left(1 + \frac{[Na]_c}{K_{Na}} + \frac{[Na]_{bl}[HCO3]_{bl}^n}{K_{Na} K_{HCO3}^n} \right) \end{gathered}} \quad (135a)$$ $$\phi_1 = exp \left(\frac{-(1-n) F V_m^{M-N(bl)}}{2RT} \right) \quad (135b)$$ $$\phi_2 = exp \left(\frac{(1-n) F V_m^{M-N(bl)}}{2RT} \right) \quad (135c)$$	[34, 55]

Table 22: The corresponding equations describing the flux transported via sodium bicarbonate symporter across the cell membrane

Sodium Bicarbonate Symporter (NBC)	Ref
$$\boxed{J_{NBCe} = g_{nbc}(V_m - E_{nbc})} \quad (136)$$ Where $$E_{nbc} = \frac{RT}{F(n-1)} ln \frac{[Na]_i[HCO3]_i^n}{[Na]_o[HCO3]_o^n} \quad (137)$$	[28, 34]
$$\boxed{J^{M,N(net)}_{NBCn} = [E]_t \frac{(g^M_{ENaHCO_3} Na^M HCO_3^M) g^N_E - (g^N_{ENaHCO_3} Na^N HCO_3^N) g^M_E}{R_M R_{NN} + R_N R_{MM}}} \quad (138a)$$ $$\boxed{J^{M,N(net)}_{Na,NBCn} = J^{M,N(net)}_{NBC}} \quad (138b)$$ $$\boxed{J^{M,N(net)}_{HCO_3,NBCn} = J^{M,N(net)}_{NBC}} \quad (138c)$$ where $[E]_t = [E]_M + [ENa]_M + [ENaHCO_3]_M + [ENaHCO_3]_N + [ENa]_N + [E]_N$ $Na^M = \frac{[A]_M}{K^M_{Na}}, HCO_3^M = \frac{[HCO_3]_M}{K^M_{NaHCO_3}} \mid Na^N = \frac{[Na]_N}{K^N_{Na}}, HCO_3^N = \frac{[HCO_3]_N}{K^N_{NaHCO_3}}$ $R_M = (1 + Na^M + Na^M HCO_3^M) \mid R_N = (1 + Na^N + Na^N HCO_3^N)$ $R_{MM} = (g^M_E + g^M_{ENaHCO_3} Na^M HCO_3^M) \mid R_{NN} = (g^N_E + g^N_{ENaHCO_3} Na^N HCO_3^N)$	[34, 56]
$$\boxed{J_{NBCn} = n''_{NBCn} \frac{k_5^+ k_6^+ [Na^+]_{cell(i)} [HCO3^-]_{cell(i)} - k_5^- k_6^- [Na^+]_e [HCO3^-]_e}{k_5^+ [Na^+]_i [HCO3^-]_i + k_5^- k_6^+ + k_6^- [Na^+]_e [HCO3^-]_e}} \quad (139)$$	[6, 34]

Table 23: The corresponding equations describing the flux transported via sodium bicarbonate symporter across the cell membrane

3.5. Sodium Phosphate Symporter (NaPO4)

Sodium Phosphate Symporter (NaPO4)	Ref
$$\boxed{J^{M,N(net)}_{Na,NaPO_4} = [E]_t\left(\frac{R_{NN}\left(g^M_{ENa}Na^M + g^M_{ENaPO_4}Na^M PO_4^M + g^M_{ENaPO_4Na}Na^M PO_4^M Na''^M\right)}{R_M R_{NN} + R_N R_{MM}} - \frac{R_{MM}\left(g^N_{EA}Na^N + g^N_{ENaPO_4}Na^N PO_4^N + g^N_{ENaPO_4Na}Na^N PO_4^N Na''^N\right)}{R_M R_{NN} + R_N R_{MM}}\right)} \tag{140a}$$ $$\boxed{J^{M,N(net)}_{PO_4,NaPO_4} = [E]_t\left(\frac{R_{NN}\left(g^M_{ENaPO_4}Na^M PO_4^M + g^M_{ENaPO_4Na}Na^M PO_4^M Na''^M\right)}{R_M R_{NN} + R_N R_{MM}} - \frac{R_{MM}\left(g^N_{ENaPO_4}Na^N PO_4^N + g^N_{ENaPO_4Na}Na^N PO_4^N Na''^N\right)}{R_M R_{NN} + R_N R_{MM}}\right)} \tag{140b}$$ where $[E]_t = [E]_M + [ENa]_M + [ENaPO_4]_M + [ENaPO_4Na]_M + [ENaPO_4Na]_N + [ENaPO_4]_N + [ENa]_N + [E]_N$ $Na^M = \frac{[Na]_M}{K^M_{Na}}$, $PO_4^M = \frac{[PO_4]_M}{K^M_{NaPO_4}}$, $Na''^M = \frac{[Na]_M}{K^M_{NaPO_4Na}}$ | $Na^N = \frac{[Na]_N}{K^N_{Na}}$, $PO_4^N = \frac{[PO_4]_N}{K^N_{NaPO_4}}$, $Na''^N = \frac{[Na]_N}{K^N_{NaPO_4Na}}$ $R_M = 1 + Na^M + Na^M PO_4^M + Na^M PO_4^M Na''^M$ | $R_N = 1 + Na^N + Na^N PO_4^N + Na^N PO_4^N Na''^N$ $R_{MM} = g^M_E + g^M_{ENa}Na^M + g^M_{ENaPO_4}Na^M PO_4^M + g^M_{ENaPO_4Na}Na^M PO_4^M Na''^M$ $R_{NN} = g^N_E + g^N_{ENa}Na^N + g^N_{ENaPO_4}Na^N PO_4^N + g^N_{ENaPO_4Na}Na^N PO_4^N Na''^N$	[34, 57]

Table 24: The corresponding equations describing the flux transported via sodium phosphate symporter across the cell membrane

3.6. Sodium Glucose Symporter (SGLT)

Sodium Glucose Symporter (SGLT)	**Ref**
$J_{SGLT}^{M-N(a)} = P_{SGLT}^{M-N(a)} exp\left(\frac{V_m^{M-N(a)}F}{RT}\right) \times \frac{[glucose]_N[Na]_N - [glucose]_M[Na]_M exp\left(-\frac{V_m^{M-N(a)}F}{RT}\right)}{1 - exp\left(-\frac{V_m^{M-N(a)}F}{RT}\right)} \quad (141)$	[58]

Table 25: The corresponding equations describing the flux transported via sodium glucose symporter across the cell membrane

3.7. Amino Acid Transporters

Amino Acid Transporters	**Ref**
$J_{AAT}^{M-N(a)} = P_{AAT}^{M-N(a)} exp\left(\frac{V_m^{M-N(a)}F}{RT}\right) \times \frac{[AminoAcid]_N[Na]_N - [AminoAcid]_M[Na]_M exp\left(-\frac{V_m^{M-N(a)}F}{RT}\right)}{1 - exp\left(-\frac{V_m^{M-N(a)}F}{RT}\right)} \quad (142)$	[58]

Table 26: The corresponding equations describing the flux transported via amino acid salt symporter across the cell membrane

4. Antiporters (Exchangers) model

4.1. Chloride Bicarbonate Antiporter (Cl/HCO3)

Chloride Bicarbonate Antiporter (Cl/HCO3)	**Ref**
$$\boxed{\mathbf{J_{Cl,BCE}} = E_t \frac{[g^M_{EHCO_3} g^N_{ECl} HCO^M_3(Cl^N) - g^N_{EHCO_3} g^M_{ECl} HCO^N_3(Cl^M)]}{R_M R_{00} + R_N R_{ee}}} \quad (143a)$$ $$\boxed{\mathbf{J_{HCO3,BCE}} = E_t \frac{[g^M_{EHCO_3} g^N_{ECl}(Cl^M HCO^N_3) - g^N_{EHCO_3} g^M_{ECl}(Cl^N HCO^M_3)}{R_M R_{00} + R_N R_{ee}}} \quad (143b)$$ where $[E]_t = [E]_M + [EHCO_3]_M + [ECl]_M + [E]_N + [EHCO_3]_N + [ECl]_N$ $HCO^M_3 = \frac{[HCO_3]_M}{K^M_{HCO_3}}, Cl^M = \frac{[Cl]_M}{K^M_{Cl}} \mid HCO^N_3 = \frac{[HCO_3]_N}{K^N_{HCO_3}}, Cl^N = \frac{[Cl]_N}{K^N_{Cl}}$ $R_M = 1 + HCO^M_3 + Cl^M \mid R_N = 1 + HCO^N_3 + Cl^N$ $R_{MM} = g^M_{EHCO_3} HCO^M_3 + g^M_{ECl}\, Cl^M \mid R_{NN} = g^N_{EHCO_3} HCO^N_3 + g^N_{ECl}\, Cl^N$	[34, 59]
$$\boxed{J_{BCE} = P_{BCE} \frac{[Cl]_l[HCO3]_c - [Cl]_c[HCO3]_l}{K_{Cl}K_{HCO3}\left(\frac{(1 + \frac{[Cl]_c}{K_{Cl}} + \frac{[HCO3]_c}{K_{HCO3}})(\frac{[Cl]_l}{K_{Cl}} + \frac{[HCO3]_l}{K_{HCO3}})}{(1 + \frac{[Cl]_l}{K_{Cl}} + \frac{[HCO3]_l}{K_{HCO3}})(\frac{[Cl]_c}{K_{Cl}} + \frac{[HCO3]_c}{K_{HCO3}})}\right)}} \quad (144)$$	[34, 38]
Basolateral $$\boxed{J_{BCE} = n''_{BCE} \frac{k^+_{Cl}k^+_{HCO_3}[Cl]_{M(e)}[HCO3]_{N(i)} - k^-_{Cl}k^-_{HCO_3}[Cl]_{N(i)}[HCO3]_{M(e)}}{k^+_{Cl}[Cl]_{M(e)} + k^+_{HCO_3}[HCO3]_{N(i)} + k^-_{HCO_3}[HCO3]_{M(e)} + k^-_{Cl}[Cl]_{N(i)}}} \quad (145)$$	[6, 60]

Table 27: The corresponding equations describing the flux and current transported via chloride bicarbonate antiporter (exchangers) across the cell membrane

4.2. Sodium Calcium Exchanger (NCX)

Sodium Calcium Exchanger (NCX)	Ref
$\boxed{I_{NCX} = k_{NCX}\left(\dfrac{[Na]_i^{n_{NCX}}[Ca]_o exp\left(\frac{(n_{NCX}-2)rV_mF}{2RT}\right) - [Na]_o^{n_{NCX}}[Ca]_i exp\left(-\frac{(n_{NCX}-2)(1-r)V_mF}{2RT}\right)}{1 + d_{NCX}\left([Na]_o^{n_{NCX}}[Ca]_i + [Na]_i^{n_{NCX}}[Ca]_o\right)}\right)}$ (146)	[15]
$\boxed{I_{NCX} = g_{NCX}\Big(\dfrac{1}{(1 + \left(\frac{K^{Ca}_{NCX,m}}{[Ca]_{i(M)}}\right)^{\eta_{NCX,h}}}\Big) \left(\dfrac{[Na]_i^{n_{NCX}}[Ca]_o exp\left(\frac{(n_{NCX}-2)rV_mF}{2RT}\right) - [Na]_o^{n_{NCX}}[Ca]_i exp\left(-\frac{(n_{NCX}-2)(1-r)V_mF}{2RT}\right)}{1 + d_{NCX}\left([Na]_o^{n_{NCX}}[Ca]_i + [Na]_i^{n_{NCX}}[Ca]_o\right)}\right)}$ (147)	[3, 61]
$\boxed{I_{NCX} = I^{max}_{NCX}\Big(\dfrac{1}{1 + (\frac{K^{Ca}_{m,NCX}}{[Ca]_{i(M)}})^{\eta_{Hill}}}\Big) \left(\dfrac{[Na]^{n_{NCX}}_{i(M)}[Ca]_{N(o)}exp(\frac{rV_mF}{RT}) - [Na]^{n_{NCX}}_{N(o)}[Ca]_{i(M)}exp(-\frac{(1-r)V_mF}{RT})}{\lambda(1 + k_{sat}exp(-\frac{(1-r)V_mF}{RT}))}\right)}$ $\lambda = [Na]_o^{n_{NCX}}[Ca]_i + [Na]_i^{n_{NCX}}[Ca]_o + K_{m,Cao}[Na]_i^{n_{NCX}} + K^{n_{NCX}}_{m,Nai}[Ca]_o(1 + \dfrac{[Ca]_i}{K_{m,Cai}}) + K_{m,Cai}[Na]_o^{n_{NCX}}\left(1 + \dfrac{[Na]_i^{n_{NCX}}}{K_{m,Nai}}\right)^{n_{NCX}}$ (148)	[53, 62]

Table 28: The corresponding equations describing the flux and current transported via sodium calcium exchanger across the cell membrane

4.3. Sodium Hydrogen Exchanger (NHE)

Sodium Hydrogen Exchanger (NHE)	**Ref**
Ammonium competitor $\boxed{\mathbf{J^{NHE}_{Na^+}} = E_t \frac{g^M_{ENa}Na^M(g^N_{EH}H^N + g^N_{ENH4}NH^N_4) - g^N_{ENa}Na^N(g^M_{EH}H^M + g^M_{ENH4}NH^M_4)}{R_M R_{NN} + R_N R_{MM}}}$ (149) $\boxed{\mathbf{J^{NHE}_{H^+}} = E_t \frac{g^M_{EH}H^M(g^N_{ENa}Na^N + g^N_{ENH4}NH^N_4) - g^N_{EH}H^N(g^M_{ENa}Na^M + g^M_{ENH4}NH^M_4)}{R_M R_{NN} + R_N R_{MM}}}$ (150) $\boxed{\mathbf{J^{NHE}_{NH_4{}^+}} = E_t \frac{g^M_{ENH4}NH^M_4(g^N_{ENa}Na^N + g^N_{EH}H^N) - g^N_{ENH4}NH^N_4(g^M_{ENa}Na^M + g^M_{EH}H^M)}{R_M R_{NN} + R_N R_{MM}}}$ (151) where $[E]_t = [E]_M + [ENa]_M + [EH]_M + [ENH_4]_M + [E]_N + [ENa]_N + [EH]_N + [ENH_4]_N$ $Na^M = \frac{[Na]_M}{K^M_{Na}}$, $H^M = \frac{[H]_M}{K^M_H}$, $NH^M_4 = \frac{[NH_4]_M}{K^M_{NH_4}}$ | $Na^N = \frac{[Na]_N}{K^N_{Na}}$, $H^N = \frac{[H]_N}{K^N_H}$, $NH^N_4 = \frac{[NH_4]_N}{K^N_{NH_4}}$ $R_M = 1 + Na^M + H^M + NH^M_4$ | $R_N = 1 + Na^N + H^N + NH^N_4$ $R_{MM} = g^M_{ENa}Na^M + g^M_{EH}\ H^M + g^M_{ENH_4}NH^M_4$ |$R_{NN} = g^N_{ENa}Na^N + g^N_{EH}\ H^N + g^N_{ENH_4}NH^N_4$	[34, 63]
No competitor $\boxed{\mathbf{J^{NHE}_{Na}} = E_t \frac{g^M_{ENa}g^N_{EH}(Na^M H^N) - g^N_{ENa}g^M_{EH}(Na^N H^M)}{R_M R_{NN} + R_N R_{MM}}}$ (152) $\boxed{\mathbf{J^{NHE}_{H}} = E_t \frac{g^M_{EH}g^N_{ENa}(H^M Na^N) - g^N_{EH}g^M_{ENa}(H^N Na^M)}{R_M R_{NN} + R_N R_{MM}}}$ (153)	[64, 65]
$\boxed{J_{NHE} = P_{NHE} \frac{([Na]_{M(bl)}[H]_{N(c)} - [Na]_{N(c)}[H]_{M(bl)})}{K_{Na}K_H\left(\left(1 + \frac{[Na]_{M(bl)}}{K_{Na}} + \frac{[H]_{M(bl)}}{K_H}\right)\left(\frac{[Na]_{N(c)}}{K_{Na}} + \frac{[H]_{N(c)}}{K_H}\right) + \left(1 + \frac{[Na]_{N(c)}}{K_{Na}} + \frac{[H]_{N(c)}}{K_H}\right)\left(\frac{[Na]_{M(bl)}}{K_{Na}} + \frac{[H]_{M(bl)}}{K_H}\right)\right)}}$ (154)	[34, 38]

Table 29: The corresponding equations describing the flux and current transported via sodium hydrogen exchanger across the membrane

Declaration of Competing Interest

There are no conflicts of interest to declare.

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