Development of a cardiac model for the study of sudden cardiac death in infants

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Ventricular hiPSC-CMs model formulation

1 Extracellular and intracellular ionic concentrations

$\mathrm{Na}_o = 151\,\mathrm{mM}$
$\mathrm{Ca}_o = 1.8\,\mathrm{mM}$
$\mathrm{K}_o = 1.8\,\mathrm{mM}$
$\mathrm{Na}_i^0 = 9.991\,\mathrm{mM}$
$\mathrm{K}_i^0 = 150\,\mathrm{mM}$
$\mathrm{Ca}_i^0 = 0.0002\,\mathrm{mM}$
$\mathrm{Ca}_{\mathrm{SR}}^0 = 0.12\,\mathrm{mM}$

2 Cell size and dimensions

$C = 98.7109\,\mathrm{pF}$
$V_c = 8800\,\mu\mathrm{m}^3$
$V_{\mathrm{SR}} = 583.73\,\mu\mathrm{m}^3$

3 Maximum conductances and currents

$\sigma_{\text{Na}} = 3.6712302e3\,\text{S/F}$
$\sigma_{\text{CaL}} = 8.635702e-5\,\text{m}^3/(\text{F}\cdot\text{s})$
$\sigma_{\text{to}} = 29.9038\,\text{S/F}$
$\sigma_{\text{Kr}} = 29.8667\,\text{S/F}$
$\sigma_{\text{Ks}} = 2.041\,\text{S/F}$
$\sigma_{\text{K1}} = 28.1492\,\text{S/F}$
$\sigma_{\text{f}} = 30.10312\,\text{S/F}$
$\sigma_{\text{pCa}} = 0.4125\,\text{A/F}$
$\sigma_{\text{bCa}} = 0.9\,\text{S/F}$
$\sigma_{\text{bCa}} = 0.69264\,\text{S/F}$
$g_{\text{rel}} = 17\,\text{s}^{-1}$
$P_{\text{NaK}} = 1.841424\,\text{A/F}$
$K_{\text{NaCa}} = 1633.33\,\text{A/F}$
$V_{\text{max,up}} = 0.728832\,\text{mM/s}$
$V_{\text{leak}} = 4.4444e-4\,\text{s}^{-1}$

4 Buffers

Sarcoplasmic reticulum

$$\text{Ca}_{\text{SR}_{\text{buf}}} = \frac{1}{1+\frac{\text{B}_{\text{SR}}\cdot K_{\text{buf}_{\text{SR}}}}{(\text{Ca}_{\text{SR}}+K_{\text{buf}_{\text{SR}}})^2}}$$

Cytosol

$$\frac{\partial \text{CaB}_{\text{TnC}}}{\partial t} = \text{k}^{\text{on}}_{\text{TnC}}\text{Ca}_i\cdot(\text{B}^{\text{T}}_{\text{TnC}}-\text{CaB}_{\text{TnC}}) - \text{k}^{\text{off}}_{\text{TnC}}\text{CaB}_{\text{TnC}}$$
$$\frac{\partial \text{CaB}_{\text{CAM}}}{\partial t} = \text{k}^{\text{on}}_{\text{CAM}}\text{Ca}_i\cdot(\text{B}^{\text{T}}_{\text{CAM}}-\text{CaB}_{\text{CAM}}) - \text{k}^{\text{off}}_{\text{CAM}}\text{CaB}_{\text{CAM}}$$
$$\frac{\partial \text{CaB}_{\text{SLH}}}{\partial t} = \text{k}^{\text{on}}_{\text{SLH}}\text{Ca}_i\cdot(\text{B}^{\text{T}}_{\text{SLH}}-\text{CaB}_{\text{SLH}}) - \text{k}^{\text{off}}_{\text{SLH}}\text{CaB}_{\text{SLH}}$$
$$\frac{\partial \text{CaB}_{\text{SR}}}{\partial t} = \text{k}^{\text{on}}_{\text{SR}}\text{Ca}_i\cdot(\text{B}^{\text{T}}_{\text{SR}}-\text{CaB}_{\text{SR}}) - \text{k}^{\text{off}}_{\text{SR}}\text{CaB}_{\text{SR}}$$
$$\frac{\partial \text{CaB}_{\text{Rhod-2}}}{\partial t} = \text{k}^{\text{on}}_{\text{Rhod-2}}\text{Ca}_i\cdot(\text{B}^{\text{T}}_{\text{Rhod-2}}-\text{CaB}_{\text{Rhod-2}}) - \text{k}^{\text{off}}_{\text{Rhod-2}}\text{CaB}_{\text{Rhod-2}}$$

$k^{\text{TnC}}_{\text{on}} = 32.7\,\mu\text{M}^{-1}\text{s}^{-1}$
$k^{\text{TnC}}_{\text{off}} = 19.6\,\text{s}^{-1}$
$B_{\text{TnC}} = 70\,\mu\text{M}$
$k^{\text{CAM}}_{\text{on}} = 35\,\mu\text{M}^{-1}\text{s}^{-1}$
$k^{\text{CAM}}_{\text{off}} = 200\,\text{s}^{-1}$
$B_{\text{CAM}} = 24\,\mu\text{M}$
$k^{\text{SLH}}_{\text{on}} = 100\,\mu\text{M}^{-1}\text{s}^{-1}$
$k^{\text{SLH}}_{\text{off}} = 30\,\text{s}^{-1}$

$B_{\mathrm{SLH}} = 50\,\mu\mathrm{M}$
$k_{\mathrm{on}}^{\mathrm{SR}} = 100\,\mu\mathrm{M}^{-1}\mathrm{s}^{-1}$
$k_{\mathrm{off}}^{\mathrm{SR}} = 60\,\mathrm{s}^{-1}$
$B_{\mathrm{SR}} = 20\,\mu\mathrm{M}$
$k_{\mathrm{on}}^{\mathrm{Rhod\text{-}2}} = 100\,\mu\mathrm{M}^{-1}\mathrm{s}^{-1}$
$k_{\mathrm{off}}^{\mathrm{Rhod\text{-}2}} = 150\,\mathrm{s}^{-1}$
$B_{\mathrm{Rhod\text{-}2}} = 20\,\mu\mathrm{M}$

5 Other constants

$K_{\mathrm{up}} = 0.00025\,\mathrm{mM}$
$K_{\mathrm{pCa}} = 0.0005\,\mathrm{mM}$
$F = 96485.3415\,\mathrm{C/M}$
$R = 8.314472\,\mathrm{J/(M \cdot K)}$
$T = 310\,\mathrm{K}$
$L_0 = 0.025\,\mathrm{dimensionless}$

6 Initial conditions

$h_0 = 0.75\,\mathrm{dimensionless}$
$j_0 = 0.75\,\mathrm{dimensionless}$
$m_0 = 0\,\mathrm{dimensionless}$
$d_0 = 0\,\mathrm{dimensionless}$
$f_{\mathrm{Ca}_0} = 1\,\mathrm{dimensionless}$
$f_{1,0} = 1\,\mathrm{dimensionless}$
$f_{2,0} = 1\,\mathrm{dimensionless}$
$r_0 = 0\,\mathrm{dimensionless}$
$q_0 = 1\,\mathrm{dimensionless}$
$X_{r_1,0} = 0\,\mathrm{dimensionless}$
$X_{r_2,0} = 1\,\mathrm{dimensionless}$
$X_{s_0} = 0\,\mathrm{dimensionless}$
$X_{f_0} = 0.1\,\mathrm{dimensionless}$
$V_0 = -70e - 3\,\mathrm{V}$
$\mathrm{O}_0 = 0\,\mathrm{dimensionless}$
$\mathrm{R}_{1,0} = 0\,\mathrm{dimensionless}$
$\mathrm{R}_{2,0} = 0\,\mathrm{dimensionless}$
$\mathrm{C}_0 = 1\,\mathrm{dimensionless}$

7 Membrane potential

$\frac{dV}{dt} = -\frac{1}{C}\left(I_{\mathrm{Na}} + I_{\mathrm{CaL}} + I_{\mathrm{f}} + I_{\mathrm{Kr}} + I_{\mathrm{Ks}} + I_{\mathrm{to}} + I_{\mathrm{NaCa}} + I_{\mathrm{NaK}} + I_{\mathrm{pCa}} + I_{\mathrm{bNa}} + I_{\mathrm{bCa}} - I_{\mathrm{stim}}\right)$

8 Ionic currents

Na^+ current

$I_{\mathrm{Na}} = \sigma_{\mathrm{Na}} m^3 \cdot h \cdot j \cdot (V - E_{\mathrm{Na}})$

h gate

$$\frac{dh}{dt} = \frac{h_\infty - h}{\tau_h}$$

$$h_\infty = \frac{1}{\sqrt{1 + e^{\frac{V+72.1}{5.7}}}}$$

$$\alpha_h = \begin{cases} 0.057 \cdot e^{-\frac{V+80}{6.8}}, & \text{if } V < -40 \text{ mV} \\ 0, & \text{otherwise} \end{cases}$$

$$\beta_h = \begin{cases} 2.7 \cdot e^{0.079V} + 3.1 \cdot 10^5 \cdot e^{0.3485V}, & \text{if } V < -40 \text{ mV} \\ \frac{0.77}{0.13 \cdot \left(1 + e^{\frac{V+10.66}{-11.1}}\right)}, & \text{otherwise} \end{cases}$$

$$\tau_h = \begin{cases} \frac{1.5}{\alpha_h + \beta_h}, & \text{if } V < -40 \text{ mV} \\ 2.542, & \text{if } V \geq -40 \text{ mV} \end{cases}$$

j gate

$$\frac{dj}{dt} = \frac{j_\infty - j}{\tau_j}$$

$$j_\infty = h_\infty$$

$$\alpha_j = \begin{cases} \frac{(-25428 e^{0.2444V} - 6.948 \cdot 10^{-6} \cdot e^{-0.04391V})(V + 37.78)}{1 + e^{0.311(V+79.23)}}, & \text{if } V < -40 \text{ mV} \\ 0, & \text{otherwise} \end{cases}$$

$$\beta_j = \begin{cases} \frac{0.02424 e^{-0.01052V}}{1 + e^{-0.1378(V+40.14)}}, & \text{if } V < -40 \text{ mV} \\ \frac{0.6 e^{0.057V}}{1 + e^{-0.1(V+32)}}, & \text{otherwise} \end{cases}$$

$$\tau_j = \frac{7}{\alpha_j + \beta_j}$$

m gate

$$\frac{dm}{dt} = \frac{m_\infty - m}{\tau_m}$$

$$m_\infty = \frac{1}{\left(1 + e^{\frac{-34.1-V}{5.9}}\right)^{1/3}}$$

$$\alpha_m = \frac{1}{1 + e^{\frac{-60-V}{5}}}$$

$$\beta_m = \frac{0.1}{1 + e^{\frac{V+35}{5}}} + \frac{0.1}{1 + e^{\frac{V-50}{200}}}$$

$$\tau_m = \alpha_m \cdot \beta_m$$

L-type Ca^{2+} current

$$I_{\mathrm{CaL}} = \sigma_{\mathrm{CaL}} \frac{4VF^2}{RT} \frac{\mathrm{Ca}_i \cdot e^{\frac{2VF}{RT}} - 0.341 \cdot \mathrm{Ca}_o}{e^{\frac{2VF}{RT}} - 1} \cdot d \cdot f_1 \cdot f_2 \cdot f_{\mathrm{Ca}}$$

d gate

$$\frac{dd}{dt} = \frac{d_\infty - d}{\tau_d}$$
$$d_\infty = \frac{1}{1 + e^{-\frac{V+9.1}{7}}}$$
$$\alpha_d = \frac{1}{1 + e^{\frac{-60-V}{5}}}$$
$$\beta_d = \frac{1.4}{1 + e^{\frac{V+5}{5}}}$$
$$\gamma_d = \frac{1}{1 + e^{\frac{50-V}{20}}}$$
$$\tau_d = \alpha_d \cdot \beta_d \cdot \gamma_d$$

f_{Ca} gate

$$\frac{df_{\mathrm{Ca}}}{dt} = C_{f_{\mathrm{Ca}}} \frac{f_{\mathrm{Ca},\infty} - f_{\mathrm{Ca}}}{\tau_{f_{\mathrm{Ca}}}}$$
$$\alpha_{f_{\mathrm{Ca}}} = \frac{1}{1 + \left(\frac{\mathrm{Ca}_i}{0.0006}\right)^8}$$
$$\beta_{f_{\mathrm{Ca}}} = \frac{0.1}{1 + e^{\frac{\mathrm{Ca}_i - 0.0009}{0.0001}}}$$
$$\gamma_{f_{\mathrm{Ca}}} = \frac{0.1}{1 + e^{\frac{\mathrm{Ca}_i - 0.00075}{0.0008}}}$$
$$f_{\mathrm{Ca},\infty} = \frac{\alpha_{f_{\mathrm{Ca}}} + \beta_{f_{\mathrm{Ca}}} + \gamma_{f_{\mathrm{Ca}}}}{1.3156}$$
$$\tau_{f_{\mathrm{Ca}}} = 2\,\mathrm{ms}$$
$$C_{f_{\mathrm{Ca}}} = \begin{cases} 0, & \text{if } (f_{\mathrm{Ca}_\infty} > f_{\mathrm{Ca}}) \text{ and } (V > -60\,\mathrm{mV}) \\ 1, & \text{otherwise} \end{cases}$$

f_1 gate

$$\frac{df_1}{dt} = \frac{f_{1,\infty} - f_1}{\tau_{f_1}}$$
$$f_{1,\infty} = \frac{1}{1 + e^{\frac{V+26}{3}}}$$
$$\tau_{f_1} = \left(1102.5 e^{-\left[\frac{(V+27)^2}{15}\right]^2} + \frac{200}{1 + e^{\frac{13-V}{10}}} + \frac{180}{1 + e^{\frac{V+30}{10}}} + 20\right) \cdot \begin{cases} 1 + 1433 \cdot (\mathrm{Ca}_i - 50 \cdot 10^{-6}), & \frac{df_1}{dt} > 0 \\ 1, & \text{otherwise} \end{cases}$$

f_2 gate

$$\frac{df_2}{dt} = \frac{f_{2,\infty} - f_2}{\tau_{f_2}}$$

$$f_{2,\infty} = \frac{0.67}{1 + e^{\frac{V+35}{4}}} + 0.33$$

$$\tau_{f_2} = \left(600e^{-\frac{(V+25)^2}{170}} + \frac{31}{1 + e^{\frac{25-V}{10}}} + \frac{16}{1 + e^{\frac{V+30}{10}}}\right)$$

Funny current

$$I_{\mathrm{f}} = \sigma_{\mathrm{f}} \cdot X_{\mathrm{f}} \cdot (V - E_{\mathrm{f}})$$

X_f gate

$$\frac{dX_f}{dt} = \frac{X_{f\infty} - X_f}{\tau_{X_f}}$$

$$X_{r_1\infty} = \frac{1}{1 + e^{\frac{V+77.85}{5}}}$$

$$\tau_{X_f} = \frac{1900}{1 + e^{\frac{V+15}{10}}}$$

Transient outward current

$$I_{\mathrm{to}} = \sigma_{\mathrm{to}} \cdot r \cdot q \cdot (V - E_{\mathrm{K}})$$

r gate

$$\frac{dr}{dt} = \frac{r_\infty - r}{\tau_r}$$

$$r_\infty = \frac{1}{1 + e^{\frac{22.3-V}{18.75}}}$$

$$\tau_r = \frac{14.40516}{1.037e^{0.09(V+30.61)} + 0.369e^{-0.12(V+23.84)}} + 2.75352$$

q gate

$$\frac{dq}{dt} = \frac{q_\infty - q}{\tau_q}$$

$$q_\infty = \frac{1}{1 + e^{\frac{V+53}{13}}}$$

$$\tau_q = \frac{39.102}{0.57e^{0.08(V+44)} + 0.065e^{0.1(V+45.93)}} + 6.06$$

Rapid delayed rectifier K$^+$ current

$$I_{\mathrm{K}_r} = \sigma_{\mathrm{K}_r}\sqrt{\frac{K_0}{5.4}} \cdot X_{\mathrm{r}_1} \cdot X_{\mathrm{r}_2} \cdot (V - E_{\mathrm{K}})$$

X_{r_1} gate

$$\frac{dX_{r_1}}{dt} = \frac{X_{r_1\infty} - X_{r_1}}{\tau_{X_{r_1}}}$$

$$X_{r_1\infty} = \frac{1}{1 + e^{\frac{V_{1/2} - V}{4.9}}}$$

$$V_{1/2} = -1000 \cdot \left[\frac{RT}{FQ} \ln \frac{\left(\frac{1+\mathrm{Ca}_o}{2.6}\right)^4}{L_0 \left(1 + \frac{\mathrm{Ca}_o}{0.58}\right)^4} - 0.019 \right]$$

$$\alpha_{X_{r_1}} = \frac{450}{1 + e^{\frac{-45 - V}{10}}}$$

$$\beta_{X_{r_1}} = \frac{6}{1 + e^{\frac{V + 30}{11.5}}}$$

$$\tau_{X_{r_1}} = \alpha_{X_{r_1}} \cdot \beta_{X_{r_1}}$$

X_{r_2} **gate**

$$\frac{dX_{r_2}}{dt} = \frac{X_{r_2\infty} - X_{r_2}}{\tau_{X_{r_2}}}$$

$$X_{r_2\infty} = \frac{1}{1 + e^{\frac{V + 88}{50}}}$$

$$\alpha_{X_{r_2}} = \frac{3}{1 + e^{\frac{-60 - V}{20}}}$$

$$\beta_{X_{r_2}} = \frac{1.12}{1 + e^{\frac{V - 60}{20}}} \tau_{X_{r_2}} = \alpha_{X_{r_1}} \cdot \beta_{X_{r_1}}$$

Slow delayed rectifier K$^+$ current

$$I_{\mathrm{K}_s} = \sigma_{\mathrm{K}_s} \cdot X_s^2 \left[1 + \frac{0.6}{1 + \left(\frac{3.8 \cdot 10^{-5}}{\mathrm{Ca}_i}\right)^2} \right] \cdot (V - E_{\mathrm{K}_s})$$

X_s **gate**

$$\frac{dX_s}{dt} = \frac{X_{s_\infty} - X_s}{\tau_{X_s}}$$

$$X_{s_\infty} = \frac{1}{1 + e^{\frac{-20 - V}{16}}}$$

$$\alpha_{X_s} = \frac{1100}{\sqrt{1 + e^{\frac{-10 - V}{6}}}}$$

$$\beta_{X_s} = \frac{1}{1 + e^{\frac{V - 60}{20}}} \tau_{X_s} = \alpha_{X_s} \cdot \beta_{X_s}$$

Inward rectifier K$^+$ current

$$I_{\mathrm{K}_1} = \sigma_{\mathrm{K}_1} x_{\mathrm{K}_1,\infty} \cdot \sqrt{\frac{K_o}{5.4}} (V - E_{\mathrm{K}})$$

$$X_{K_1\infty} = \frac{\alpha_{K_1}}{\alpha_{K_1} + \beta_{K_1}}$$

$$\alpha_{X_{K_1}} = \frac{3.91}{1 + e^{0.5942(V - E_K - 200)}}$$

$$\beta_{X_{K_1}} = \frac{-1.509 \cdot e^{0.0002(V-E_K+100)} + e^{0.5886(V-E_K-10)}}{1+e^{0.4547(V-E_K)}}$$

$\mathbf{Na^+/Ca^{2+}}$ pump current

$$I_{\mathrm{NaCa}} = K_{\mathrm{NaCa}} \frac{e^{\frac{\gamma \cdot VF}{RT}} \cdot \mathrm{Na}_i^3 \cdot \mathrm{Ca}_o - e^{\frac{(\gamma-1)VF}{RT}} \cdot \mathrm{Na}_o^3 \cdot \mathrm{Ca}_i \cdot \alpha}{(K_{\mathrm{m_{Ca}}} + \mathrm{Ca}_o) \cdot (K_{\mathrm{m_{Na}}}^3 + \mathrm{Na}_o^3) \cdot \left(1 + K_{\mathrm{sat}} e^{\frac{(\gamma-1)VF}{RT}}\right)}$$

$\mathbf{Na^+/K^+}$ pump current

$$I_{\mathrm{NaK}} = \frac{\frac{\mathrm{Na}_i \cdot P_{\mathrm{NaK}} \cdot \mathrm{K}_o}{\mathrm{K}_o + \mathrm{K_{mk}}}}{(\mathrm{Na}_i + \mathrm{K_{mNa}}) \cdot \left(1 + 0.1245 e^{\frac{-0.1VF}{RT}} + 0.0353 e^{\frac{-VF}{RT}}\right)}$$

9 $\mathbf{Ca^{2+}}$ dynamics

$$\frac{d\mathrm{Ca}_i}{dt} = \left(j_{\mathrm{leak}} - j_{\mathrm{up}} + j_{\mathrm{rel}} - \frac{I_{\mathrm{CaL}} - 2I_{\mathrm{NaCa}} + I_{\mathrm{pCa}} + I_{\mathrm{bCa}}}{2FV_c}\right) - \sum_j \frac{\partial \mathrm{CaB}_j}{\partial t}$$
$$\frac{d\mathrm{Ca_{SR}}}{dt} = \mathrm{Ca_{SR_{buf}}} \frac{V_c}{V_{\mathrm{SR}}} (j_{\mathrm{up}} - j_{\mathrm{leak}} - j_{\mathrm{rel}})$$
$$j_{\mathrm{up}} = V_{\mathrm{max,up}} \frac{1}{1 + \frac{K_{\mathrm{up}}^2}{\mathrm{Ca}_i^2}}$$
$$j_{\mathrm{leak}} = V_{\mathrm{leak}} \cdot (\mathrm{Ca_{SR}} - \mathrm{Ca}_i)$$
$$j_{\mathrm{rel}} = g_{\mathrm{rel}} \cdot \mathrm{O} \cdot (\mathrm{Ca_{SR}} - \mathrm{Ca}_i)$$

9.1 RyR scheme

$$\frac{d\mathrm{O}}{dt} = k_{\mathrm{co}}\mathrm{C} + k_{\mathrm{io}}\mathrm{R}_1 - (k_{\mathrm{oc}}O + k_{oi}O)$$
$$\frac{d\mathrm{C}}{dt} = k_{\mathrm{oc}}\mathrm{O} + k_{\mathrm{ic}}\mathrm{R}_2 - (k_{\mathrm{co}}C + k_{ci}C)$$
$$\frac{d\mathrm{R}_2}{dt} = k_{\mathrm{ci}}\mathrm{C} + k_{\mathrm{i_1i_2}}\mathrm{R}_1 - (k_{\mathrm{ic}}\mathrm{R}_1 + k_{\mathrm{i_2i_1}}\mathrm{R}_1)$$
$$\frac{d\mathrm{R}_1}{dt} = k_{\mathrm{ci}}\mathrm{C} + k_{\mathrm{i_1i_2}}\mathrm{R}_1 - (k_{\mathrm{ic}}\mathrm{R}_1 + k_{\mathrm{i_2i_1}}\mathrm{R}_1)$$
$$k_{\mathrm{Ca}_{SR}} = \frac{1 + (150\,\mu\mathrm{M}/\mathrm{Ca_{SR}})^{30}}{1 + (\mathrm{Ca_{SR}}/300\,\mu\mathrm{M})^5}$$
$$k_{\mathrm{co}} = k_{\mathrm{a}} \cdot \frac{(\mathrm{Ca}_i/\mathrm{Ca}_i^*)^3}{1 + (\mathrm{Ca}_i/\mathrm{Ca}_i^*)^3} \cdot \frac{1}{k_{\mathrm{Ca}_{SR}}}$$
$$f_2 = 1 + \left(\frac{200\,\mu\mathrm{M}}{\mathrm{Ca_{SR}}}\right)^2$$
$$k_{\mathrm{ci}} = 10^{-4} \cdot \mathrm{Ca}_i \cdot f_2$$

$k_{\mathrm{a}} = 3\,\mathrm{S/F}$
$\mathrm{Ca}_i^* = 1\,\mu\mathrm{M}$
$k_{\mathrm{oc}} = k_{i1i2} = 0.01\,\mathrm{ms}^{-1}$
$k_{\mathrm{1d}} = 2\,\mathrm{mM}$
$k_{\mathrm{ic}} = k_{\mathrm{io}}$
$k_{\mathrm{ci}} = k_{\mathrm{oi}}$

Ca^{2+} pump current

$I_{\mathrm{pCa}} = \sigma_{\mathrm{pCa}} \frac{\mathrm{Ca}_i}{\mathrm{Ca}_i + K_{\mathrm{pCa}}}$

10 Na^+ dynamics

$$\frac{d\mathrm{Na}}{dt} = -C\,\frac{I_{\mathrm{Na}} + I_{\mathrm{bNa}} + 3I_{\mathrm{NaK}} + 3I_{\mathrm{NaCa}}}{FV_c}$$

Background currents

$I_{\mathrm{bNa}} = \sigma_{\mathrm{bNa}} \cdot (V - E_{\mathrm{Na}})$
$I_{\mathrm{bCa}} = \sigma_{\mathrm{bCa}} \cdot (V - E_{\mathrm{Ca}})$

11 Reversal potentials

$$E_{\mathrm{Na}} = \frac{RT}{F} \ln \frac{\mathrm{Na}_o}{\mathrm{Na}_i}$$
$$E_{\mathrm{K}} = \frac{RT}{F} \ln \frac{\mathrm{K}_o}{\mathrm{K}_i}$$
$$E_{\mathrm{K}_s} = \frac{RT}{F} \ln \frac{\mathrm{K}_o + P_{K,Na} \cdot \mathrm{Na}_o}{\mathrm{K}_i + P_{K,Na} \cdot \mathrm{Na}_i}$$
$$E_{\mathrm{Ca}} = \frac{RT}{2F} \ln \frac{\mathrm{Ca}_o}{\mathrm{Ca}_i}$$
$E_{\mathrm{f}} = -17\,\mathrm{mV}$