Noble et al. 1998 Single Cell Model

(a) Time-dependent (delayed) K+ Current i_{Kr1}

Rapidly activating and fast deactivating component of the delayed rectifier current based on data of Heath and Terrar.

Equations:

$i_{\mathrm{Kr1}} = Xr1\ Gkr1\ \{(\mathrm{E} - \mathrm{E_K})/(1+\exp((\mathrm{E} + 9)/22.4))\}$
$\mathrm{d}xr1/\mathrm{d}t = \alpha_{xr1} - (\alpha_{xr1} + \beta_{xr1})\ xr1$
$E_0 = E - 5$
$\alpha_{xr1} = 50 / \{1 + \exp(-E_0/9)\}$
$E_0 = E - 20$
$\beta_{xr1} = 0.05 \exp(-E_0/15)$

Parameters:

$Gkr1 = 0.0021$
$xr1 = 0.01428$ (initial)

(b) Time-dependent (delayed) K+ Current i_{Kr2}

Rapidly activating and very slow deactivating component of the delayed rectifier current based on data of Heath and Terrar.

Equations:

$i_{\mathrm{Kr2}} = Xr2\ Gkr2\ \{(\mathrm{E} - \mathrm{E_K})/(1+\exp((\mathrm{E} + 9)/22.4))\}$
$\mathrm{d}xr2/\mathrm{d}t = \alpha_{xr2} - (\alpha_{xr2} + \beta_{xr2})\ xr2$
$E_0 = E - 5$
$\alpha_{xr2} = 50 / \{1 + \exp(-E_0/9)\}$
$E_0 = E + 30$
$\beta_{xr2} = 0.4 \exp\{-(E_0/30)^3\}$

Parameters:

$Gkr2 = 0.0013$
$xr2 = 0.5$ (initial)

(c) Time-dependent (delayed) K+ Current i_{Ks}

Slowly activating but rapidly deactivating component of the delayed rectifier current.

Equations:

$i_{\mathrm{Ks}} = Xs^2\ Gks\ \{\mathrm{E} - \mathrm{E_{Ks}}\}$

$E_{ks} = (RT/F) \ln\{([K]_o + PKNa[Na]_o)/([K]_i + PKNa[Na]_i)\}$

$dxs/dt = \alpha_{xs} - (\alpha_{xs} + \beta_{xs})\, xs$

$E_0 = E - 40$

$\alpha_{xs} = 14 / \{1 + \exp(-E_0/9)\}$

$E_0 = E$

$\beta_{xs} = \exp\{-E_0/45\}$

Parameters:

$Gks = 0.0026$
$xs = 0.5$ (initial)
PKNa = 0.03

(d) Time-independent (background) K+ current i_{k1} (Inward Rectifier Potassium Current)

(Inherits from DiFrancescoNoble)

Equations:

$i_{K1} = g_{K1}\ \{[K]_c/([K]_c + K_{m,K1})\}\{(E - E_K)/(1 + \exp((E - E_K - 10)\ 1.25F/RT))\}$

Parameters:

$g_{K1} = 0.5$
$K_{m,K1} = 10$

(e) The transient outward current i_{to}

(Inherits from HilgemannNobleSingle)

Equations:

i_{to} = gto*(gtos+s*(1-gtos))*r*(E-EK)

$E_0 = E + 4$

dr/dt = 333*((1/(1+exp(-E_0/steepq)))-r)

$ds/dt = \alpha_s - (\alpha_s + \beta_s)\, s$

$\alpha_s = 0.033 \exp\{-E/17\}$

$\beta_s = 33/\{1 + \exp[-0.125\ (E + 10)]\}$

Parameters:

gto = 0.005
gtos = 0
steepq = 5
r = 0 (initial)
$s = 0.99505$ (initial)

(f) Background sodium current i_{bNa}

(Inherits from DiFrancescoNoble)

Equations:

$i_{b,\,Na} = g_{b,\,Na}\,(E - E_{Na})$

Parameter:
$g_{b,\,Na} = 0.0006$

(g) Na-K exchange pump current i_p

(Inherits from DiFrancescoNoble)

Equations:

$i_p = \hat{\imath}_p\ \{[K]_c / ([K]_c + K_{m,\,K})\}\{[Na]_i / ([Na]_i + K_{m,\,Na})\}$

Parameters:

$\hat{\imath}_p = 0.7$
$K_{m,\,K} = 1$
$K_{m,\,Na} = 40$

(h) Na-Ca exchange current i_{NaCa}

Equations:

$$i_{NaCa,Cyt} = \{(1\text{-INaCaFract})\ k_{NaCa}\ \{\exp[2\gamma(n_{NaCa} - 2)EF/(2RT)][Na]_i^{\,n_{NaCa}}[Ca]_o - \exp[-2(1-\gamma)(n_{NaCa} - 2)EF/(2RT)][Na]_o^{\,n_{NaCa}}[Ca]_i\} / \{1 + d_{NaCa}([Na]_o^{\,n_{NaCa}}[Ca]_i + [Na]_i^{\,n_{NaCa}}[Ca]_o)\}\} / (1 + [Ca]_i / 0.0069)$$

$$i_{NaCa,DS} = \{\text{INaCaFract}\ k_{NaCa}\ \{\exp[2\gamma(n_{NaCa} - 2)EF/(2RT)][Na]_i^{\,n_{NaCa}}[Ca]_o - \exp[-2(1-\gamma)(n_{NaCa} - 2)EF/(2RT)][Na]_o^{\,n_{NaCa}}[Ca]_{ds}\} / \{1 + d_{NaCa}([Na]_o^{\,n_{NaCa}}[Ca]_i + [Na]_i^{\,n_{NaCa}}[Ca]_o)\}\} / (1 + [Ca]_{ds} / 0.0069)$$

Parameters:

$d_{NaCa} = 0.0$
$n_{NaCa} = 3$
$k_{NaCa} = 0.0005$
$\gamma = 0.5$
INaCaFract = 0.001

(i) Background Calcium current i_{bCa}

(Inherits from DiFrancescoNoble)

Equation:

$i_{b, Ca} = g_{b, Ca} (E - E_{Ca})$

Parameter:

$g_{b, Ca} = 0.00025$

(j) Fast sodium current i_{Na}

(Inherits from DiFrancescoNoble)

Equations:

$i_{Na} = m^3 h\, g_{Na} (E - E_{mh})$

$E_{mh} = (RT/F) \ln\{([Na]_o + 0.12[K]_c)/([Na]_i + 0.12[K]_i)\}$
$dm/dt = \alpha_m - (\alpha_m + \beta_m)\, m$
$dh/dt = \alpha_h - (\alpha_h + \beta_h)\, h$
$E_0 = E + 41$
$\alpha_m = 200\, E_0 / \{1 - \exp(-0.1\, E_0)\}$
$\alpha_m |_{|E0| < 0.00001} = 2000$
$\beta_m = 8000 \exp[-0.056(E + 66)]\}$
$\alpha_h = 20 \exp[-0.125(E + 75)]\}$
$\beta_h = 2000 / \{1 + 320\exp[-0.1(E + 75)]\}$

Parameter:

$g_{Na} = 2.5$
$h = 0.9939474$ (initial)
$m = 0.0017$ (initial)

(k) The L-Type Calcium current i_{CaL}

Equations:

$i_{CaL, Cyt} = (1\text{-ICaFract}) dff_2 (i_{CaL, Ca} + i_{CaL, K} + i_{CaL, Na})$
$i_{CaL, DS} = \text{ICaFract}\ dff_{2DS} (i_{CaL, Ca} + i_{CaL, K} + i_{CaL, Na})$

$i_{CaL, Ca} = 4P_{Ca} (E - V_{surf}) (F/RT) / \{1 - \exp[-(E - V_{surf})2F/RT]\}$
$\times \{[Ca]_i \exp(V_{surf}\, 2F/RT) - [Ca]_o \exp(-2(E - 50)\, F/RT)\}$
$i_{CaL, K} = 0.002P_{Ca} (E - V_{surf}) (F/RT) / \{1 - \exp[-(E - V_{surf})F/RT]\}$
$\times \{[K]_i \exp(V_{surf}\, F/RT) - [K]_c \exp(-(E - V_{surf})\, F/RT)\}$
$i_{CaL, Na} = 0.01P_{Ca} (E - V_{surf}) (F/RT) / \{1 - \exp[-(E - V_{surf})F/RT]\}$

$\times \{[Na]_i \exp(V_{surf} F/RT) - [Na]_c \exp(-(E - V_{surf}) F/RT) \}$

$dd/dt = \alpha_d - (\alpha_d + \beta_d) d$
$df/dt = \alpha_f - (\alpha_f + \beta_f) f$

$E_0 = E + 24 - V_{shift}$
$\alpha_d = 30 E_0 / \{1 - \exp(-0.25 E_0)\}$
$\alpha_d |_{|E0| < 0.0001} = 120$
$\alpha_d = 3.0 * \alpha_d$
$\beta_d = -12 E_0 / \{ 1 - \exp(0.1 E_0)\}$
$\beta_d |_{|E0| < 0.0001} = 120$
$\beta_d = 3.0 * \beta_d$

$E_0 = E + 34$
$\alpha_f = 6.25 E_0 / \{\exp(0.25 E_0)-1\}$
$\alpha_f |_{|E0| < 0.0001} = 25$
$\alpha_f = 0.3 * \alpha_f$
$\beta_f = 12 / \{ 1 + \exp[-0.25(E_0)]\}$
$\beta_f = 0.3 * \beta_f$

$df_2/dt = \{1 - ([Ca]_i/(KmCytInact+[Ca]_i)) - f_2)$
$df_{2DS}/dt = RateDSInact\{1 - ([Ca]_{ds}/(KmDSInact+[Ca]_{ds})) - f_{2DS} \}$

Parameters:
$V_{shift} = 5$

$P_{Ca} = 0.1$
$V_{surf} = 50$
$d = 0.0$ (initial)
$f = 1.0$ (initial)
$f_2 = 1.0$ (initial)
$f_{2DS} = 0.9682754$ (initial)

KmCytInact = 100000
KmDSInact = 0.001
RateDSInact = 20
ICaFract = 1.0

(I) Persistent Sodium current i_{pNa}

Equation:

$i_{p, Na} = g_{p, Na} (1/(1+\exp(-(E+52)/8))) (E - E_{Na})$

Parameter:

$g_{p, Na} = 0.004$

(m) Intracellular sodium concentration

Equations:

$d[Na]_i/dt = -\{i_{Na} + i_{p,\,Na} + i_{b,\,Na} + i_{CaL,\,Na} + (n_{NaK}/(n_{NaK} - 1))i_p + (n_{NaCa}/(n_{NaCa} - 2))i_{NaCa}\}/V_iF$

Parameters:

$n_{NaCa} = 3$

$n_{NaK} = 1.5$

$[Na]_i = 5.5997$ (initial)

(n) Intracellular calcium concentration

(Inherits itr and iup from HilgemannNoble)

Equations:

i_{up} = FractionUptakeCalciumSites*α_{up} - FractionBackSRSites*β_{up}

FractionUptakeCalciumSites = $[Ca]_i$/K2

FractionBackSRSites = $[Ca]_{up}$*K1/K2

K1 = Kcyca*Kxcs/Ksrca;

K2 = $[Ca]_i$+($[Ca]_{up}$*K1)+Kcyca*Kxcs+Kcyca

$i_{tr} = \alpha_{tr}([Ca]_{up} - [Ca]_{rel})$

i_{rel} = (OpenReleaseChannelFraction*KmRelease+LeakRate)*$[Ca]_{rel}$

PrecursorFraction = 1 - ActivatorFraction - ProductFraction

RegulatoryBindingSite = $[Ca]_i$/($[Ca]_i$+KmCaCyt)

RegulatoryBindingSite = RegulatoryBindingSite + (1-RegulatoryBindingSite)($[Ca]_{ds}$/($[Ca]_{ds}$+KmCaDS))

RegulatoryBindingSite = RegulatoryBindingSite^2

ActivationRate = 500.0*RegulatoryBindingSite

InactivationRate = 60.0+(500.0*RegulatoryBindingSite)

dActivatorFraction/dt = (PrecursorFraction*ActivationRate) -(ActivatorFraction*InactivationRate)

dProductFraction/dt = (ActivatorFraction*InactivationRate)-(1.0*ProductFraction)

If E < -50 then dActivatorFraction/dt = 5*dActivatorFraction/dt

If E < -50 then dProductFraction/dt = 5*dProductFraction/dt

OpenReleaseChannelFraction = (ActivatorFraction/(ActivatorFraction+0.25))^2

$d[Ca]_{up}/dt = i_{up}*V_i/V_{up} - i_{tr}$

$d[Ca]_{rel}/dt = i_{tr}*V_{up}/V_{rel} - i_{rel}$

$d[Ca]_i/dt = -\{i_{CaL,\,Ca,\,Cyt} + i_{b,\,Ca} - (2/(n_{NaCa} - 2))i_{NaCa,\,Cyt}\}/2V_iF - i_{up}$

$+ i_{rel} * V_{rel}/V_i$
$-$ d[Ca-Calmodulin]/dt - d[Ca-Troponin]/dt - d[Ca-Indicator]/dt
$+ [Ca]_{ds}$.volds.kdecay

$$d[Ca]_{ds}/dt = -\{ i_{CaL, Ca, DS} \} / 2\text{volds} V_i F - [Ca]_{ds}.\text{kdecay}$$

d[Ca-Calmodulin]/dt = (Calmodulin - [Ca-Calmodulin])* $[Ca]_i$ *αCalmodulin
- [Ca-Calmodulin]*βCalmodulin

d[Ca-Troponin]/dt = (Troponin - [Ca-Troponin])* $[Ca]_i$ *αTroponin
- [Ca-Troponin]*βTroponin

d[Ca-Indicator]/dt = (Indicator - [Ca-Indicator])* $[Ca]_i$ *αIndicator
- [Ca-Indicator]*βIndicator

Parameters:

Kcyca = 0.0003
Kxcs = 0.4
Ksrca = 0.5
α_{up} = 0.4
β_{up} = 0.03
α_{tr} = 50.0

$[Ca]_{up}$ = 0.2872393 (initial)
$[Ca]_{rel}$ = 0.2846761 (initial)
$[Ca]_i$ = 0.0000082 (initial)
$[Ca]_o$ = 2.0
$[Ca]_{ds}$ = 0.0000171 (initial)

KmCaCyt = 0.0005
KmCaDS = 0.01
volds = 0.1
kdecay = 10
KmRel = 250.0

α_{act} = 600.0
β_{act} = 500.0
ActivatorFraction = 0.00191 (initial)
α_{prod} = 60.0
β_{prod} = 500.0
ProductFraction = 0.28546 (initial)

LeakRate = 0.05

SRFract = 0.0

Troponin = 0.05

[Ca-Troponin] = 0.0002 (initial)
αTroponin = 100000
βTroponin = 200

Calmodulin = 0.02
[Ca-Calmodulin] = 0.0003 (initial)
αCalmodulin = 100000
βCalmodulin = 50

Indicator (Fura) = 0.0
[Ca-Indicator] = 0.0 (initial)
αIndicator = 100000
βIndicator = 84

(o) Extracellular potassium concentration

Equations:

$$d[K]_o / dt = \{i_K + i_{K1} + i_{CaL,K} - (1/(n_{NaK} - 1))i_p + i_{to}\} / VF - 0.7*([K]_o - [K]_b)$$

Parameters:
n_{NaK} = 1.5
$[K]_o$ = 4.0 (initial)
$[K]_b$ = 4.0 (initial)

(p) Intracellular potassium concentration

Equations:

$$d[K]_i / dt = -\{i_K + i_{K1} + i_{CaL,K} - (1/(n_{NaK} - 1))i_p + i_{to}\} / V_i F$$

Parameters:
n_{NaK} = 1.5
$[K]_i$ = 139.3050 (initial)

Model Cell Parameters

Temperature = 37 ^{o}C

Capacitance = 0.000095 μF
Preplength = 74 μm
Radius = 12 μm
Cell Volume = 3.14.preplength.radius^2
Cytosolic Volume = 0.49.Cell Volume
SR Uptake Volume = 0.01.Cell Volume

SR Release Volume = 0.1.Cell Volume
Diadic Space Volume = 0.1.Cytosolic Volume
Extracellular Volume = 0.4.Cell Volume

Initial Membrane Potential = -92.4993529 mV

Stimulus Current = -3.0 nA
On at 0.06 s
Off at 0.0625 s