Supplementary Information

Analysis of Circulating Waves in Tissue Rings derived from Human Induced Pluripotent Stem Cells

Model Equations

The model we used refers to classic Priebe & Beuckelmann membrane model[1] and modified PB model by Bernus et al[2] and Hyperpolarization-activated current model by Verkerk et al[3].

Equilibrium Potentials:

$$E_{Na} = \frac{RT}{F} \ln\left(\frac{[Na^+]_e}{[Na^+]_i}\right) \quad (S\text{-}1)$$

$$E_{Ca} = \frac{RT}{2F} \ln\left(\frac{[Ca^{2+}]_e}{[Ca^{2+}]_i}\right) \quad (S\text{-}2)$$

$$E_{to} = \frac{RT}{F} \ln\left(\frac{0.043 \times [Na^+]_e + [K^+]_e}{0.043 \times [Na^+]_i + [K^+]_i}\right) \quad (S\text{-}3)$$

$$E_K = \frac{RT}{F} \ln\left(\frac{[K^+]_e}{[K^+]_i}\right) \quad (S\text{-}4)$$

Na^+ current:

$$I_{Na} = g_{Na} \times m^3 \times v^2 \times (V_m - E_{Na}) \quad (S\text{-}5)$$

$$\alpha_m = \frac{[0.32 \times (V_m + 47.13)]}{1 - \exp^{[-0.1 \times (V_m + 47.13)]}} \quad (S\text{-}6)$$

$$\beta_m = 0.08 \times \exp^{\frac{-V_m}{11}} \quad (S\text{-}7)$$

$$\frac{dm}{dt} = (1 - m) \times \alpha_m - m \times \beta_m \quad (S\text{-}8)$$

$$v_\infty = 0.5 \times [1 - \tanh(7.74 + 0.12 \times V_m)] \quad (S\text{-}9)$$

$$\tau_v = 0.25 + 2.24 \times \frac{1 - \tanh(7.74 + 0.12 \times V_m)}{1 - \tanh[0.07 \times (V_m + 92.4)]} \quad (S\text{-}10)$$

$$\frac{dv}{dt} = \frac{v_\infty(V_m) - v}{\tau_v(V_m)} \quad (S\text{-}11)$$

Ca^{2+} current:

$$I_{Ca} = g_{Ca} \times d_\infty \times f \times f_{Ca} \times (V_m - E_{Ca}) \quad (S\text{-}12)$$

$$d_\infty = \frac{\alpha_d}{\alpha_d + \beta_d} \quad (S\text{-}13)$$

$$\alpha_d = \frac{14.98 \times \exp^{\{-0.5 \times [\frac{(V_m - 22.36)}{16.68}]^2\}}}{16.68 \times \sqrt{2\pi}} \quad \text{(S-14)}$$

$$\beta_d = \frac{0.1471 - 5.3 \times \exp^{\{-0.5 \times [\frac{(V_m - 6.2)}{14.93}]^2\}}}{14.93 \times \sqrt{2\pi}} \quad \text{(S-15)}$$

$$\alpha_f = \frac{0.00687}{1 + \exp^{-\frac{(6.1546 - V_m)}{6.12}}} \quad \text{(S-16)}$$

$$\beta_f = \frac{0.069 \times \exp^{[-0.11 \times (V_m + 9.825)]} + 0.011}{1 + \exp^{[-0.278 \times (V_m + 9.825)]}} + 0.000575 \quad \text{(S-17)}$$

$$\frac{df}{dt} = (1 - f) \times \alpha_f - f \times \beta_f \quad \text{(S-18)}$$

$$f_{Ca} = \frac{1}{1 + \frac{[Ca^{2+}]_i}{0.0006}} \quad \text{(S-19)}$$

Transient outward current:

$$I_{to} = g_{to} \times r_\infty \times t_o \times (V_m - E_{to}) \quad \text{(S-20)}$$

$$r_\infty = \frac{\alpha_r}{\alpha_r + \beta_r} \quad \text{(S-21)}$$

$$\alpha_r = \frac{0.5266 \times \exp^{[-0.0166 \times (V_m - 42.2912)]}}{1 + \exp^{[-0.0943 \times (V_m - 42.2912)]}} \quad \text{(S-22)}$$

$$\beta_r = \frac{0.00005186 \times V_m + 0.5149 \times \exp^{[-0.1344 \times (V_m - 5.0027)]}}{1 + \exp^{[-0.1348 \times (V_m - 0.00005186)]}} \quad \text{(S-23)}$$

$$\alpha_{to} = \frac{0.00005612 \times V_m + 0.0721 \times \exp^{[-0.173 \times (V_m + 34.2531)]}}{1 + \exp^{[-0.1732 \times (V_m + 34.2531)]}} \quad \text{(S-24)}$$

$$\beta_{to} = \frac{0.0001215 \times V_m + 0.0767 \times \exp^{[-1.66 \times 10^{-9} \times (V_m + 34.0235)]}}{1 + \exp^{[-0.1604 \times (V_m + 34.0235)]}} \quad \text{(S-25)}$$

$$\frac{dt_o}{dt} = (1 - t_o) \times \alpha_{t_o} - t_o \times \beta_{t_o} \quad \text{(S-26)}$$

$$\tau_{t_o}(V_m) = \frac{1}{P \times \alpha_{t_o}(V_m) + P \times \beta_{t_o}(V_m)} \quad \text{(S-27)}$$

$$t_{o\infty}(V_m) = \frac{\alpha_{t_o} \times (V_m - V_{shift})}{\alpha_{t_o}(V_m - V_{shift}) + \beta_{t_o}(V_m - V_{shift})} \quad \text{(S-28)}$$

$$\frac{dt_o}{dt} = \frac{t_{o\infty} - t_o}{\tau_{t_o}} \quad \text{(S-29)}$$

Delayed rectifier K^+ current:

$$I_K = g_K \times X^2 \times (V_m - E_K) \quad \text{(S-30)}$$

$$X_{\infty} = \frac{0.972}{1+\exp^{-(2.036+0.0834\times V_m)}} \tag{S-31}$$

$$\tau_X = 380 \times \exp^{-\frac{(V_m+25.5)^2}{156}} + 166 \times [1 + \tanh(0.558 + 0.0169 \times V_m)] \tag{S-32}$$

$$\frac{dX}{dt} = \frac{X_{\infty}-X}{\tau_X} \tag{S-33}$$

Inward rectifier K^+ current:

$$I_{K_1} = g_{K_1} \times K_{1_{\infty}} \times (V_m - E_K) \tag{S-34}$$

$$K_{1_{\infty}} = \frac{\alpha_{K_1}}{\alpha_{K_1}+\beta_{K_1}} \tag{S-35}$$

$$\alpha_{K_1} = \frac{0.1}{1+\exp^{[0.06\times(V_m-E_K-200)]}} \tag{S-36}$$

$$\beta_{K_1} = \frac{3\times\exp^{0.0002\times(V_m-E_K+100)}+\exp^{0.1\times(V_m-E_K-10)}}{1+\exp^{-0.5\times(V_m-E_K)}} \tag{S-37}$$

Background current:

$$I_{Ca,b} = g_{Ca,b} \times (V_m - E_{Ca}) \tag{S-38}$$

$$I_{Na,b} = g_{Na,b} \times (V_m - E_{Na}) \tag{S-39}$$

Na^+-K^+ pump:

$$I_{NaK} = g_{NaK} \times f_{NaK} \times f'_{NaK} \tag{S-40}$$

$$f_{NaK} = \frac{1}{1+0.1245\times\exp^{-0.0037\times V_m}+0.0365\times\sigma\times\exp^{-0.037\times V_m}} \tag{S-41}$$

$$f'_{NaK} = \frac{1}{1+(\frac{10}{[Na^+]_i})^{1.5}} \times \frac{[K^+]_e}{[K^+]_e+1.5} \tag{S-42}$$

$$\sigma = 0.1428 \times (\exp^{\frac{[Na^+]_e}{67.3}} - 1) \tag{S-43}$$

Na^+/Ca^{2+} exchanger:

$$I_{NaCa} = g_{NaCa} \times f_{NaCa} \tag{S-44}$$

$$f_{NaCa} = \frac{[Na^+]_i^3\times[Ca^{2+}]_e\times\exp^{0.013\times V_m}-[Na^+]_e^3\times[Ca^{2+}]_i\times\exp^{-0.024\times V_m}}{(669921+[Na^+]_e^3)\times(1.38+[Ca^{2+}]_e)\times(1+0.1\times\exp^{-0.024\times V_m})} \tag{S-45}$$

Hyperpolarization-activated current:

$$I_f = y \times g_f \times (V_m - E_f) \tag{S-46}$$

$$\frac{dy}{dt} = \frac{y_\infty - y}{\tau_y} \quad \text{(S-47)}$$

$$\tau_y = \frac{1000}{0.36 \times \frac{(V_m+148.8)}{\exp^{0.066\times(V_m+148.8)}-1} + 0.1 \times \frac{(V_m+87.3)}{1-\exp^{-0.21\times(V_m+87.3)}}} - 54 \quad \text{(S-48)}$$

if $V_m < -80mV$:

$$y_\infty = \frac{0.99921}{1+\exp^{\frac{V_m+97.134}{8.1752}}} + 0.01329 \quad \text{(S-49)}$$

if $V_m \geq -80mV$:

$$y_\infty = \exp^{-\frac{V_m}{12.861}} \times 0.0002501 \quad \text{(S-50)}$$

Concentration of major ions in and out of the cell membrane (units: mM)

$[Ca^{2+}]_i$	$[Ca^{2+}]_e$	$[Na^+]_i$	$[Na^+]_e$	$[K^+]_i$	$[K^+]_e$
0.0004	2	10	138	140	4

Other parameters:

$R = 8.314J/K$; $T = 273 + 37(K)$; $F = 96.5/mmol$; $P = \frac{1}{1.7}$; $V_{shift} = -4mV$; $E_f = -22mV$

References

1. Priebe, L. & Beuckelmann, D. J. Simulation study of cellular electric properties in heart failure. *Circ Res* **82**, 1206–1223 (1998).
2. Bernus, O., Wilders, R., Zemlin, C. W., Verschelde, H. & Panfilov, A. V. A computationally efficient electrophysiological model of human ventricular cells. *Am. J. Physiol. - Hear. Circ. Physiol.* (2002). doi:10.1152/ajpheart.00731.2001
3. Verkerk, A. O., Van Borren, M. M. G. J. & Wilders, R. Calcium transient and sodium-calcium exchange current in human versus rabbit sinoatrial node pacemaker cells. *Sci. World J.* **2013**, (2013).