Extended Methods

The Luo-Rudy (LRd) model of the cardiac ventricular action potential[1] was used to investigate the pacemaking mechanism in BP cells. The following protocol was simulated: After 10 minutes at rest (to achieve steady-state), I_{K1} suppression (81% and 100%) was simulated by adjusting the channel conductance. Simulated transmembrane currents were observed during initial transitory oscillations of membrane potential, V_m, and during the stable oscillatory steady-state. Pacemaker cycle-length (CL) was computed as the interval between peaks of neighboring APs. Calcium transients were generated by the calcium-induced calcium-release (CICR) process, where calcium entry starting at the AP upstroke $(dV_m/dt)_{max}$ provided the trigger for Ca^{2+} release from the sarcoplasmic reticulum (SR). The effects of βAS were simulated based on experimental observations[2]. They include: shifting I_{Na} fast inactivation in the hyperpolarizing direction (-3.4 mV)[2,3], increasing I_{Ks} conductance (60%)[4], increasing the rate of I_{NaK} (20%)[2] and increasing $I_{Ca,L}$ (300%). The rate of $[Ca^{2+}]_i$ uptake into the network SR, I_{up}, was also increased (110%) to account for a 40% increase in the rate of decline of $[Ca^{2+}]_i$. The sensitivity of BP pacemaking rate to these changes was tested at various expression levels of I_{NaCa} (control[1] and 100% increase).

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