## Supplemental Equations

<u>Ionic</u> Compartment	<u>Rapid</u> Buffer(s)	Modified Equations
Ca <sub>i</sub>	СаМ	$J_{CaB_{cytosol}} = T\dot{n}C_l + T\dot{n}C_{h_c} + M\dot{y}o_c$
	SRB	$\beta_{Ca_{i}} = \left(1 + \frac{B_{max_{CaM}} \cdot \frac{k_{off_{CaM}}}{k_{on_{CaM}}}}{\left(\frac{k_{off_{CaM}}}{k_{on_{CaM}}} + Ca_{i}\right)^{2}} + \frac{B_{max_{SR}} \cdot \frac{k_{off_{Sr}}}{k_{on_{Sr}}}}{\left(\frac{k_{off_{Sr}}}{k_{on_{Sr}}} + Ca_{i}\right)^{2}}\right)^{-1}$
		$\dot{Ca}_{i} = \beta_{Ca_{i}} \cdot \left( -J_{serca} \cdot \frac{V_{sr}}{V_{myo}} - J_{CaB_{cytosol}} + \frac{J_{Ca_{slmyo}}}{V_{myo}} \cdot (Ca_{sl} - Ca_{i}) \right)$
Caj	SLL <sub>j</sub> SLH <sub>i</sub>	$\beta_{Ca_{j}} = \left(1 + \frac{B_{max_{SL_{low_{j}}}} \cdot \frac{k_{off_{sl_{l}}}}{k_{on_{sl_{l}}}}}{\left(\frac{k_{off_{sl_{l}}}}{k_{on_{sl_{l}}}} + Ca_{j}\right)^{2}} + \frac{B_{max_{SL_{high_{j}}}} \cdot \frac{k_{off_{sl_{h}}}}{k_{on_{sl_{h}}}}}{\left(\frac{k_{off_{sl_{h}}}}{k_{on_{sl_{h}}}} + Ca_{j}\right)^{2}}\right)^{-1}$
	5011	$\int \left( \frac{k_{off_{sl_l}}}{k_{on_{sl_l}}} + Ca_j \right)^2 \left( \frac{k_{off_{sl_h}}}{k_{on_{sl_h}}} + Ca_j \right)^2 \right)$
		$\dot{Ca}_{j} = \beta_{Ca_{j}} \cdot \left( -I_{Ca_{tot_{junc}}} \cdot \frac{C_{mem}}{V_{junc} \cdot 2 \cdot Frdy} + \frac{J_{Ca_{juncsl}}}{V_{junc}} \cdot (Ca_{sl} - Ca_{j}) \right)$
		$+ J_{SR_{Ca_{rel}}} \cdot \frac{V_{sr}}{V_{junc}} + J_{SR_{leak}} \cdot \frac{V_{myo}}{V_{junc}} \bigg)$
Ca <sub>sl</sub>	SLL <sub>sl</sub>	$\left( B_{max_{SL_{lowsl}}} \cdot \frac{k_{off_{Sl_l}}}{k_{onsl_l}}  B_{max_{SL_{high_{Sl}}}} \cdot \frac{k_{off_{Sl_h}}}{k_{onsl_l}} \right)^{-1}$
	SLH <sub>sl</sub>	$\beta_{Ca_{sl}} = \left(1 + \frac{B_{max_{SL_{low_{sl}}}} \cdot \frac{k_{off_{sl_{l}}}}{k_{on_{sl_{l}}}}}{\left(\frac{k_{off_{sl_{l}}}}{k_{on_{sl_{l}}}} + Ca_{sl}\right)^{2}} + \frac{B_{max_{SL_{high_{sl}}}} \cdot \frac{k_{off_{sl_{h}}}}{k_{on_{sl_{h}}}}}{\left(\frac{k_{off_{sl_{h}}}}{k_{on_{sl_{h}}}} + Ca_{sl}\right)^{2}}\right)^{-1}$
		$\dot{Ca}_{sl} = \beta_{sl} \cdot \left( -I_{Ca_{tot_{sl}}} \cdot \frac{C_{mem}}{V_{sl} \cdot 2 \cdot Frdy} + \frac{J_{Ca_{juncsl}}}{V_{sl}} \cdot (Ca_j - Ca_{sl}) \right)$
		$+\frac{J_{Ca_{slmyo}}}{V_{sl}}\cdot(Ca_i-Ca_{sl})\bigg)$

<u>Ionic</u> <u>Compartment</u>	<u>Rapid</u> Buffer(s)	Modified Equations
Ca <sub>SR</sub>	Csqn <sub>b</sub>	$\beta_{Ca_{SR}} = \left(1 + \frac{B_{max_{csqn}} \cdot \frac{k_{off_{csqn}}}{k_{on_{csqn}}}}{\left(\frac{k_{off_{csqn}}}{k_{on_{csqn}}} + Ca_{SR}\right)^2}\right)^{-1}$
		$\dot{Ca}_{SR} = \beta_{Ca_{SR}} \cdot \left( J_{serca} - \left( J_{SR_{leak}} \cdot \frac{V_{myo}}{V_{sr}} + J_{SR_{Ca_{rel}}} \right) \right)$
Naj	Na <sub>Bj</sub>	$\beta_{Na_j} = \left(1 + \frac{B_{max_{Na_j}} \cdot \frac{k_{off_{Na}}}{k_{on_{Na}}}}{\left(\frac{k_{off_{Na}}}{k_{on_{Na}}} + Na_j\right)^2}\right)^{-1}$
		$\dot{Na_{j}} = \beta_{Na_{j}} \cdot \left( -I_{Na_{tot_{junc}}} \cdot \frac{C_{mem}}{V_{junc} \cdot Frdy} + \frac{J_{Na_{juncsl}}}{V_{junc}} \cdot (Na_{sl} - Na_{j}) \right)$
Na <sub>sl</sub>	Na <sub>Bsl</sub>	$\beta_{Na_{sl}} = \left(1 + \frac{B_{max_{Na_{sl}}} \cdot \frac{k_{off_{Na}}}{k_{on_{Na}}}}{\left(\frac{k_{off_{Na}}}{k_{on_{Na}}} + Na_{sl}\right)^2}\right)^{-1}$
		$\dot{Na}_{sl} = \beta_{Na_{sl}} \cdot \left( -I_{Na_{tot_{sl}}} \cdot \frac{C_{mem}}{V_{sl} \cdot Frdy} + \frac{J_{Na_{juncsl}}}{V_{sl}} \cdot (Na_{j} - Na_{sl}) \right)$
		$+\frac{J_{Na_{slmyo}}}{V_{sl}}\cdot(Na_{i}-Na_{sl})\bigg)$