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Supplemental information

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Running title: Modelling lysosomal calcium signalling in cardiac cells

Supplementary Material

Parameters		Units	Value	Ref.
Volume	Total cell (V_{tot})	pL	33	[1]
	Lysosome (V_{ls})	pL	2% V_{tot}	[2, 3]
TPC	Maximum open probability (P_{Omax})		0.014	[2, 4]
	Variance (P_{Osd}^2)		2.25	this study
	Mean (P_{Omean})		23	[2]
	Leak rate ($j_{clc,leak}$, $j_{tpc,leak}$)	s^{-1}	1.13E-05	this study
Lysosome	TPC flux density into junction (j_{clc})	s^{-1}	9.708	this study
	TPC flux density into cytosol (j_{tpc})	s^{-1}	12.135	this study
	[*NAADP*] for CTRL protocol	nM	1	this study
	[*NAADP*] for NAADP-AM protocol	nM	15	this study
	[*NAADP*] for ISO protocol	nM	15	this study
	Diffusion flux rate to junction ($J_{ls,j}$)	um^3/s	1.4219E-15	this study
	Diffusion flux rate to cytosol ($J_{ls,i}$)	um^3/s	1.3858E-15	this study

Table S1. Baseline parameters for the lysosome compartment.

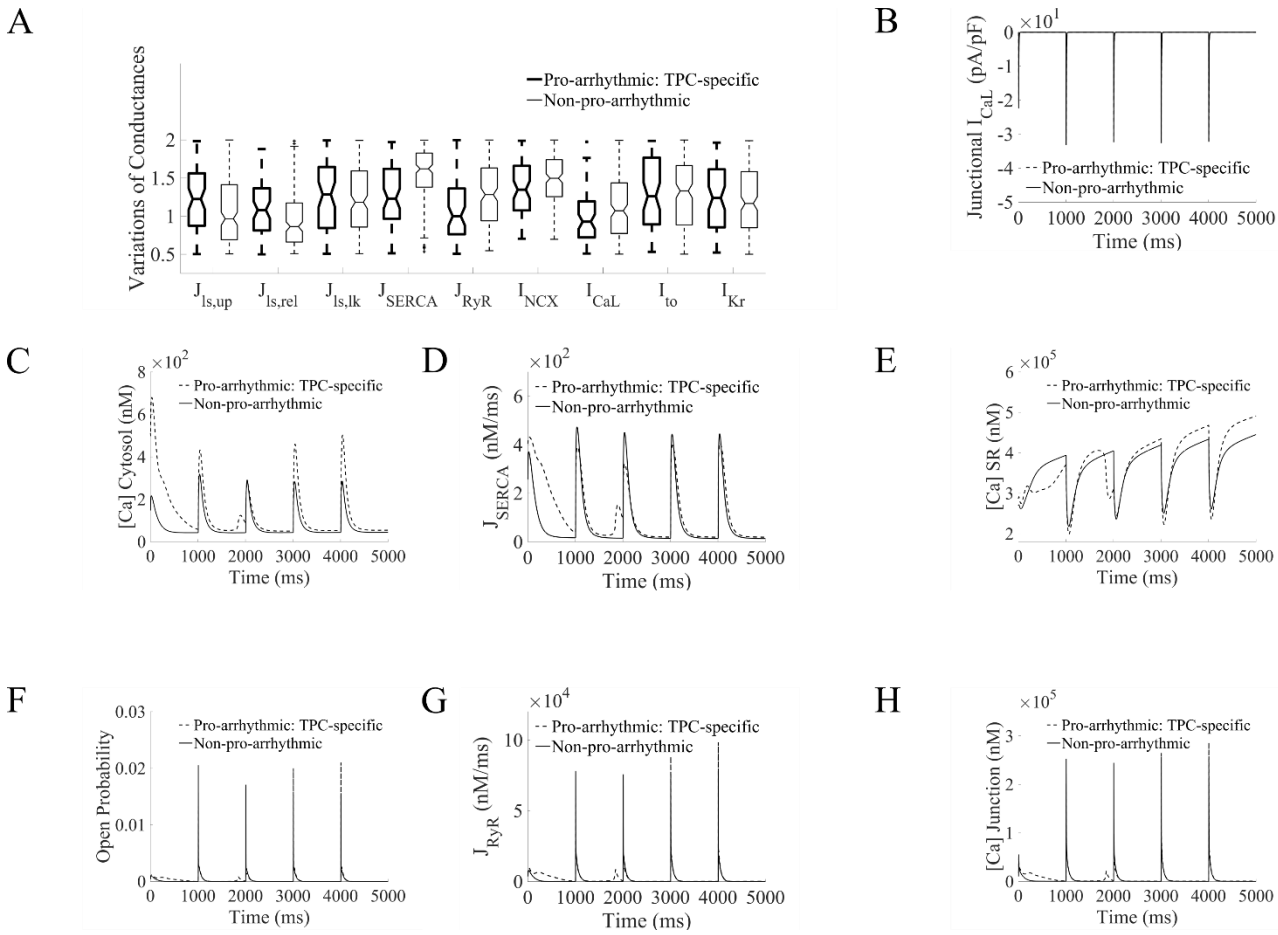

Figure S1. Ionic properties and calcium fluxes underlying spontaneous calcium events under fast pacing at 10 Hz and sustained β-adrenergic stimulation. **S1A:** Comparison of ionic properties of TPC-specific proarrhythmic models (blue), and non-proarrhythmic models (magenta) in WT. **S1B-S1H:** Traces of junctional L-type calcium current, cytosolic, SR and junctional calcium concentrations, SERCA and RyR fluxes, and RyR open probability, comparing TPC-specific pro-arrhythmic models, and non-proarrhythmic models in WT.

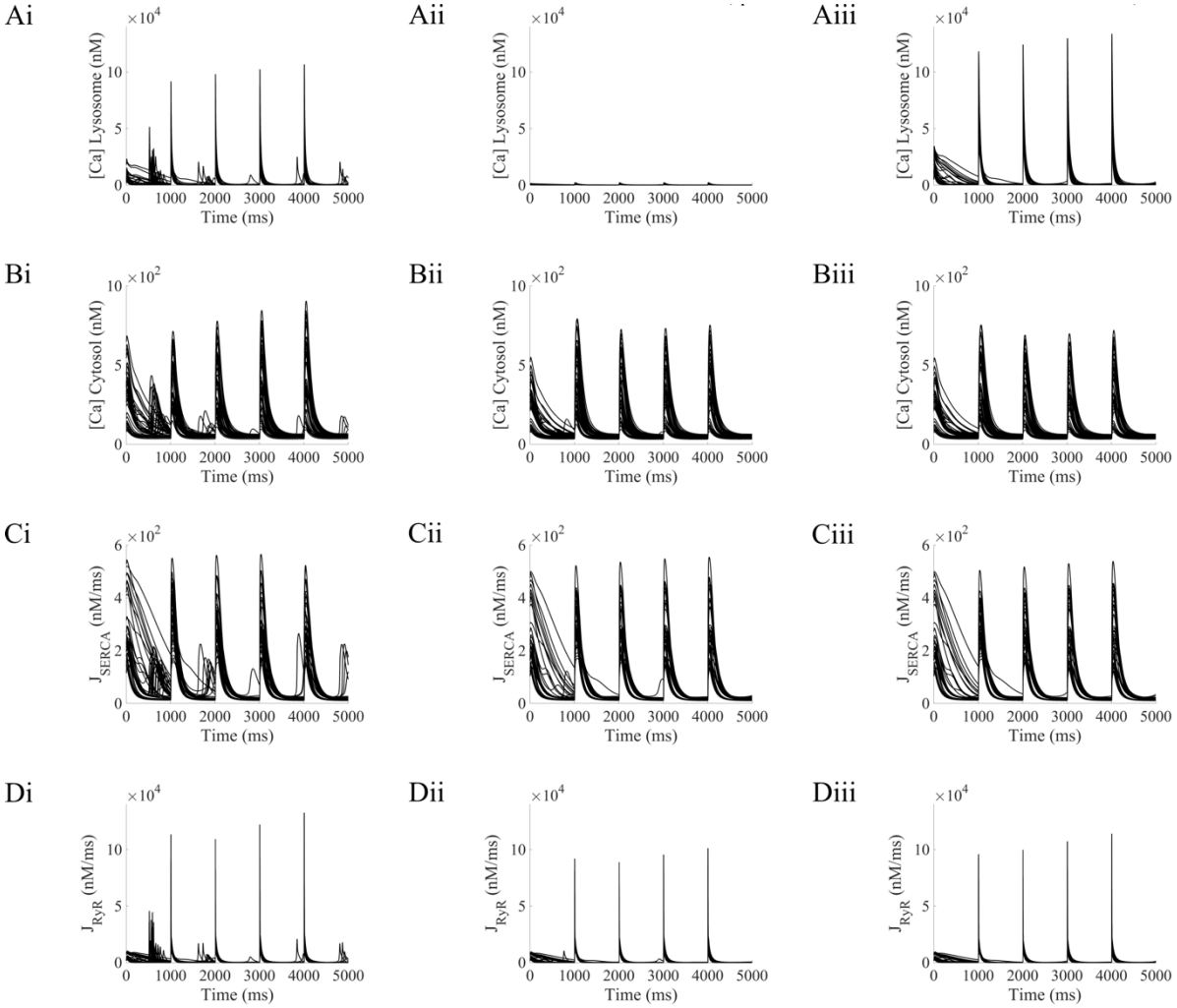

Figure S2. Lysosomal calcium release promotes spontaneous calcium release in TPC-specific pro-arrhythmic profiles under fast pacing and β-adrenergic stimulation, by increasing the junctional-SR calcium gradient. **S2Ai-S2Di:** Lysosomal calcium concentration, cytosolic calcium concentration, and SR reuptake and release fluxes, respectively, in basal conditions. **S2Aii-S2Dii:** Calcium concentrations and fluxes under lysosomal uptake block ($J_{ls,up} = 0$). **S2Aiii-S2Diii:** Calcium concentrations and fluxes under lysosomal release block ($J_{ls,rel} = 0$). All results presented under preliminary fast pacing at 25 Hz.

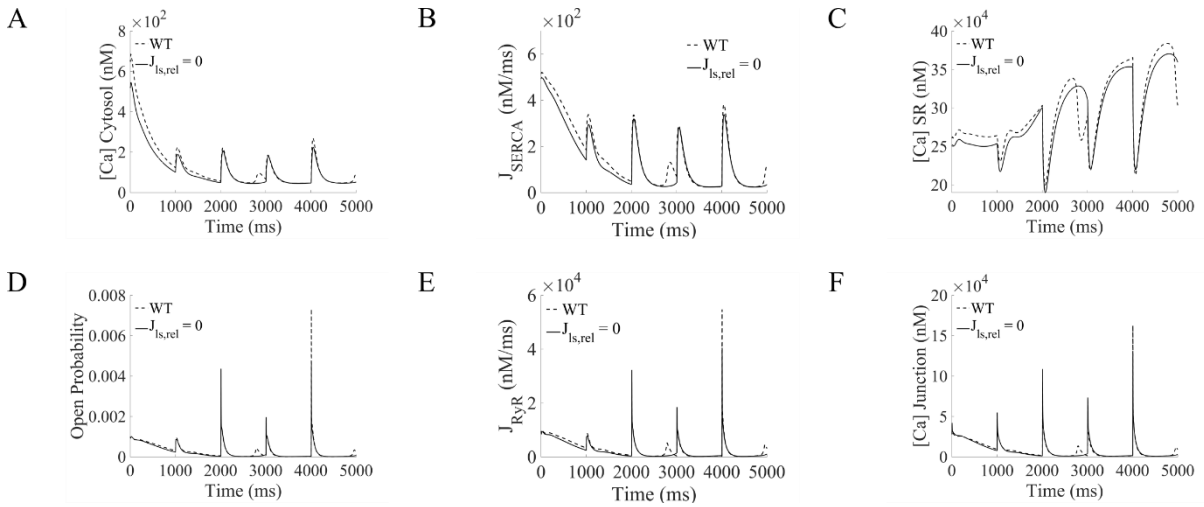

Figure S3. Loss of each lysosomal flux reduced spontaneous calcium release from SR in TPC-specific pro-arrhythmic models under fast pacing and β-adrenergic stimulation. **S3A-S3F:** Traces of cytosolic, SR and junctional calcium concentrations, SERCA and RyR fluxes, and RyR open probability, comparing scenarios in WT (blue), and blocking lysosomal calcium release ($J_{ls,rel} = 0$, magenta). The beats presented in the results are at 1Hz following 25Hz fast pacing protocol.

Supplemental References

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