Coupling the Electrical and Calcium Signaling in a Heart Cell

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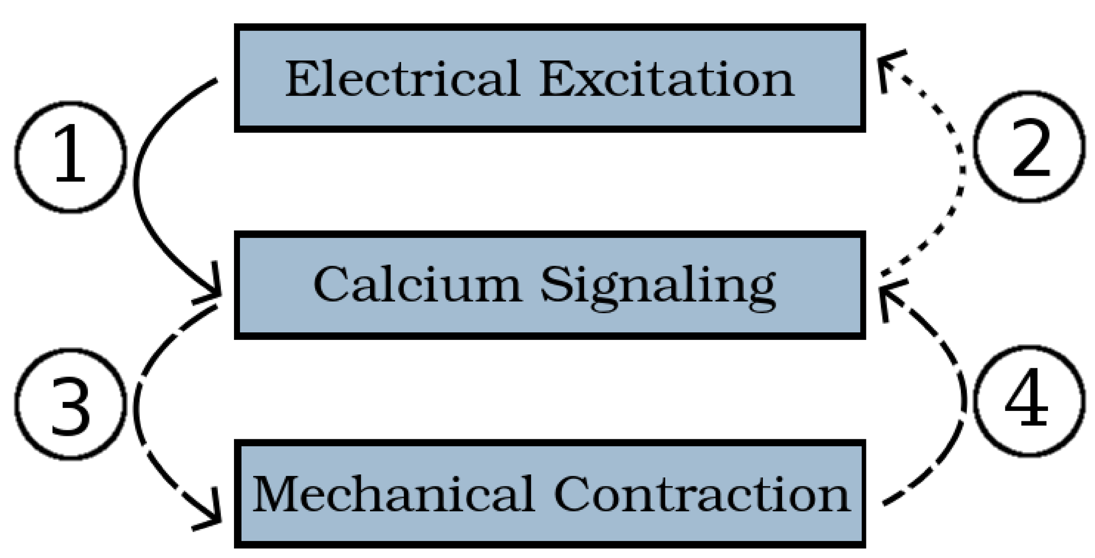
Problem

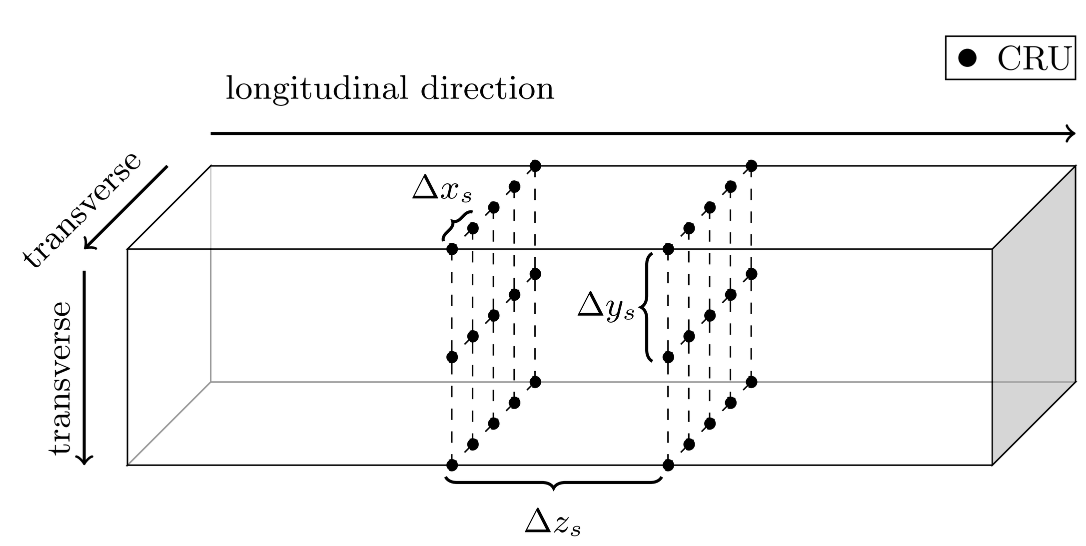
The rhythm of the heartbeat is governed by the collective contraction of individual heart cells, regulated by the chemical concentration of calcium ions in each cell's cytosol. To model these calcium concentrations in a heart cell fully requires the coupling of three interconnected systems:



Our work ②, ③, ④ extends an earlier implementation ① to complete the model and to couple all three systems fully. The initial simulations reported here compare one-way coupling ① to two-way coupling ①–② of the electrical and calcium systems.

Model

The mathematical model of the full cell is given by a system of eight time-dependent partial differential equations in the three-dimensional cell domain:

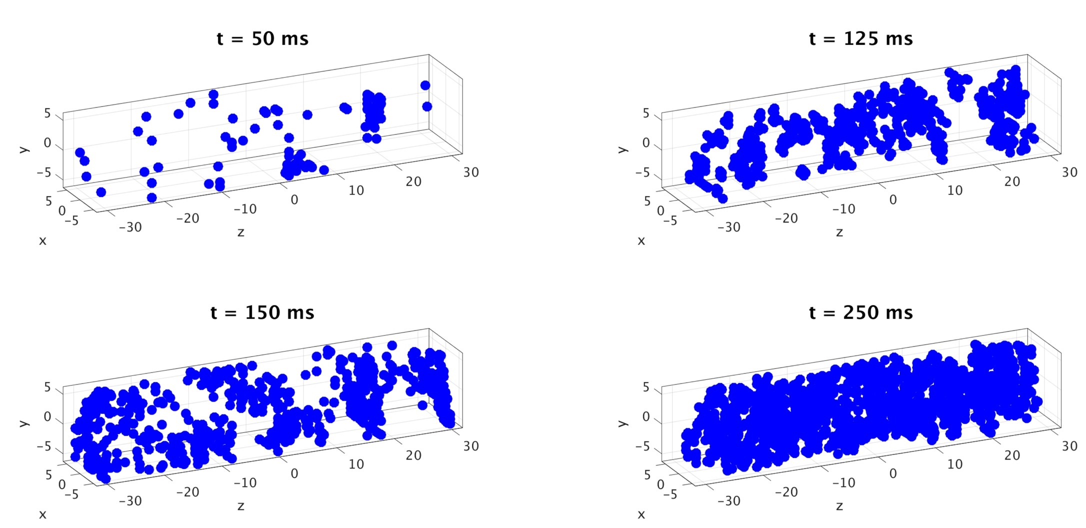


The vital calcium release units (CRUs), through which calcium is injected into the cytosol from the store, are distributed in an approximately regular net throughout the cell, modeled as a lattice of $15 \times 15 \times 31 = 6{,}975$ point sources throughout the interior of the domain.

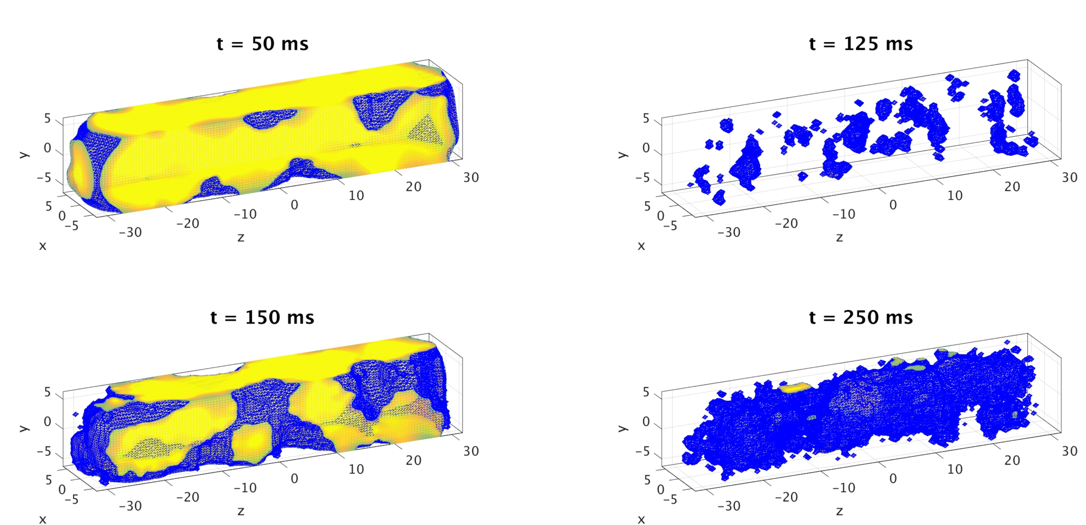
Coupling Electrical → Calcium

For one-way coupling ①, the calcium concentration repeatedly reaches high levels throughout the cell, before decreasing to low levels permanently.

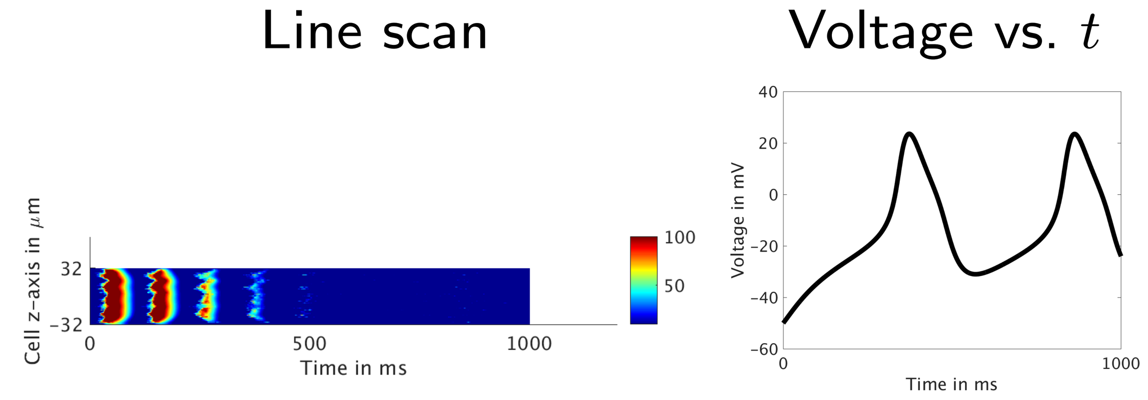
Snapshots of open CRUs throughout cell



Snapshots of calcium concentration isosurfaces



Line scan　　Voltage vs. t

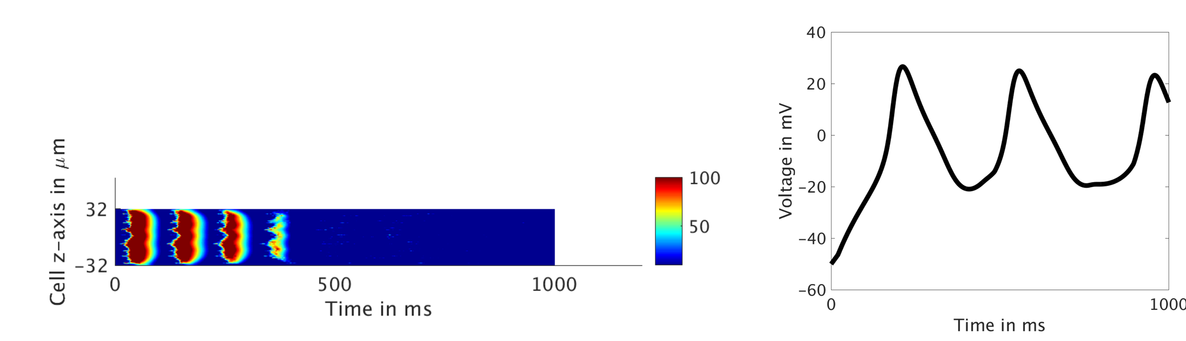


The voltage is unaffected by the fluctuations in calcium concentration. This is not physiologically realistic.

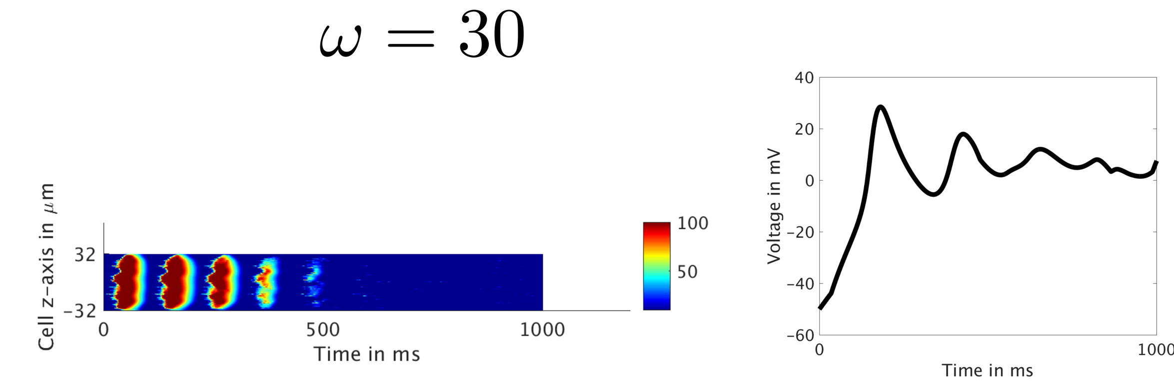
Coupling Electrical ↔ Calcium

For two-way coupling ①–②, we demonstrate the electrical effect of the previous calcium release patterns by linking the calcium system back to the electrical system via the current generated by calcium efflux.

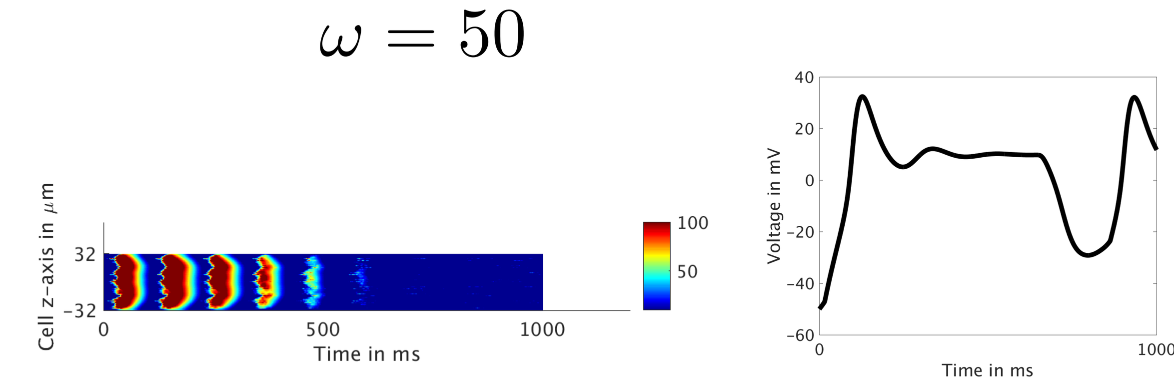
A parameter study of the coupling strength ω in ② shows that as the effect of calcium concentration on the voltage increases, the formerly periodic behavior of the voltage is destabilized by the sharp fluctuations in current caused by the calcium oscillations.



$\omega = 30$



$\omega = 50$



$\omega = 100$

Conclusions

- Our extended model completes the links between the electrical, calcium, and mechanical systems; initial simulations study coupling between the electrical and calcium systems.
- A parameter study of the coupling strength indicates that the feedback and feedforward between electrical excitation and calcium signaling influence the shape of the voltage to physiologically realistic levels.

References

[1] Alexander et al., *SPORA* 1(1), 2015
[2] Banyasz et al., *Heart Rhythm* 9(1), 2012
[3] Full technical report: HPCF–2016–15
`hpcf.umbc.edu` > Publications

Acknowledgments

- REU Site: `hpcreu.umbc.edu`
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