Examining the Electrical Excitation, Calcium Signaling, and Mechanical Contraction Cycle of a Heart Cell

UMBC REU Site: Interdisciplinary Program in High Performance Computing

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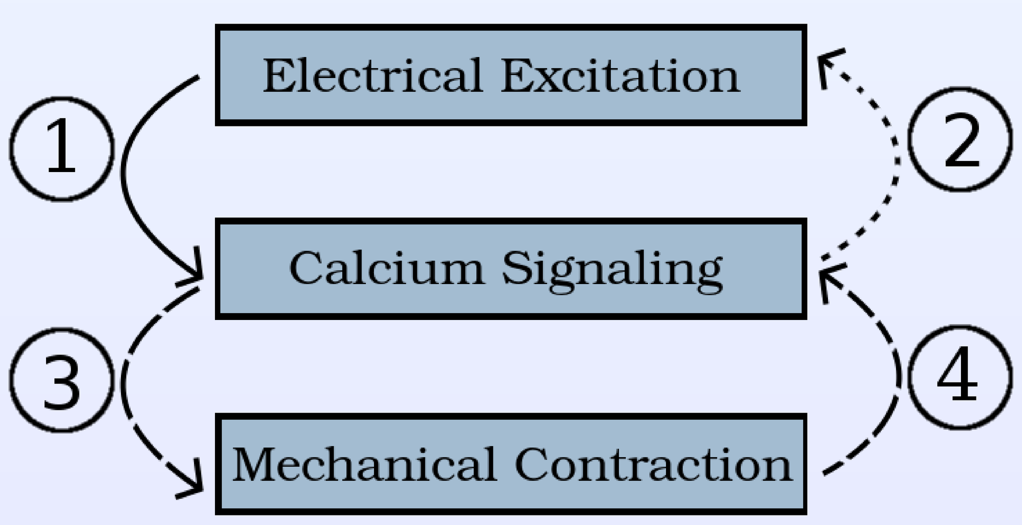
Goal

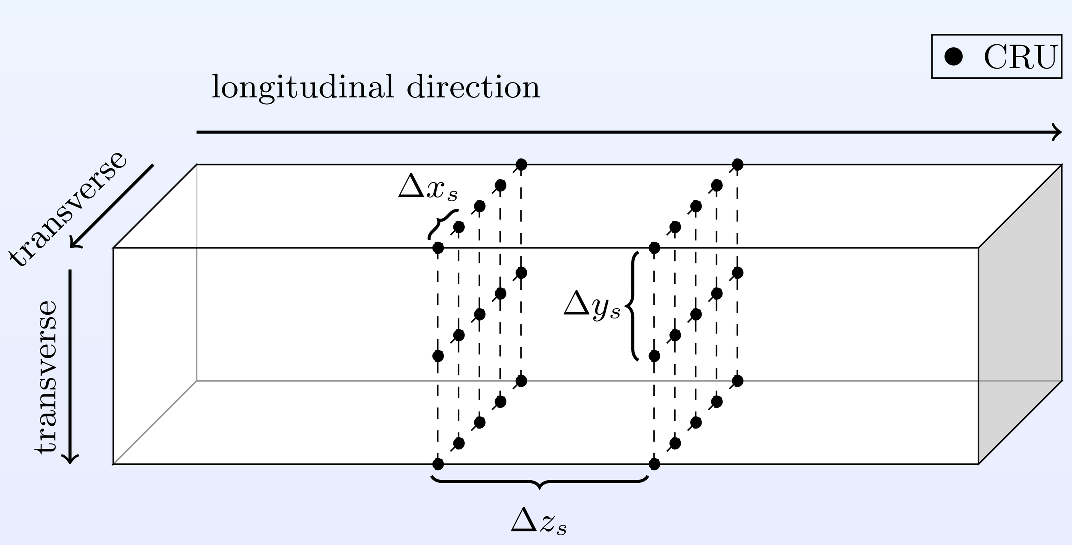
In order to better understand the heart, this work studies the connection between the electrical excitation and mechanical contraction components of the calcium induced calcium release (CICR) cycle in a single heart cell. The heart beats when a collection of heart cells contract through this CICR process, driven by the voltage in the electrical system and ultimately depending on the calcium concentration in the cytosol.



This work creates a model and executes simulations linking all components of the CICR cycle, including the mechanical component with Links ③ and ④.

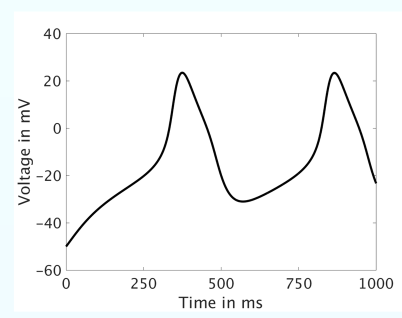
Model

This work models a heart cell through the use of seven coupled time-dependent non-linear reaction-diffusion equations. Calcium releases from the store in the sacroplasmic reticulum (SR) into the cytosol through calcium release units (CRUs).



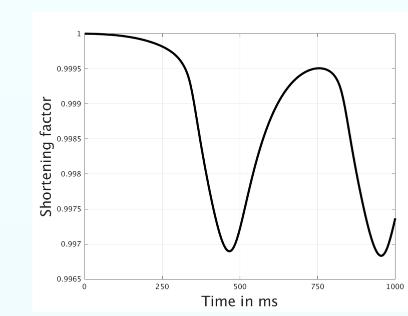
The CRUs form a regular net modeled by a lattice of $15 \times 15 \times 31 = 6{,}975$ point sources throughout the interior of the 3-D cell.

Seven-Variable Simulations



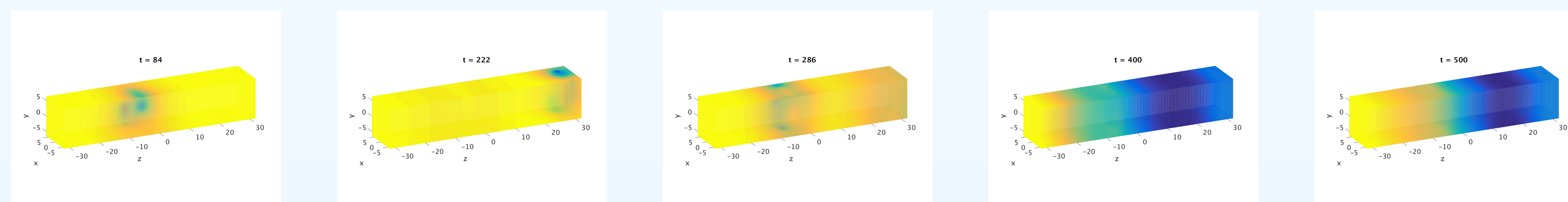
Driving voltage

Voltage stimulates release of calcium from the store $s(\mathbf{x}, t)$, limited by its depletion, via CRUs to the cytosol $c(\mathbf{x}, t)$. This calcium binds to actin-myosin cross-bridges $b_3^{(c)}(\mathbf{x}, t)$, which contract the cell. $\Rightarrow$



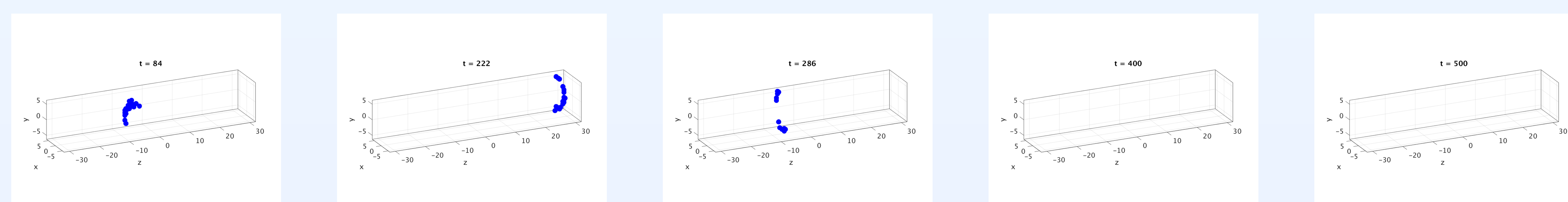
Shortening factor

Isosurfaces of the store SR calcium $s(\mathbf{x}, t)$ with $s_{crit} = 5{,}000\ \mu$M



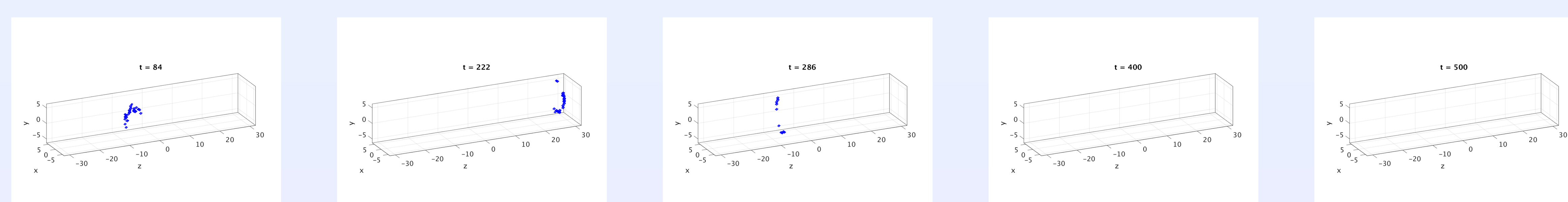
$t = 100$ ms $t = 200$ ms $t = 300$ ms $t = 400$ ms $t = 500$ ms

Plots of open calcium release units (CRUs)



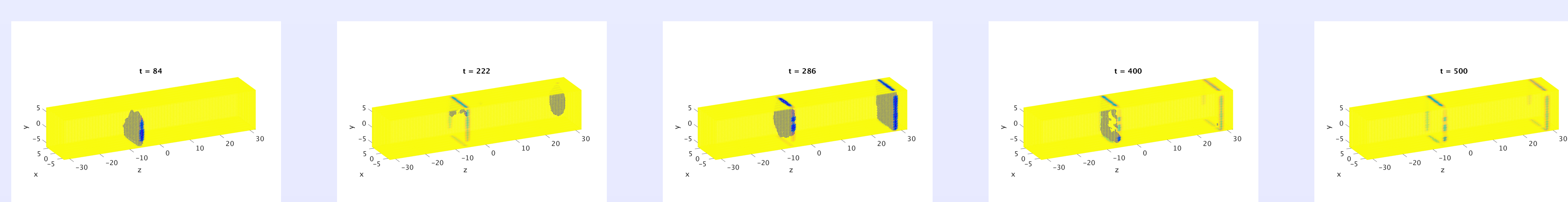
$t = 100$ ms $t = 200$ ms $t = 300$ ms $t = 400$ ms $t = 500$ ms

Isosurfaces of cytosol calcium $c(\mathbf{x}, t)$ with $c_{crit} = 65\ \mu$M



$t = 100$ ms $t = 200$ ms $t = 300$ ms $t = 400$ ms $t = 500$ ms

Isosurfaces of inactive actin-myosin cross-bridges $b_3^{(c)}(\mathbf{x}, t)$ with $b_{3_{crit}}^{(c)} = 120\ \ \mu$M



$t = 100$ ms $t = 200$ ms $t = 300$ ms $t = 400$ ms $t = 500$ ms

- Created first fully coupled simulations including mechanical contraction.
- Identified set of parameter values showing realistic effects.

Simulations used FVM with $32 \times 32 \times 128$ mesh for 1 million DOF in each time step.

References

[1] Kallista Angeloff, Carlos Barajas, et al., *Spora*, vol. 2, 2016.

[2] Full technical report: HPCF–2017–15 `hpcf.umbc.edu` > Publications

Acknowledgments

- REU Site: `hpcreu.umbc.edu`
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