Modeling 3-D Calcium Waves from Stochastic Calcium Sparks in a Sarcomere Using COMSOL

Zana A. Coulibaly[1], Leighton T. Izu[2] and Bradford E. Peercy[1]

1. University of Maryland, Baltimore County, Department of Mathematics and Statistics, 1000 Hilltop Circle, Baltimore, MD 2150;
2. University of California Davis, Department of Pharmacology, 451 Health Science Dr., Davis CA 95616.

Introduction: We utilize COMSOL General Form PDE interface and MATLAB to model stochastic calcium waves in a basic unit of a heart muscle (a sarcomere). Calcium is released stochastically from sites modeled as point sources and distributed on z-disc (planes) in an hexagonal pattern. The release sites are sensitive to calcium levels and after opening and releasing calcium, undergo a refractory period during which they stay closed and after which are able to open.

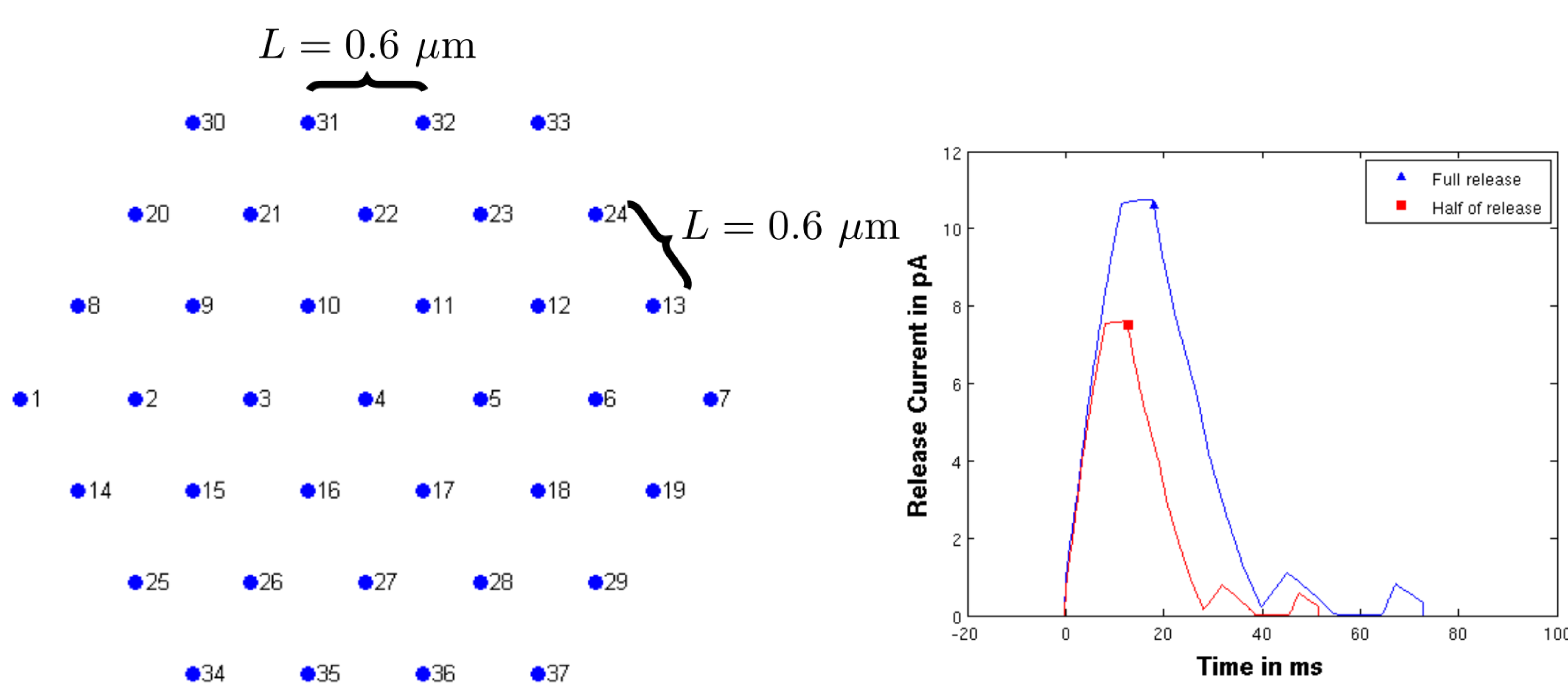

Figure 1. (Left) Release units distribution. (Right) Release Current.

Model: We model the release of calcium in cardiac cells with the following system of reaction-diffusion equations

$$\frac{\partial c}{\partial t} = \nabla \cdot (D_c \nabla c) - J_{\text{pump}} + J_{\text{leak}} + J_{\text{release}} + \sum_i R_i(c, b_i, B_i),$$

$$\frac{\partial b_i}{\partial t} = \nabla \cdot (D_{b_i} \nabla b_i) + R_i(c, b_i, B_i),$$

$$\frac{\partial B_i}{\partial t} = \nabla \cdot (D_{B_i} \nabla B_i) - R_i(c, b_i, B_i),$$

with buffer reactions $c + b_i \underset{k_i^-}{\overset{k_i^+}{\rightleftharpoons}} B_i$

and release

$$J_{\text{release}}(c, \mathbf{x}) = \sum_j \sigma(t, T_j^m) S(t; T_{open}) \delta(\mathbf{x} - \hat{\mathbf{x}}_j)$$

Release Mechanism: The stochastic aspect of the release is modeled using MATLAB through the indicator function

$$S(t, T_{open}) = \begin{cases} 1 & \text{if } \alpha \le J_{\text{prob}}(c), \\ 0 & \text{if } \alpha > J_{\text{prob}}(c), \end{cases}$$

with probability

$$J_{\text{prob}}(c) = P_{\max} \frac{c^m}{K_{\text{prob}}^m + c^m},$$

α is a number from a uniform distribution.

Results: The simulations obtained over a sarcomere domain shows individual stochastic releases of calcium self-organizing into propagating waves.

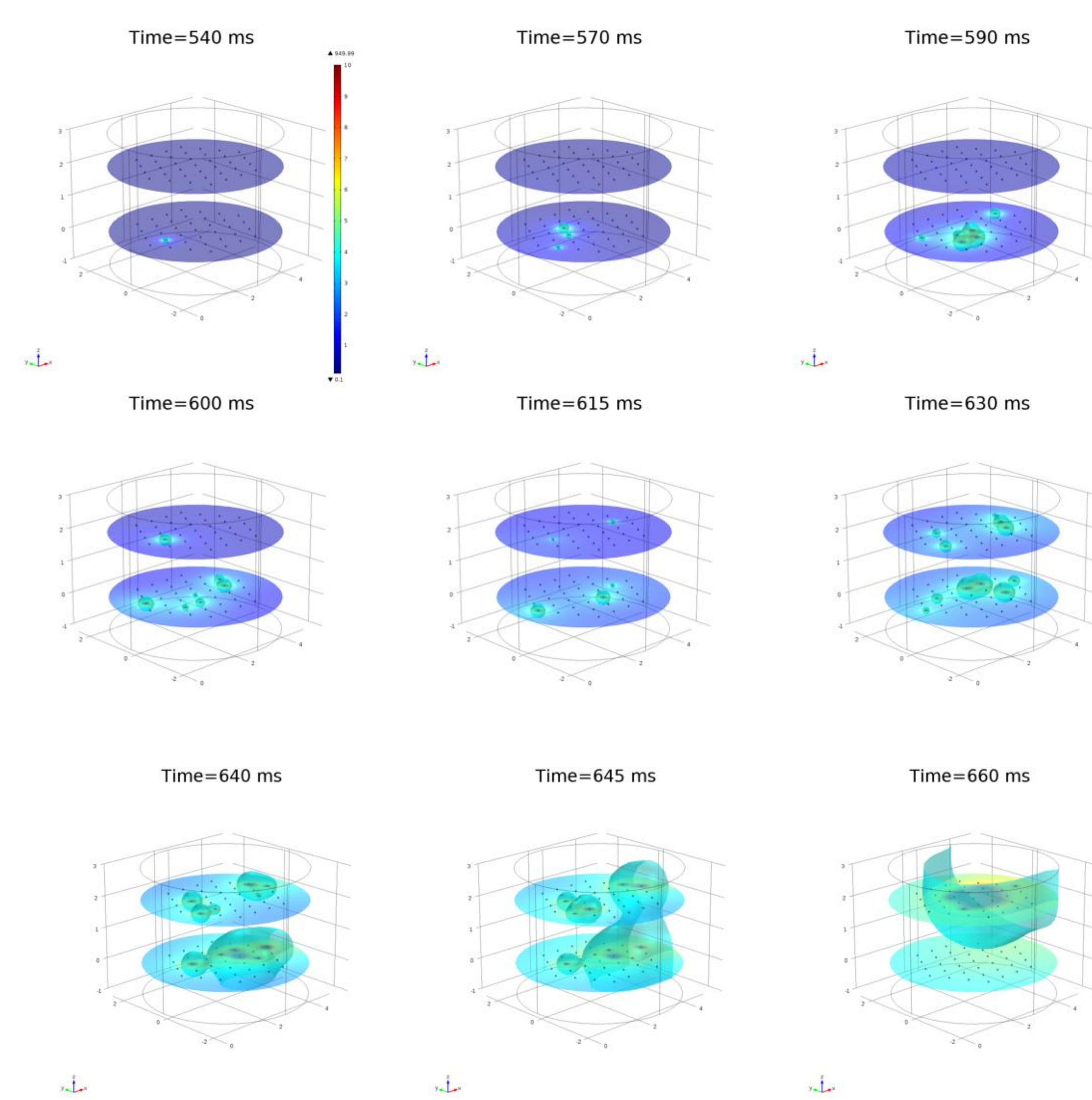

Figure 2. Simulation obtained from stochastic release of calcium at half release strength. Stochastic release of calcium generates a self-organized wave that propagates through the sarcomere in 660 ms.

Reference: *Proceedings of the COMSOL Conference 2013*, Boston, MA.

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