Modeling 3D Calcium Waves from Stochastic Calcium sparks in a Sarcomere Using COMSOL Multiphysics©

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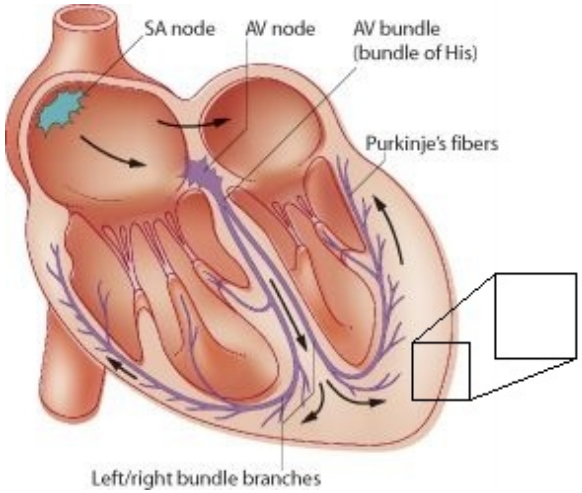
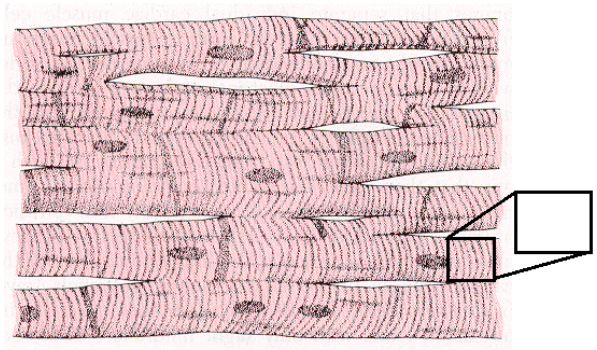
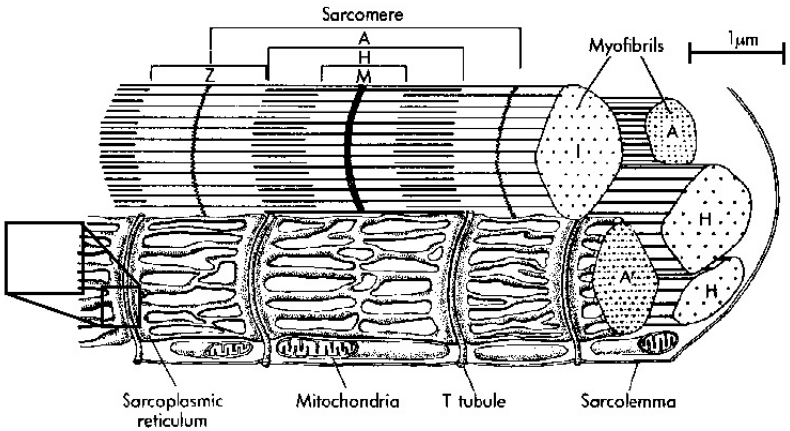
Cardiac Myocyte Schematic



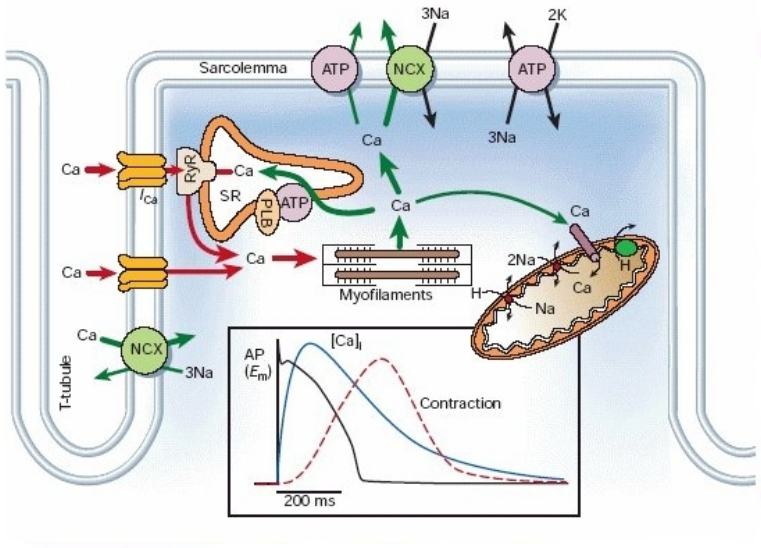
(a) Heart muscle.



(b) Heart tissues.



(c) Sarcomere schematics.



(d) Calcium dynamics. [Bers, 2002]

Our goal is to model calcium dynamics in a sarcomere. This involves:

- modeling the random release of calcium from calcium release units (CRU),
- modeling the diffusion and interaction of calcium with other chemical species,
- changing the distribution of CRUs on a z-disc.

Main equations [Izu 2001, Gobbert 2008]

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

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

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

Buffer reaction

$$c + b_i \underset{k_i^-}{\overset{k_i^+}{\rightleftharpoons}} B_i.$$

Stochastic Release Mechanism

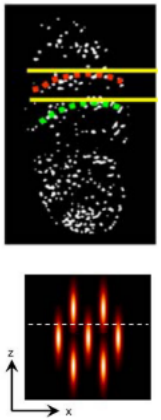
$$J_{\text{release}}(c, \mathbf{x}) = \sum_j \sigma(t, T_j^m) S(t; T_{open}) \delta(\mathbf{x} - \hat{\mathbf{x}}_j),$$

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

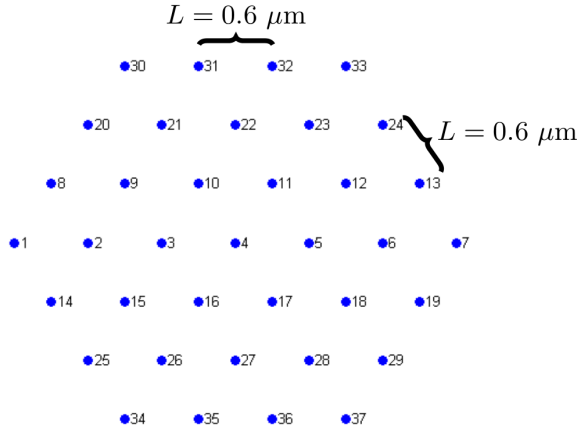
$$J_{\text{prob}}(c) = P_{\max} \frac{c^m}{K_{\text{prob}}^m + c^m}, \alpha \sim U[0, 1].$$

⇒ A CRU is allowed to open every ms. After opening, a CRU undergoes a refractory period of about 100 ms.

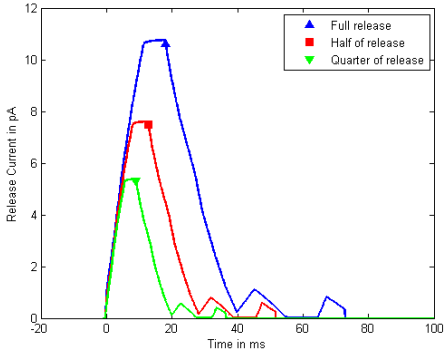
Comsol-Matlab Implementation



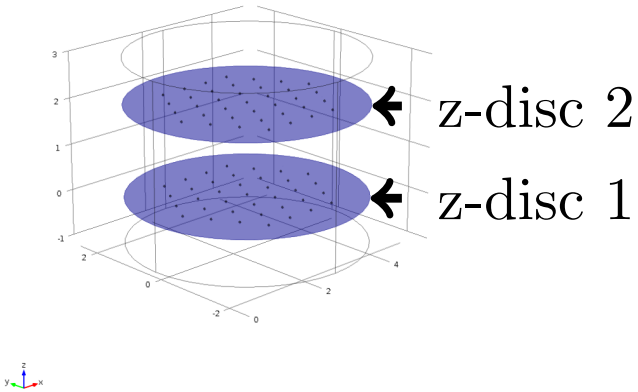
(a) CRU spacing [Izu 2006].



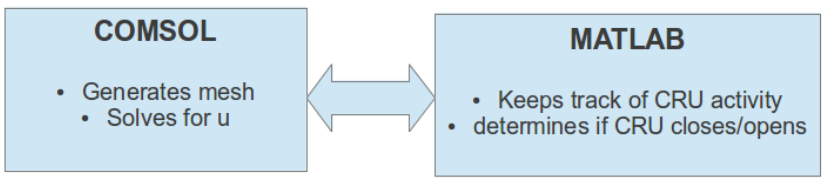
(b) CRU spacing in simulations.



(c) Release current [Soeller 2012].



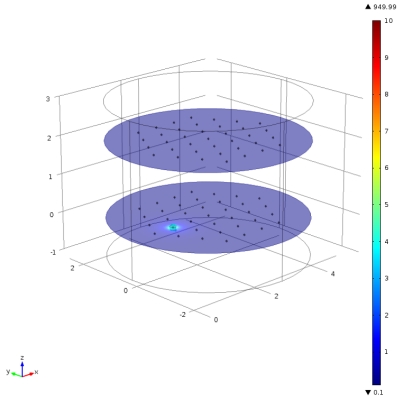
(d) The sarcomere domain.



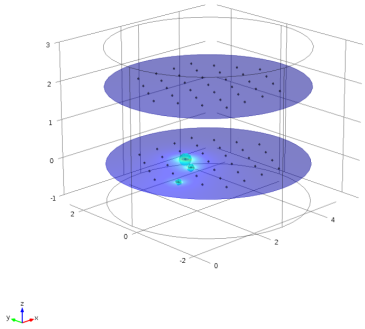
(e) **Programming logic.**

Stochastic sparks organizing into a wave

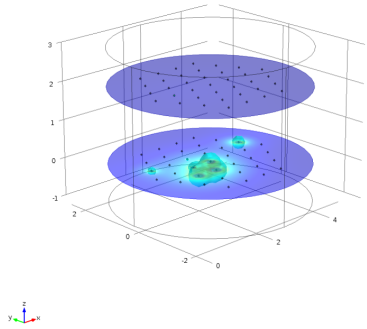
Time=540 ms



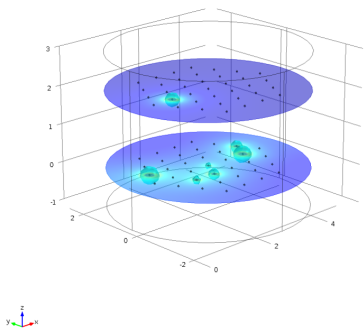
Time=570 ms



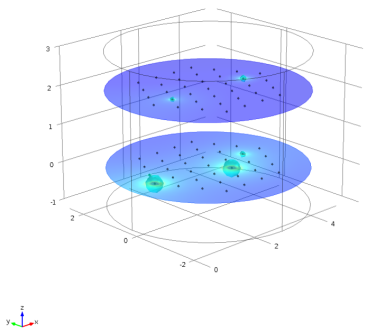
Time=590 ms



Time=600 ms



Time=615 ms



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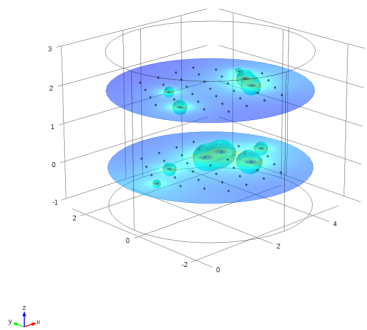
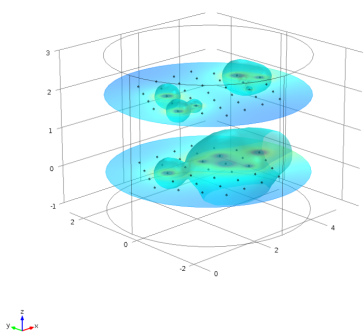


Time=640 ms



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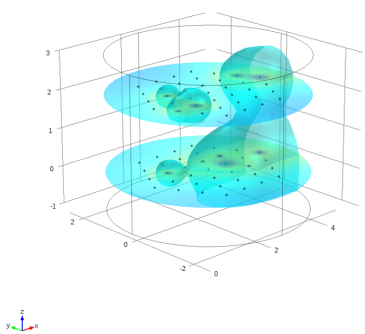
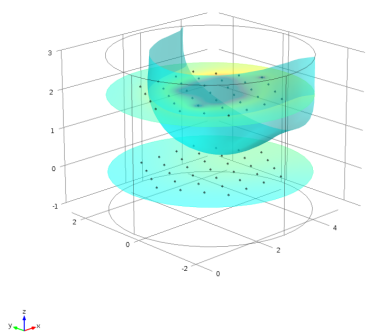
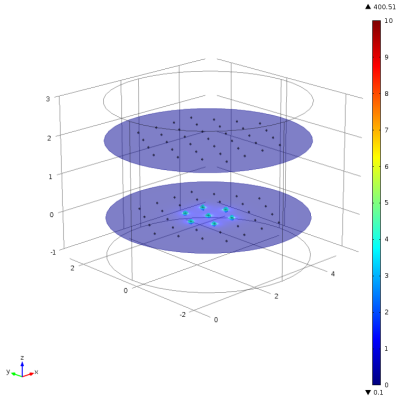


Time=660 ms

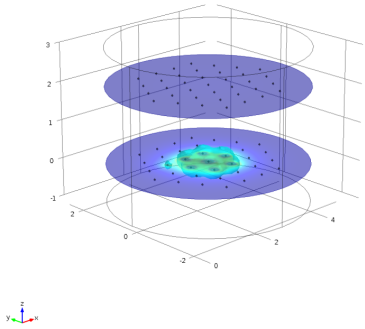


Forced sparks organizing into a wave

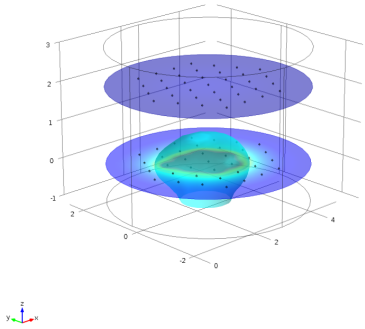
Time=2 ms



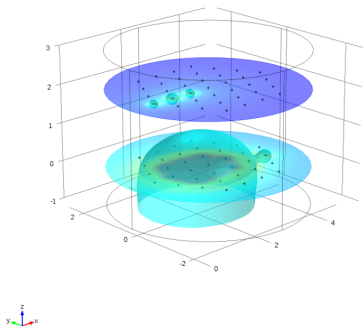
Time=8 ms



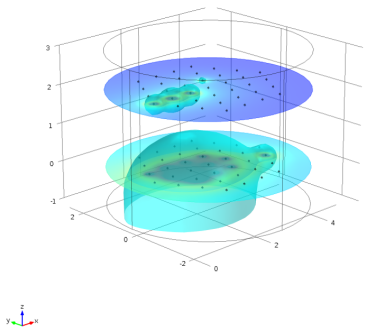
Time=15 ms



Time=30 ms



Time=33 ms



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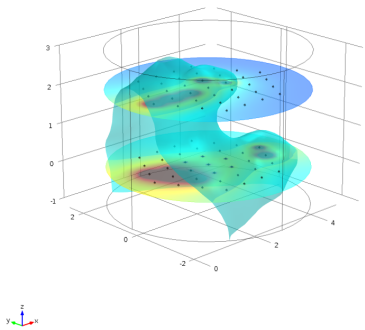

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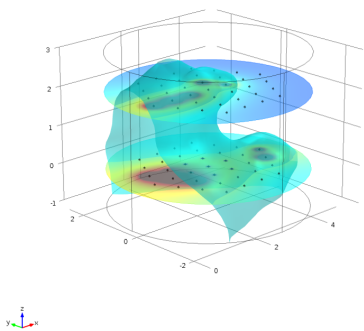
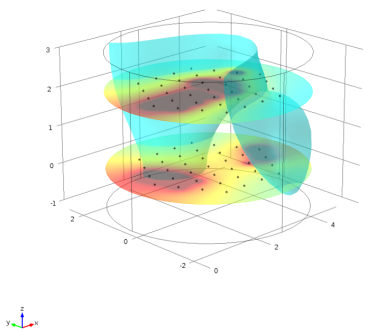


Time=50 ms



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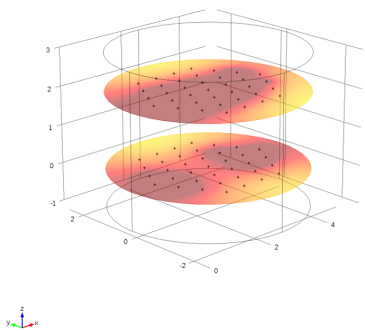

- Izu et al., *Evolution of Cardiac Calcium Waves from Stochastic Calcium Sparks* , Biophysical Journal Volume 80, 2001.
- Bers, *Cardiac Excitation-contraction Coupling*, Nature Volume 45, 2002.
- Izu et al., *Three-Dimensional Distribution of Ryanodine Receptor Clusters in Cardiac Myocytes*, Biophysical Journal Volume 91, 2006.
- Gobbert, *Long-time Simulations on High Resolution Meshes to Model Calcium Waves in a Heart Cell*, SIAM Journal of Scientific Computing, 2008.