Three-dimensional modeling of Ca^{2+} dynamics in single cardiac cells

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Ca^{2+} release from the sarcoplasmic reticulum (SR) contributes to the cardiac rhythm under resting and stimulated conditions (Lakatta *et al*., 2003; Imtiaz *et al*., 2010). We have developed a detailed three-dimensional mathematical model to study Ca^{2+} sparks and waves in single cardiac cells.

The fundamental building block of our three-dimensional model is a calcium cycling unit (CCU). Each CCU is composed of: 1) a ryanodine receptor (RyR) cluster - formulation of the RyR in the cluster is based on experimental data from lipid bi-layer measurements; 2) terminal SR; 3) network SR; 4) SERCA which transports Ca^{2+} from the bulk cytoplasm to the network SR; 5) various Ca^{2+} buffers in all the compartments of the CCU. Geometric dimensions and other parameter values were based on available experimental data.

A cardiac cell was formulated by defining a three dimensional bulk cytoplasmic space which also contained cytoplasmic buffers. An algorithm was developed to distribute CCUs in the three-dimensional space in required density and arrangement. The cardiac cell model could be stimulated locally and globally to study emergence of sparks, and generation and propagation of Ca^{2+} waves.

Our model provides the ability to incorporate experimental data characterizing RyRs during resting and stimulated conditions into detailed three dimensional simulations. This model can be used in further studies investigating role of Ca^{2+} in cardiac pacemaking and contraction.

Imtiaz MS, von der Weid PY, Laver DR, van Helden DF. (2010) SR Ca^{2+} store refill - a key factor in cardiac pacemaking. *Journal of Molecular and Cellular Cardiology* **49,** 412-426.

Lakatta EG, Maltsev VA, Bogdanov KY, Stern MD, Vinogradova TM. (2003) Cyclic variation of intracellular calcium: a critical factor for cardiac pacemaker cell dominance. *Circulation Research* **92**: e45-50.