# Modeling excitation contraction coupling of a cardiac myocyte

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Electrophysiological cardiomyocyte models commonly have simplified calcium dynamics between grouped cell subcompartments. A recent development is biophysically detailed models with spatially resolved calcium cycling and calcium release units (CRUs) which simulate important subcellular spatiotemporal dynamics including calcium sparks and calcium waves. We have developed a highly detailed rabbit ventricular myocyte model with spatiotemporally resolved calcium which reproduces experimentally measured steep gradients in CRUs, graded $Ca2^{+}$ release and calcium-induced calcium release (CIRC) gain [1].

The excitation-contraction coupling is the crucial process for the contraction of the heart chambers and it is therefore an active area of research. The myocyte contracts as a response to an action potential, which travels along the membrane into the T-tubules. The voltage-dependent L-type calcium channels are opened by the depolarization and $Ca2^{+}$ enters the cell. The increased calcium concentration activates ryanodine receptors, which release calcium from the sarcoplasmic reticulum. Because of the high intracellular calcium concentration, the cell contracts. Afterwards, the calcium is pumped outwards and the contraction ends. In this model the intracellular calcium concentration of the cellular subcompartments is spatially resolved, as are the local action of calcium buffers. Each CRU is represented by a detailed model of local CICR which simulates realistic spatial calcium gradients, the local electric field, and individual stochastic gating of the channels. The membrane potential is modelled using an ordinary differential equation electrophysiological ionic currents model. The diffusion of calcium ions is represented by a set of coupled partial differential equations which are solved in a finite elements framework (DUNE). Modeling such a multiscale problem involves a comprehensive parameter analysis, dealing with controversial issues like the distribution of the NCX and continuous improvements and extensions.

**Reference**

[1] J. Vierheller, W. Neubert, M. Falcke, S. H. Gilbert, and N. Chamakuri. A multiscale computational model of spatially resolved calcium cycling in cardiac myocytes: from detailed cleft dynamics to the whole cell concentration profiles," Front Physiol.6, 1–15, 2015.