Contributions of structural t-tubule heterogeneities and membrane Ca^{2+} flux localization to local Ca^{2+} signaling in rabbit ventricular myocytes

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The micro-architecture of the transverse tubular system (t-system) and the arrangement of associated proteins are central to the function of ventricular cardiomyocytes. Recently, Savio-Galimberti and collaborators used confocal imaging and digital image processing to characterize the geometry of t-system in rabbit ventricular cells [1]. The average diameter of single t-tubules was estimated to be 448 ± 172 nm with constrictions occurring every 1.87 ± 1.09 μm along their principal axis. Here, we used a modeling approach to investigate how local variations in t-tubular cross-sectional area and the distribution of membrane Ca^{2+} flux regulate Ca^{2+}-entry, diffusion and buffering in rabbits [2]. The current model includes a realistic 3D geometry of a single t-tubule and its surrounding half-sarcomeres, the spatially distributed Ca^{2+} transporting proteins along the cell membrane (L-type Ca^{2+} channel, Na^{+}/Ca^{2+} exchanger, sarcolemmal Ca^{2+} pump) as well as stationary and mobile Ca^{2+} buffers (troponin C, ATP, calmodulin, Fluo-3). A finite element software package CSMOL was used to solve the coupled reaction-diffusion PDE system describing the time-dependent concentration profiles of the above-listed species.[3]. The model was parameterized according to Sobie's et al. voltage-clamp data in rabbit ventricular myocytes with Ca^{2+} release at the sarcoplasmic reticulum disabled pharmacologically [4]. The results indicate that the constrictions and spatial arrangements of membrane Ca^{2+} proteins may cause local inhomogeneities in Ca^{2+} concentration. In addition, the activation of a catalytic Ca^{2+}-binding site on Na^{+}/Ca^{2+} exchanger on local Ca^{2+} gradients was examined in the presence or absence of fluorescent dye.

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