RyR Simulator Reference Environment

Thank you for trying out the RyR-Simulator. This document briefly summarizes what you see in the reference environment. For the theoretical and computational algorithm details, please refer to the supplementary text in our PLoS Comp Biol publication.

Default Script Execution

The default script executes ryr-simulator.R to simulate RyR clusters in a half-sarcomere model of a cardiac cell derived from electron tomography data (see Fig. 1 below).

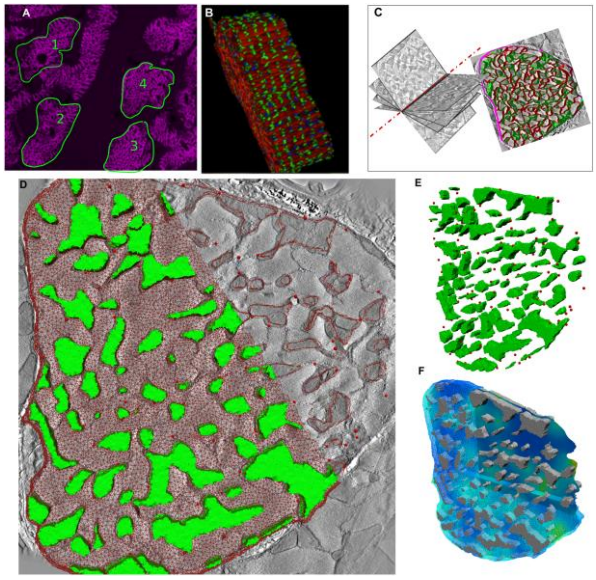

Figure 1. **A hybrid-scale spatial model of myofbirils, mitochondria and RyR clusters.**

(A): Confocal image of a tissue section from the left ventricule of an adult male Wistar rat; numbered cells were processed for RyR cluster distribution analysis and development of a novel computational fusion algorithm (see S1 Text). (B): 3D rendering of cell number 1 in (A) showing green immuno-labeling of RyR clusters and red, phalloidin staining of myofibrillar actin. (C): Electron micrographs of a 240 nm tissue section from another left ventricular sample of a similar male Wistar rat were acquired at different tilts (left) to construct a 3D electron tomogram; the stack was manually segmented (right) for myofibrils and mitochondria. More details on the data acquisition are in the Materials and Methods. (D): One image slice from the electron tomogram with an overlay of the FE computational mesh (mitochondrial regions in green) and the simulated RyR clusters (red spheres) from the computational fusion algorithm; the mesh is partly removed for visualization. (E): A 3D view of the RyR clusters and the mitochondrial regions. (F): 3D view of the predicted Fluo-4-bound Ca^{2+} at the end of 30 ms; an isosurface of the solution field is partially in view at the mid-plane of the half-sarcomere model.

When executing the script inside the reference environment, a command window will appear with scrolling numbers. These numbers represent the difference in the statistical properties between the simulated RyR cluster distribution and the RyR cluster distribution measured in fixed-tissue confocal data. At the end of the simulation, an openGL-library based 3D visualization window will appear that shows the distribution of the first set of points simulated by the program (see Fig. 2).

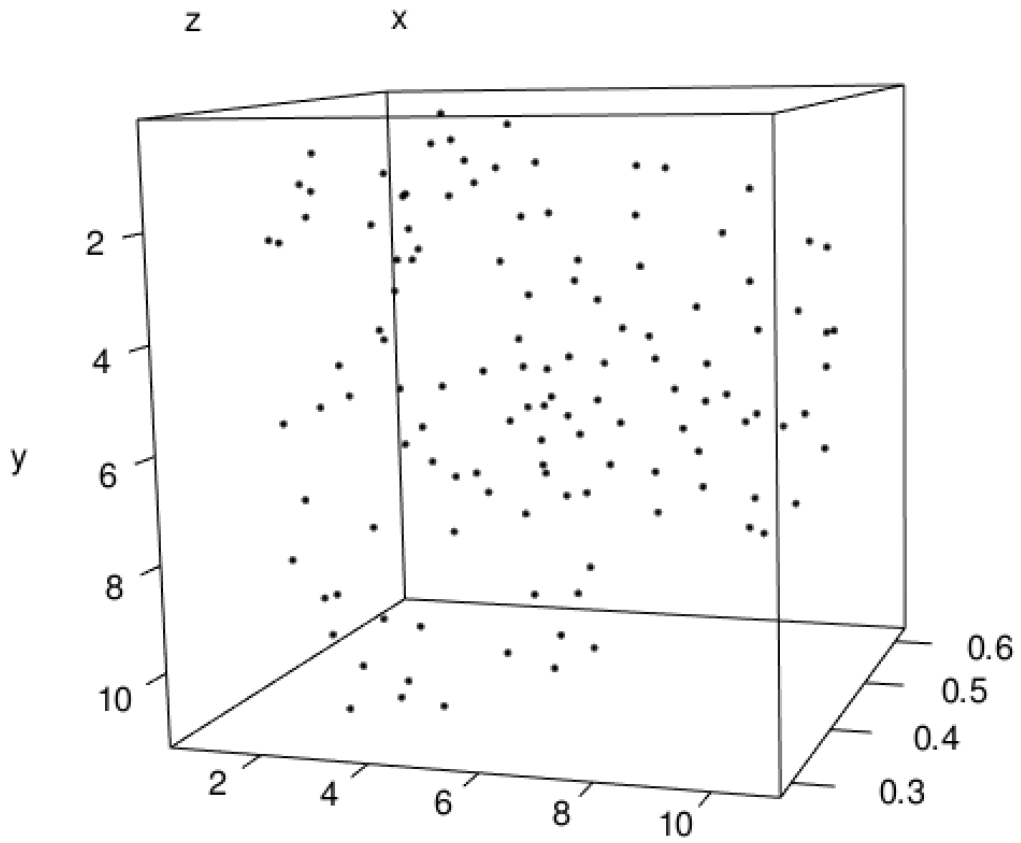

Figure 2: The spatial distribution of RyR clusters that were simulated inside the electon-tomography based template of myofibrils and mitochondria from Fig. 1 using the reference environment script.