May 15th, 6:00 PM

Coupled Influence of Heart Rate Variability and Subcellular Calcium Heterogeneity on Cardiac Electromechanical Dynamics

Vrishti M. Phadumdeo
Virginia Commonwealth University, phadumdeovm@vcu.edu

Seth H. Weinberg Ph.D
Virginia Commonwealth University, shweinberg@vcu.edu

Heart rate variability (HRV) is a normal physiological phenomena that results from autonomic regulation, stochastic pacemaking, and circadian rhythms. Many clinical studies have shown that decreased HRV correlates with an increased risk for cardiac arrhythmias, while prior work suggests that HRV impacts alternans, a beat-to-beat alternation in the cardiac action potential duration (APD) or intracellular calcium (Ca) transient. We previously showed using a nonlinear discrete-time map model that HRV disrupted alternations in both APD and peak Ca and weakened APD-Ca coupling (Phadumdeo and Weinberg, J Theoretical Biology, 2018). Here, we aim to investigate the coupled effects of HRV and subcellular heterogeneity by modeling individual Ca release units (CRUs). We simulated cardiac cells with 100 CRUs with varying heterogeneity in the initial Ca concentrations for a given pacing rate. HRV is reproduced by adding a random Gaussian distribution with zero mean and specified standard deviation to a constant baseline pacing rate. In agreement with prior experimental work, we found that in the absence of HRV, subcellular Ca heterogeneity leads to the formation of subcellular alternans in which Ca in different regions of the cell alternate out of phase, which decreases the magnitude of the whole Ca and APD and peak Ca alternans. Interestingly, as in our prior work, HRV disrupted APD and peak Ca alternation and weakened APD and peak Ca, and these effects did not depend on the amount of initial subcellular Ca heterogeneity. In contrast, for low HRV, the peak Ca variability and alternans magnitude decreases in the presence of subcellular Ca heterogeneity. Overall, our model predicts that both heart variability and subcellular calcium heterogeneity alter beat-to-beat electromechanical dynamics in cardiac cells.