Dissertation Defense Announcement
To: The George Mason University Community

Candidate: Jerome Anthony E. Alvarez

Program: PhD in Bioinformatics & Computational Biology

Date: Wednesday, November 8, 2023

Time: 11:00 AM

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Title: "A Computational Model of a Human Ventricular Cardiomyocyte: Possible Roles in Cardiovascular Disease and Arrhythmias"

Committee Chair: Dr. Aman Ullah

Committee Members: Dr. Saleet, Dr. Kim Avrama Blackwell

ABSTRACT:
Studying cardiac diseases using human tissue has proven difficult and limited, even in optimized clinical conditions. Computer simulation studies have been continuously researched by mimicking electrophysiological protocols which can now be accommodated in the present time due to their high computational load. In that regard, we have developed a stochastic human ventricular cardiomyocyte model for intracellular calcium ([Ca2+]i) handling to include 9 individual L-Type calcium (LCC) and 49 ryanodine receptor (RyR) channels as components of 20,000 Ca2+–release units (CRUs). The model presented here explores the intricacies of calcium-induced calcium-release (CICR) dynamics, with a particular focus on the interplay between LCCs and a cluster of RyRs within CRUs. This framework elucidates the fundamental aspects of excitation-contraction coupling. Various ionic pumps and currents contained in the cell membrane contribute to the overall electrophysiological behavior of the cardiac action potential (AP) morphology. Moreover, cardiac contractility is regulated by fine–tuning multiple fluxes involved in [Ca2+]i concentrations and impacts signaling pathways by spontaneous calcium release from the sarcoplasmic reticulum (SR). However, Ca2+ ions also indicate the presence of abnormalities observed in the behavior of the cardiomyocyte's AP and intracellular Ca2+ dynamics which may ultimately result to arrhythmogenic disorders. The model presented here captures the spontaneous Ca2+ release events and can be further used to explore both normal and defective mechanisms in ventricular cardiac abnormalities.