TAL TECH
SCHOOL OF SCIENCE

Calcium activation in cardiac muscle: experimental and modelling studies

Master's thesis

Student: Maike Mona Širinov
Student code: 231943LAFM
Supervisors: Marko Vendelin, Professor
Mari Kalda-Kroon, Researcher
Laboratory of Systems Biology
Department of Cybernetics
Study program: Applied Physics and Data Science

Tallinn 2025

Summary

Calcium activation plays a vital role in cardiac muscle contraction, serving as the link between electrical excitation and mechanical force generation in a process known as excitation–contraction coupling. With each heartbeat, a rapid increase in intracellular calcium triggers the contractile response of the muscle. This carefully regulated process is essential for maintaining the heart's rhythmic function and ensuring effective blood circulation throughout the body.

This thesis is divided into two main components: an experimental section and a computational section. It addresses two primary aims. The first was to introduce a method in the laboratory for measuring steady-state isometric force in permeabilized mouse cardiomyocytes across a range of calcium concentrations, providing a foundation for future investigations into contraction regulation in various mouse models. The second aim focused on refining an existing computational model to better represent the force–calcium relationship, allowing for more accurate simulations of isometric stress dynamics at varying sarcomere lengths.

The first part of the thesis provides an overview of cardiac muscle structure and function, followed by a brief review of existing experimental methods used to analyze muscle contractile properties. It also covers modeling approaches in the field, with a particular focus on cross-bridge dynamics. Additionally, this section introduces the current model structure and highlights its limitations, identifying areas where improvements are necessary. The second part explains the methods used for the experiments and modeling, followed by a section presenting the results and discussing the challenges encountered and how they were addressed.

A method for measuring isometric force in cardiomyocytes at different calcium concentrations was successfully established. Additionally, refining the model's calcium function led to the identification of rate parameters that improved its fit to isometric stress dynamics across various sarcomere lengths and significantly enhanced the force–calcium relationship. Building on these advances, potential areas for improvement in both the experimental procedure and the model have been identified to guide future work.