PUBLIC DEFENSE
OF DOCTORAL DISSERTATION
TRANSLATIONAL BIOLOGY,
MEDICINE, AND HEALTH
GRADUATE PROGRAM

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"EFFECTS OF PERFUSATE
COMPOSITION (NA+ AND CA2+)
ON CARDIAC ELECTRICAL AND
MECHANICAL FUNCTION IN
THE ISOLATED LANGENDORFF-
PERFUSED HEART"

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AT VTC

TRANSLATIONAL BIOLOGY,
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Virginia Tech’s Translational Biology, Medicine, and Health (TBMH) program is a research-intensive, integrative, and multidisciplinary doctoral program in the biomedical and health sciences. The program brings together students and faculty from the life, behavioral, physical, engineering, mathematical, and computational sciences to consider today’s major challenges in health and disease. The program seeks to develop a new generation of research scientists and thought leaders, who are prepared to identify and tackle the complex challenges for improving human health, by making and translating discoveries into preventions, diagnostics, treatments, cures, and healthier behaviors.

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In recent years, scientific rigor and reproducibility has garnered increased attention in both the scientific and public media. In several recent reports, the high attrition rate observed in clinical trials has been attributed to irreproducibility at the preclinical level. Preclinical cardiology is no exception to this rule. In our systematic review of the ex vivo Langendorff-perfused heart, we found methods reporting to be sparse at best, specifically as it pertains to documenting the ex vivo perfusate compositions employed in the Langendorff heart. Previously, our lab has demonstrated that variation in perfusate compositions can unmask disease states in genetically modified animals. In this dissertation, we exploit this concept with a therapeutic end-point in mind. We show that perfusate variation, specifically sodium and calcium elevations, can attenuate conduction slowing associated with severe hyperkalemia. Likewise, elevating sodium is capable of sustaining intrinsic rhythm where hearts would otherwise go asystolic. In doing so, elevated sodium prevents repolarization prolongation in these hearts. Together, these studies would suggest that elevating extracellular sodium, and calcium, should be considered as therapeutic targets in the context of conduction defects. However, when considering the heart’s primary role as a pump, we found that elevating sodium depresses cardiac mechanical function. This is both in a healthy and post-ischemic setting. In short, we show that electrolyte variation may influence both cardiac electrophysiology and contraction; however, an improvement in one does not guarantee an improvement in both. Maintaining proper cardiac physiological function is a complex process that is tightly regulated by the ionic makeup of the extracellular environment and in order to improve insights from preclinical studies at the clinical level it is paramount that we, as researchers, properly document employed methodologies as they pertain to perfusate composition.