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Title: First steps toward the integration of an in-silico electro-chemo-mechanical smooth muscle cell and a cardiovascular system model

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Abstract

Smooth muscle cells (SMCs) are largely responsible for maintaining vascular tone. Their ability to adapt to any local hemodynamic change is thus an integral mechanism of both cardiovascular function and systemic cardiovascular control. However, the exact processes driving smooth muscle cell contraction, and subsequent local and systemic level vascular tone adaptation to hemodynamic changes are complex and not well understood. This leaves a gap in our understanding and ability to predict and manage cardiovascular disease progression. We aim to begin addressing this knowledge gap by coupling, in-silico, a detailed electro-chemo-mechanical smooth muscle model with a systemic level integrated cardiovascular model that includes a mechanoelectric heart generating the cardiovascular drive, and a detailed circulatory system including the coronary arteries. The system and cell level models are coupled through the flow and pressure profiles obtained from the systemic level driving the muscle force generation. The model behaviors are demonstrated for the cell level control of left main coronary artery in LVOT obstructive and non-obstructive cases for both hypertrophic cardiomyopathy (HCM) and non-HCM virtual patients. The pulsatile pressure and flow changes between the obstructive and non-obstructive cases are observed to alter the contractile force of the SMC through Nitric Oxide and stretch driven pathways. A marked difference in vascular tone between the obstructive and non-obstructive cases is observed. Most interestingly, an inverse force response to obstructive pressure and flow is observed in HCM cases. In this work we demonstrate a successful preliminary coupling of arterial smooth muscle cell cardiovascular and systemic level cardiovascular models.