Title: Development of an In-Silico Smooth Muscle Cell Model to Elucidate Mechanisms of Vascular Tone Regulation

Authors:
Nicole Anderton, Mohamadamin Forouzandehmehr, Jari Hyttinen, Jussi T. Koivumäki

Keywords:
blood pressure, chemo-mechanical, electrochemical, mechanosensitive piezo

Abstract
Unregulated blood pressure is a key indicator of the development of vascular and arterial disease. Vascular smooth muscle cells (SMCs) are key components for blood pressure and flow maintenance and thus respond to stimuli, such as changes in blood pressure or flow, by modulating the vascular tone. Tone is a result of the mechanical contractile force exerted by the SMCs of the vascular wall. This force results from myosin and actin cross-bridge cycling, which is governed by the intracellular calcium concentration. Much is still unknown about the precise mechanisms of vascular SMC tone regulation and its role in vascular and arterial disease progression. Furthermore, in-silico studies describing SMC electrical, chemical and mechanical interaction are limited. Here, we begin to address these knowledge gaps and present an integrated chemo-mechanical and electrochemical SMC model, while also including a novel mechanosensitive Piezo channel. The impact of mechanical stretch over SMCs owing to pressure can be modelled through this Piezo channel. The SMC electrophysiological and mechanochemical models were tested independently and compared with previous literature results before integration. Stimulation of the coupled models with varying extracellular calcium concentrations and Piezo channel-mediated mechano-electric feedback were shown to generate contraction force transients. Our model suggests a potential piezo-stretch role in SMC tone modulation. Our novel integrated model also provides the basis for further investigation of vascular tone regulation and its impact on vascular and arterial health and disease progression.