Title: Autonomic, Metabolic, and Mechanical Control of Coronary Blood Flow

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Coronary blood flow is regulated through the combined action of metabolic, adrenergic, and mechanical (myogenic and shear) mechanisms. The adrenergic pathway, in which -receptor mediated vasodilation leads to increasing flow with increasing cardiac work rate, is important in matching oxygen delivery to oxygen demand during exercise. However, sympathetic outflow to the heart may also stimulate an -receptor mediated vasoconstriction. The -mediated constriction effect is thought to be primarily concentrated on relatively large (>100 m diameter) vessels, with the -mediated dilation effect centered on small vessels that represent the major sites of hydraulic resistance. We hypothesize that the -mediated constriction phenomenon contributes to helping match the effective impedance of the coronary circulation to changes in heart rate.

To test and refine this hypothesis we have constructed a multi-scale model of coronary flow regulation, integrating cell-level models of endothelial and smooth-muscle function, single-vessel mechanics of coronary resistance arteries, autonomic function, network-level myocardium-coronary vessel interaction. The model was used to simulate coronary hemodynamics in the left anterior descending coronary network during exercise-associated changes in myocardial oxygen demand and heart rate. Simulations reveal how -mediated dilation -mediated constriction in vessels of different sizes contribute to the maintenance of the transmural blood flow ratio between endocardium and epicardium (FR = Fendo / Fepi).