# Regional Cellular Demands, Blood Flow, and Transport Phenomena in the Contracting Heart

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**ABSTRACT: Abnormal routes of cardiac excitation, induced for example by left bundle branch block (LBBB) in humans or right ventricular outflow tract pacing in dogs, results in predictable patterns of changes in regional blood flows and metabolism. In LBBB, glucose uptake and flow are both reduced in the septal region. In the paced dogs, the septum and outflow tract are activated early, shorten rapidly without initially raising LV pressure by much, and septal blood flow is substantially reduced while flow increases in the LV free wall. Further, in both the humans with LBBB and the chronically-paced dogs, the septal wall becomes thinner, while the late-activated regions thicken by as much as 40%. In the paced dogs, the LV free wall is being passively stretched by the contraction of the early activated regions, and then contracts relatively slowly against the rising load of developing LV pressure: the prestretch is followed by a prolonged more forceful contraction presumably due to the combination of the Starling effect and the increased afterload.**

**A hypothesis, defined as a mathematical model, has been developed to explain this set of phenomena. The linked events include: (1) intravascular flow of substrate and oxygen in the blood, using partial differential equations (PDEs) accounting for intracapillary gradients, (2) cellular fatty acid and glucose metabolism, using ODEs (3) ATP generation by glycolysis and oxidative phosphorylation, (4) ATP utilization by hydrolysis at the cross bridge, by ion pumps, and for cell maintenance, (5) the processes of excitation-contraction coupling, and (6) feedback regulation of blood flow at smooth muscle receptors. The modeling used a mathematical modeling language (MML) for the PDEs and ODEs under JSim, a simulation interface (http://www.physiome.org) which is available for free download.**

**We attempt to explain the observations using a common parameter set for two regions linked in tandem, but activating them separately with a time delay representing the time for excitation to spread from septum to free wall. The early activation of one region stretches the other. Key unknowns explored in this modeling are: (a) the degree of reduction of ATP use via shortening deactivation (dominating the reduction in flow and substrate use in the early activated cell), and (b) the magnitude and mechanism of the Starling effect in increasing force, ATP use, and blood flow in the late-activated cell.**

**KEYWORDS: Myocardial blood flow, heterogeneity, cardiac pacing, excitation-contraction coupling, cellular energetics, cardiac cell model, bundle branch block, shortening deactivation, ionic regulation.**

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