## Supplemental Materials: Multiscale model of the physiological control of myocardial perfusion to delineate putative metabolic feedback mechanisms

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## S1. Aortic and left ventricular pressure

The aortic pressure  $(P_{ao})$  is continuously measured during the zero-flow pressure measurements (before and after occlusion). To estimate left ventricular pressure  $P_{lv}$ , half-sine functions were used to match AoP in the systolic phase. Figure S1 shows  $P_{ao}$  measurements and estimated  $P_{lv}$  for Pig D (control) experiment with 100 mmHg CPP. Analogous data exist for all experiments.

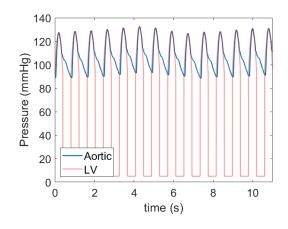
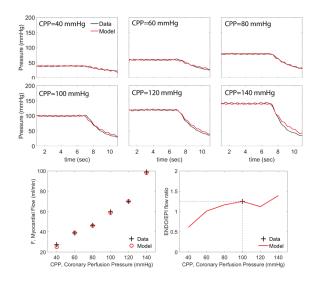
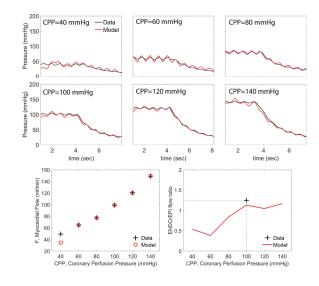


Figure S1. Measured aortic and estimated left ventricular pressure for Pig D, CPP = 100 mmHg.

## S2. Myocardial circulation model fits

Model fits to zero-flow pressure time course data for all animals/experimental conditions are illustrated below.



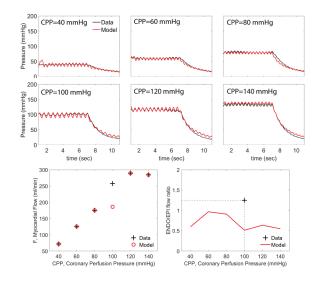


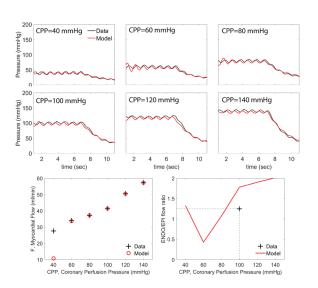
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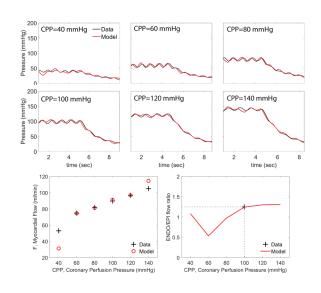
<sup>&</sup>lt;sup>2</sup>Department of Molecular and Integrative Physiology, University of Michigan, Ann Arbor, MI

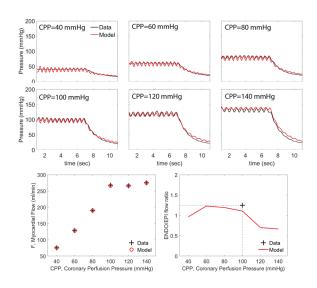
<sup>&</sup>lt;sup>3</sup>Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI

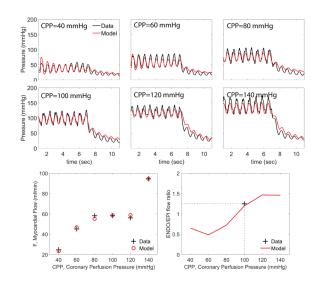
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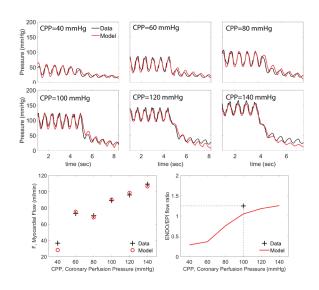


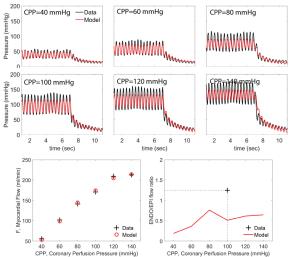


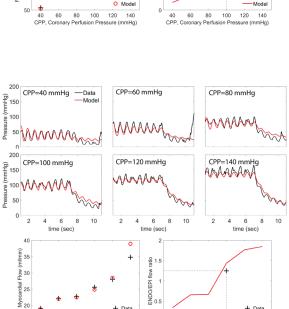


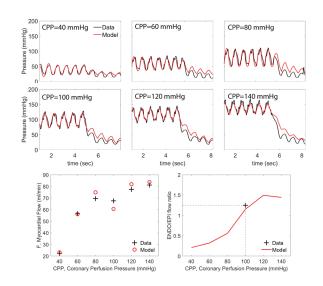


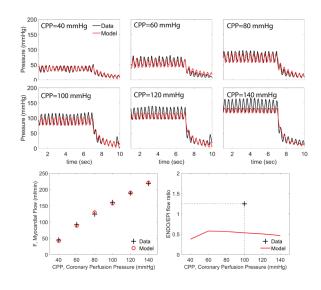






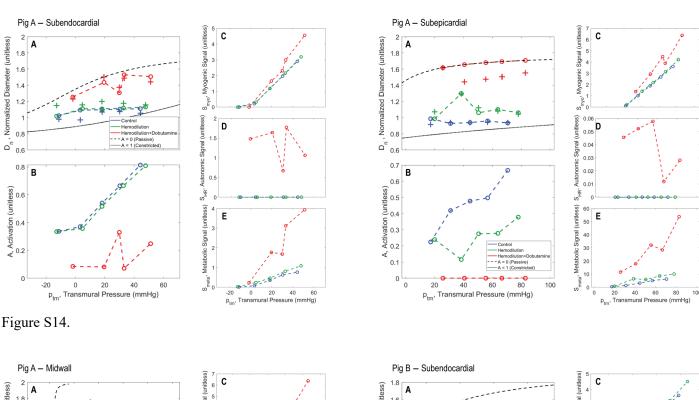






## S3. Representative vessel model fits

The representative vessel model fits with the top-ranking metabolic signal MS<sub>FM</sub> are illustrated below. Each figure plots: Panel A: equivalent diameters as functions of transmural pressure in the representative vessel, with markers "+" and "o" showing Model 1 and Model 2 results, respectively; Panel B: predicted vessel activation vs. transmural pressure; Panels C-E: predicted regulatory signals strengths as functions transmural pressure.



, Normalized Diameter (unitless) 1.6 1.2 0.3 0.8 0.25 ۵ 0.2 0.15 0.9 В 0.1 8.0 0.05 0.7 (unitless) Metabolic Signal (unitless) Ε , Activation ( 7.0 0.0 7.0 0.0 0.3 20 40 60 80 0 -20 0 20 40 60 p<sub>tm</sub>, Transmural Pressure (mmHg)

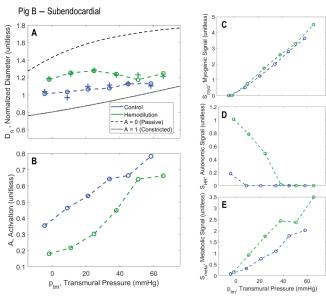


Figure S15.

Figure S17.

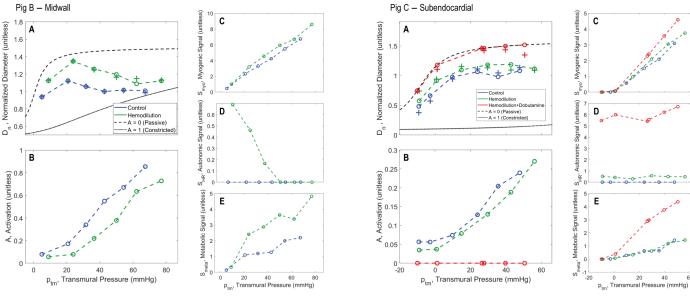


Figure S18.

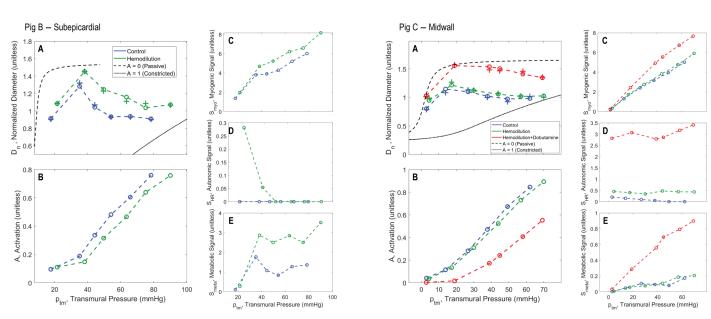
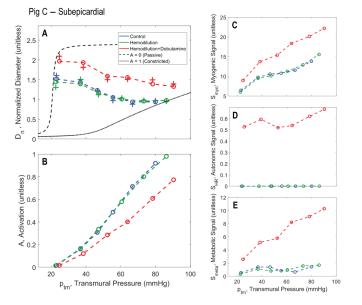


Figure S19.

Figure S21.



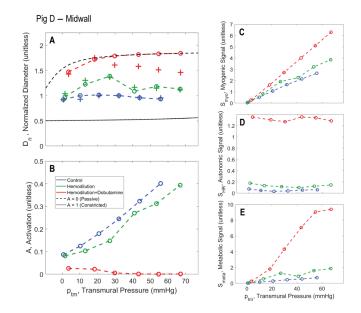
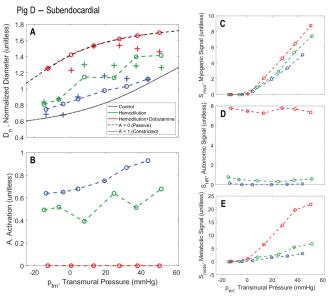


Figure S22.



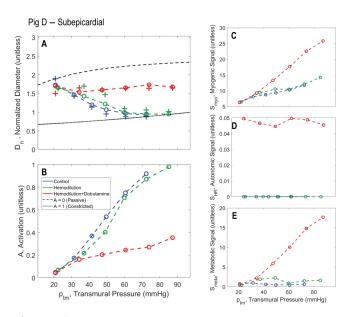


Figure S23.

Figure S25.