Final Report MRC 2016: Project 8

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1 Problem description

During blood loss, there is a sudden decrease in the pressure and volume of the systemic arteries. These changes to systemic pressure and volume affect pressure and volume throughout the cardiovascular system. In response to these changes, the baroreflex mechanism modulates vascular resistance, compliance, and cardiac contractility to return the system to normal pressures and volumes. To better understand how the baroreflex mechanism regulates pressure and volume, experimental data has been collected on how the left ventricular blood pressure and volume change during and after blood withdrawal.

The changes in left ventricular pressure and volume have been modeled using a five compartment cardiovascular model. In this study, the left ventricular unstressed volume, left ventricular minimum elastance, and systemic resistance were identified as the key parameters which are time varying to replicate the experimental data. To better understand how the baroreflex works, we set out to model these key parameters using differential equations. If differential equations for this volume, minimum elastance, and resistance can be developed to give good agreement between the model and experimental data, we can look at the form of these differential equations to gain insight into how the baroreflex functions.

2 Approaches

For the left ventricular unstressed volume and minimum elastance, the differential equations were of the form

$$\frac{dX}{dt} = \frac{\bar{X} - X}{\tau_X}$$

where $\bar{X}$ is dependent on the rolling average left ventricular pressure and volume. In the original blood withdrawal model, the time varying parameter for systemic resistance appeared to be composed of two components with different time scales. Therefore, we modeled systemic resistance as an additive resistance with slow and fast components:$R_s(t) = R_{ss}(t) + R_{sf}(t)$. The variables R_{ss} and R_{sf} were both governed by differential equations of the a similar form to those for left ventricular unstressed volume and minimum elastance. The parameters for each of these differential equations were initially estimated by fitting our modeled variables to the time varying parameters used in the original blood withdrawal model.

3 Full Model Results

The differential equations for systemic resistance, unstressed volume and minimum left heart elastance were incorporated into an existing model of the cardiovascular system. We therefore considered a system of nine differential equations, with both original parameters from the cardiovascular model and additional parameters that described the dynamics of the new variables. Sensitivity analysis on this extended system revealed that the parameters of the minimum heart elasticity differential equation are most sensitive, while the parameters of the resistance variable are moderately sensitive. Our results also suggested that it may be important to include a volume-dependent mechanical effect on the unstressed volume variable, together with the pressure-dependent baroreflex effect under inflammation.

The sensitivity analysis also allowed us to reduce the computational cost of a large parameter optimization of the system by restricting our attention to the most sensitive parameters. While the fits of the available pressure and volume data were not improved compared to using time-varying parameters, this approach can be refined to obtain better optimization of the parameters. Next steps for the project include starting the new variables from steady-state value initial conditions, choosing better nominal fit parameters, and adapting the objective function in parameter optimization.