A cardiovascular-respiratory control system model including state delay with application to congestive heart failure in humans

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Abstract. This paper considers a model of the human cardiovascular-respiratory control system with one and two transport delays in the state equations describing the respiratory system. The effectiveness of the control of the ventilation rate $V_A$ is influenced by such transport delays because blood gases must be transported a physical distance from the lungs to the sensory sites where these gases are measured. The short term cardiovascular control system does not involve such transport delays although delays do arise in other contexts such as the baroreflex loop (see [46]) for example. This baroreflex delay is not considered here. The interaction between heart rate, blood pressure, cardiac output, and blood vessel resistance is quite complex and given the limited knowledge available of this interaction, we will model the cardiovascular control mechanism via an optimal control derived from control theory. This control will be stabilizing and is a reasonable approach based on mathematical considerations as well as being further motivated by the observation that many physiologists cite optimization as a potential influence in the evolution of biological systems (see, e.g., Kenner [29] or Swan [62]). In this paper we adapt a model, previously considered (Timischl [63] and Timischl et al. [64]), to include the effects of one and two transport delays. We will first implement an optimal control for the combined cardiovascular-respiratory model with one state space delay. We will then consider the effects of a second delay in the state space by modeling the respiratory control via an empirical formula with delay while the the complex relationships in the cardiovascular control will still be modeled by optimal control. This second transport delay associated with the sensory system of the respiratory control plays an important role in respiratory stability. As an application of this model we will consider congestive heart failure where this transport delay is larger than normal and the transition from the quiet awake state to stage 4 (NREM) sleep. The model can be used to study the interaction between cardiovascular and respiratory function in various situations as well as to consider the influence of optimal function in physiological control system performance.

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1. Introduction

The cardiovascular system functions to maintain adequate blood flow to various regions of the body. This function depends upon the interaction of a large number of factors including blood pressure, cross-section of arteries, cardiac output, and partial pressures of CO₂ and O₂ in the blood. There are global control mechanisms that act on the entire system to maintain appropriate blood flow and these mechanisms are supplemented by local mechanisms in each vascular region which act to shunt blood to those regions where demand is high and away from areas where demand is low. The overall control process which stabilizes the system is quite complicated and not fully elucidated. Principles of optimal control theory will be applied to design a control mechanism for this system. For further details about the cardiovascular system and control see, e.g., Rowell [55].

When breathing is not under voluntary control or subject to neurologically induced changes, the human respiratory control system varies the ventilation rate in response to the levels of carbon dioxide CO₂ and oxygen O₂ in the body (via partial pressures \( P_{aCO_2} \) and \( P_{aO_2} \)). This chemical control system depends upon information fed back from two sensory sites which monitor the blood gas levels (producing a negative feedback control loop). These sensory sites at which the blood gas levels are measured are a physical distance from the lungs (where blood gas levels are adjusted) and thus there are transport delays (which vary depending on blood flow) in the negative feedback loop. Under normal conditions (even with delays in the feedback control loop) the control system is sufficiently stable to maintain blood levels of these gases within very narrow limits. See, e.g., [11] or [13] for more information on this system.

There are a number of links between the respiratory and cardiovascular systems. Function of the respiratory system depends on blood flow through the lungs and tissues. The amount of oxygen O₂ transported to the tissues and carbon dioxide CO₂ transported away from the tissues depends on cardiac output \( Q \) and blood flow \( F \) through the pulmonary and systemic circuits. \( Q \) and \( F \) depend in turn upon heart rate \( H \), stroke volume \( V_{str} \), resistance in the vascular system \( R \), and blood pressure \( P \). Arterial blood pressure \( P_{ast} \) is controlled via the baroreceptor negative feedback loop which has important effects on \( H \), \( V_{str} \), \( R \), and hence \( Q \). Systemic resistance which impacts blood pressure is also influenced by local metabolic control acting on the resistance of the blood vessels of various tissues. This local control is in turn influenced by local concentrations of CO₂ and O₂, thus illustrating another important link between the two systems. The effect of concentration of O₂ on the resistance of the systemic blood vessels is included in this model. Furthermore, \( P_{aCO_2} \) and \( P_{aO_2} \) can affect cardiac output and contractility as well (see, e.g., Richardson et al. [54]). Neither these blood gas effects nor synchronization of heart rate and ventilation are included in this model.

An optimal control approach will be used to model the complex interactions in the cardiovascular-respiratory control system. The cardiovascular and respiratory controls are represented by a linear negative feedback control which minimizes a quadratic cost functional defining optimal performance. Reasons and motivation for incorporating an optimal control approach is given in Section 3. This modeling...