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# Control aspects of the human cardiovascular-respiratory system under a nonconstant workload[☆]

Pio Gabrielle B. Calderon[a], Mustafa Habib[b], Franz Kappel[c], Aurelio A. de los Reyes V[a,*]

[a] Institute of Mathematics, University of the Philippines Diliman, C.P. Garcia St., U.P. Campus, Diliman, 1101 Quezon City, Philippines
[b] Department of Mathematics, University of Engineering and Technology, Lahore, Pakistan
[c] Institute for Mathematics and Scientific Computing, University of Graz, Heinrichstraße 36, A-8010 Graz, Austria

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## ABSTRACT

The human cardiovascular system (CVS) and respiratory system (RS) work together in order to supply oxygen ($O_2$) and other substrates needed for metabolism and to remove carbon dioxide ($CO_2$). Global and local control mechanisms act on the CVS in order to adjust blood flow to the different parts of the body. This, in turn, affects the RS since the amount of $O_2$ and $CO_2$ transported, respectively to and away from the tissues depends on the cardiac output and blood flow in both the systemic and pulmonary circuits of the CVS. Local metabolic control is influenced by local concentrations of blood gases affecting systemic resistance, resulting to vasoconstriction/vasodilation. Thus, the exchange of blood gases demands a tight coordination between blood flow and ventilation of the lungs. In this work, a model of the cardiovascular-respiratory system (CVRS) is considered to obtain an optimal control for time-dependent ergometric workloads by using the Euler-Lagrange formulation of the optimal control problem. The essential controls in the CVRS model are variations in the heart rate and alveolar ventilation through which the central nervous system restricts the arterial partial pressure of $CO_2$ ($P_{a,CO_2}$) close to 40 mmHg. Further, penalization terms in the cost functional are included to match the metabolic need for $O_2$ and the metabolic production of $CO_2$ with $O_2$- and $CO_2$-transport by blood.

## 1. Introduction

One of the central tasks of the cardiovascular system (CVS) is to maintain an appropriate environment in various tissue regions of the body to guarantee optimal survival and function of the corresponding cells. As a major transport system, the CVS is responsible for supplying nutrients including oxygen ($O_2$) and substrates to the body tissues needed for metabolism, at the same time, removing carbon dioxide ($CO_2$) and other waste products of metabolism. In addition, the CVS also transports hormones to different parts of the body. The distribution of substances to various tissue regions is achieved by blood flow through the vessels of the two circuits of the CVS, the systemic and the pulmonary circuit. The systemic circuit distributes the substances in the body, whereas the pulmonary circuit, together with the lungs, is primarily responsible for the exchange of the blood gases $O_2$ and $CO_2$. In order for the CVS to accomplish its task, several control actions are necessary to adjust blood flow in different body regions. These control actions involve neural control, hormonal control, local control mechanisms or a combination of these. Neural control is responsible for the transmission of signals in the sympathetic and parasympathetic branches of the autonomic nervous system in response to signals generated by stretch receptors in various parts of the CVS. Hormonal control is characterized by hormones and ions secreted into the CVS and transported to various tissue regions. Local control mechanisms provide the ability of each tissue to control its own local blood flow necessary to meet its metabolic needs, such as delivery of oxygen and nutrients (glucose, amino acids, fatty acids, etc.) to the tissues and removal of $CO_2$ and hydrogen ions from the tissues [1–3].

The respiratory system (RS) is primarily responsible for the exchange of gases between the body tissues and the surrounding environment. Together with the CVS, it provides $O_2$ to the tissues and removes $CO_2$. The lungs extract $O_2$ from the surrounding air and supply it to the body tissues. Carbon dioxide produced by metabolism is removed from the tissues by the blood to the lungs and is lost to the outside air. The functions of the RS include pulmonary ventilation, which refers to the movement of air

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[☆] This paper is dedicated to Peter Kotanko, MD, Research Director (Renal Research Institute New York), Adjunct Professor of Medicine, Nephrology (The Mount Sinai Hospital, New York) on the occasion of his 60-th birthday.

[*] Corresponding author.
*E-mail address:* adlreyes@math.upd.edu.ph (A.A. de los Reyes V).

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between the surrounding atmosphere and the lung alveoli via inhalation and exhalation; diffusion of $O_2$ and $CO_2$ between the alveoli and the blood; transport of $O_2$ and $CO_2$ through the blood and body fluids to and from the tissue cells. In addition, when levels of $O_2$ and $CO_2$ in the body vary due to metabolic demands, the RS responds by regulating the ventilation rate. This mechanism, referred to as the chemical control system, monitors the blood gas levels from the two sensory sites. The information is fed back to the central respiratory center, influencing ventilation and producing a negative feedback control loop [1,4–6].

There are a number of key links requiring tight coordination between CVS and RS. The amount of $O_2$ and $CO_2$ transported to and away from the tissues, respectively, depends on the cardiac output and blood flow through the systemic and pulmonary circuits. Thus, cardiac output and ventilation must be coordinated for efficient loading and unloading of these blood gases. This coordination includes ventilation-perfusion matching, synchronization of heart rate and ventilation, and influence of blood gases on cardiovascular function. The two systems are also linked intimately to satisfy requirements of stable metabolism. The local metabolic control influences the systemic resistance by varying the degree of vasoconstriction/vasodilation. This local control is also affected by the local concentrations of $O_2$ and $CO_2$, demonstrating another important link between CVS and RS. Evidently, the two systems are intimately linked together based on the corresponding control actions. See for instance, [7–10].

Investigations of control mechanisms for the CVS are usually restricted to situations where a constant workload was imposed onto the system. In such a situation, the CVS tends to a new equilibrium state [8,11–13]. By imposing a time-varying workload onto the CVS, an equilibrium state is no more attainable. In fact, there is not even a state variable of the CVS tending to a constant value. Therefore, the question arises if there are quantities which are controlled to nominal values in a wide range of different situations. It has been observed physiologically that the arterial pressure of $CO_2$ is tightly regulated to about 40 mmHg [1]. Hence, in order to understand the actions of control mechanisms during a time-dependent workload, a combined cardiovascular-respiratory system (CVRS) must be considered.

In the current study, a mathematical model for the CVRS adapted from [8] is used to describe the overall response of the CVRS under a time-varying workload. The essential CVRS controls in the model include the baroreceptor and chemoreceptor loop. The signals generated by the baroreceptors in the aorta, which contain information on blood pressure, are used by the control center in the medulla in order to generate signals transmitted by the autonomous nervous system to the sine node in the heart in order to adjust the heart frequency accordingly. The influence of these signals on the contractility of the ventricles is not considered directly. According to the Bowditch effect, which states that heart rate and contractility of the ventricles are controlled concordantly, the contractility of the ventricle is assumed to be regulated by the heart frequency. For comprehensive studies concerning baroreflex regulation of heart rate and interaction of pulsatility and baroreceptor dynamics, refer to [14–26], and [27]. On the other hand, chemoreceptors are found in the carotid bodies located at the carotid sinuses and also in the aortic bodies. These sensors monitor the systemic arterial levels of $O_2$ and $CO_2$. Information from the sensory sites is collected, integrated, and translated into a ventilatory drive signal by the respiratory controller located in the medulla and pons. This ventilatory drive is conveyed to the respiratory muscles to regulate breathing. Based on information transmitted from the sensors regarding variations in blood gases, the respiratory center responds with changes in ventilation so as to restore the steady state of the system [1,8].

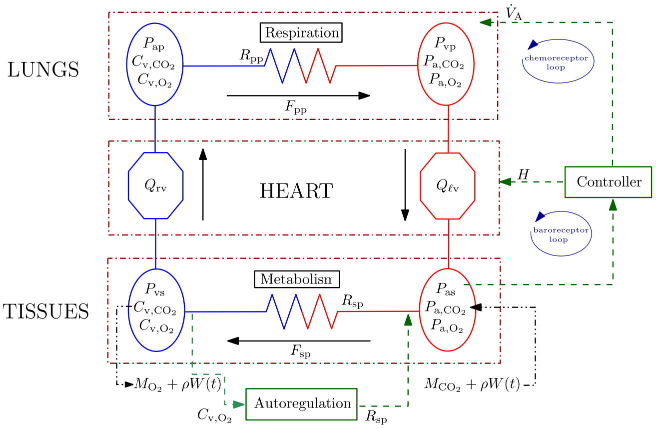

**Fig. 1.** Block diagram of the model depicting blood flow across the cardiovascular and respiratory parts as well as control loops considered.

An optimal control approach is used to model the interactions of the control mechanisms in the system. This modeling approach has been previously applied to study transition from rest to exercise under a constant workload [10,12,13], describe the response of CVRS under orthostatic stress conditions [28,29], and model congestive heart failure in humans [7]. The goal of the modeling effort in this study is to obtain an optimal control for nonconstant ergometric workload by using the Euler–Lagrange formulation of the optimal control problem. Moreover, the metabolic need for $O_2$ and the metabolic production of $CO_2$ had to be matched accordingly to some extent with $O_2$- and $CO_2$-transport by blood. This supports the approach in [30] that the metabolic demands of organs and tissues control the circulation and blood pressure.

This paper is organized as follows. Section 2 presents a cardiovascular-respiratory model adapted from Chapter 3 of [8]. The control problem is presented in Section 3 where two different cost functionals are presented depending on the type of workload function imposed onto the system. Numerical considerations involving penalization terms in the cost functional and the computation of the control are included in Section 4. Numerical results, their interpretations and discussion for constant and sinusoidal workload are given in Section 5. Conclusions and future directions of the work are presented in the last section.

## 2. The model

We consider the model for the combined cardiovascular-respiratory system (CVRS) model presented in Chapter 3 of [8]. Fig. 1 shows the block diagram of the model depicting the different compartments and the blood flow across the cardiovascular and respiratory parts. The model under study is an average flow model where the ventilation considered is minute ventilation and the blood flow is unidirectional and non-pulsatile. Further, blood pressures are interpreted as mean values over the length of a pulse.

The model assumes that the cardiovascular system (CVS) is comprised of four main compartments including the arterial (a) and venous (v) parts of the systemic (s) and pulmonary (p) circuit. These compartments are connected to each other via regions consisting of smaller vessels (capillaries, arterioles and venules) which make up the systemic (sp) and pulmonary (pp) peripheral region. Vessels in the four main compartments are assumed to be compliance vessels, while those in the peripheral regions are resistance vessels. The dynamics of the cardiovascular system is described using nine state variables, consisting of the pressure in each of the main compartments ($P_{as}$, $P_{vs}$, $P_{ap}$, $P_{vp}$), the contractilities of the left