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Modelling of long-term and short-term mechanisms of arterial pressure control in the cardiovascular system: An object-oriented approach

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ABSTRACT

A mathematical model that provides an overall description of both the short- and long-term mechanisms of arterial pressure regulation is presented. Short-term control is exerted through the baroreceptor reflex while renal elimination plays a role in long-term control. Both mechanisms operate in an integrated way over the compartmental model of the cardiovascular system. The whole system was modelled in MODELICA, which uses a hierarchical object-oriented modelling strategy, under the DYMOLA simulation environment. The performance of the controlled system was analysed by simulation in light of the existing hypothesis and validation tests previously performed with physiological data, demonstrating the effectiveness of both regulation mechanisms under physiological and pathological conditions.

1. Introduction

The regulatory control of the cardiovascular system has been more intensively studied than any other physiological system [1], which can be attributed at least in part to the high rate of cardiovascular diseases.

The mechanisms responsible for maintaining arterial blood pressure may be divided into short-term processes, which are effective over a period of seconds to hours, and mid- and long-term processes, which operate over days to weeks [2]. The short-term mechanism is largely based on neural control through the receptors in the heart and blood vessels, which sense blood pressure, together with the autonomic nervous system (ANS), which regulates cardiac function and the diameter of the resistance and capacitance vessels. Mid-term control is basically of a hormonal nature whereas the renal system plays the central role in long-term control.

Cardiovascular modelling and control present a particular challenge and require both a multi-scale and multi-physics approach [3]. Several mathematical models of the closed loop cardiovascular system have been developed [4,5] and distinct simulation development tools have been used for graphic notation of the structure of physiological regulation's systems, including that of the cardiovascular control system [6–8].

Traditionally, mathematical models are presented through a series of differential and algebraic equations with the option of a block diagram representing the interconnections of various subsystems [9]. In recent years, various specialized and general-purpose modelling software applications have been applied to the modelling and control of physiological systems, and are commonly divided into structure-oriented and equation-oriented. Most software follows a causal modelling approach and requires either the explicit coding of mathematical model equations or the representation of systems in a graphical notation such as a block diagram, as occurs in SIMULINK [10,11], thus differing substantially from the more common representation of physiological knowledge.

The object-oriented approach can offer many advantages in physiological system modelling and control when dynamics are given by a set of differential algebraic equations (DAE) [12]. This object-oriented approach can be implemented using modelling language such as MODELICA [13], or SIMSCAPE [14,15] among others, which allow the system, subsystem, or component levels of a whole physiological system to be described in increasing detail using a hierarchical structure.

While several MODELICA applications have been reported in different fields of engineering, few studies have considered biomedical system modelling [16–18], particularly cardiovascular modelling and control [19], although a SIMSCAPE application in this field has recently been reported [20].

In this paper we describe the use of the MODELICA modelling language under the DYMOLA simulation environment for the object-oriented modelling of the cardiovascular regulatory system,

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considering both the short- and long-term pressure control mechanisms. For this task we followed a hierarchical structure that has previously been validated to represent the cardiovascular dynamics as a multi-compartmental system. The results were obtained under both physiological and pathological conditions, namely, hypertension due to either increased values of peripheral resistance, heart rate or intravascular volume by liquid intake, and hypotension due to either diminished values of vascular elastance, heart rate or severe haemorrhage, taking into account the validation tests previously performed with physiological data.

2. Methods

The cardiovascular model represented here is constituted by a set of nonlinear equations describing its dynamics and is based on previous studies by Ferrari et al. [21]. However, unlike in this previous study, a multi-compartmental acausal modelling approach was followed.

2.1. Modeling of the cardiovascular control system

The cardiovascular system model will be described using seven compartments, namely, the two ventricles, the arterial and venous pulmonary circulation and the systemic circulation constituted by the aorta, peripheral circulation and vena cava (Fig. 1), where the arterial compartment is considered as a simple windkessel model.

Each compartment is modelled using a mathematical relationship between blood volume $V_i(t)$, input flow rate $F_{i_{in}}(t)$ and output flow rate $F_{i_{out}}(t)$ relative to the ith compartment given as

$$\frac{dV_i(t)}{dt} = F_{i_{in}}(t) - F_{i_{out}}(t) \quad i = 1,\ldots,7 \tag{1}$$

with flow rate $F_{ij}(t)$ between compartments i and j defined in general by

$$F_{ij}(t) = \frac{P_i(t) - P_j(t)}{R_{ij}} \quad i = 1,\ldots,7 \text{ and } j = i-1 \tag{2}$$

or in the case of flow rate through a valve by

$$F_{ij}(t) = \frac{lim(P_i(t) - P_j(t))}{R_{ij}} \tag{3}$$

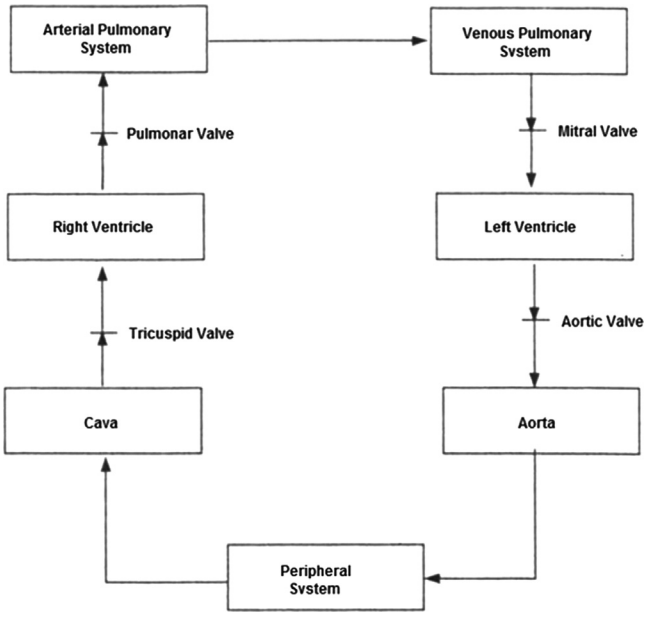

Fig. 1. Compartmental model of the circulatory system.

where R_{ij} stands for the resistance to the flow between compartments i and j, while the function $\lim(x) = \max(x, 0)$.

The relation between pressure $P_i(t)$ and volume $V_i(t)$ in each systemic and pulmonary compartment is given by

$$P_i(t) = E_i V_i(t) \quad i = 1,\ldots,5 \tag{4}$$

where E_i stands for the elastance of compartment i, while the heart contraction and ejection processes are described in each ventricle according to [21] by the linearized pressure–volume relation

$$P_V(t) = \begin{cases} P_{Vl}(t) + E_{Vs}(t)(V_V(t) - V_{V0}) & \text{systole} \\ E_{Vd}(V_V(t) - V_{V0}) & \text{diastole} \end{cases} \tag{5}$$

where $P_{Vl}(t)$ is the isovolumetric pressure at the initial linearization point V_{V0} with peak value of P_{Vpk}, while E_{Vd} and $E_{Vs}(t)$ represent the diastolic and systolic ventricular elastances, with both $P_{Vl}(t) = P_{Vpk}a(t)$ and $E_{Vs}(t) = E_{Vd} + E_{Vs}a(t)$ showing the time-dependence of the ventricular pressure with the activation function given by $a(t) = (1/2)(1 - \cos(2\pi t/t_s))$ during the systole period $0 \le t \le t_s$ and being null during the diastole period $t_s \le t \le t_c$, with t_c representing the cardiac cycle time (inverse of heart rate H_c) and $t_s = 0.16 + 0.3t_c$.

Short-term control of arterial pressure is achieved by the baroreceptor system, which Mitamura et al. [22] reported to regulate the heart rate, the ventricular elastances, the cava elastance and the peripheral system resistance as a function of the mean aortic pressure value through a first-order filter with transfer function $H_j(s)$

$$H_j(s) = \frac{k_j}{\tau_j s + 1} \quad j = 1\ldots4 \tag{6}$$

and a dead zone as shown in Fig. 2, where k_j and τ_j stand for the corresponding gain and time constant of each filter, while s denotes the Laplace complex variable.

Long-term control of arterial pressure is accomplished by the renal system through the elimination of urine. In order to model this effect it was assumed [23] that there is a linear relation between the renal excretion flow rate $J_u(t)$ and the plasmatic volume $V_p(t)$, stated as

$$J_u(t) = \begin{cases} K_{ud}\left(\frac{V_p(t) - V_{pn}}{V_{pn}}\right) + J_{un}, & V_p(t) < V_{pn} \\ K_{uo}\left(\frac{V_p(t) - V_{pn}}{V_{pn}}\right) + J_{un}, & V_p(t) \ge V_{pn} \end{cases} \tag{7}$$

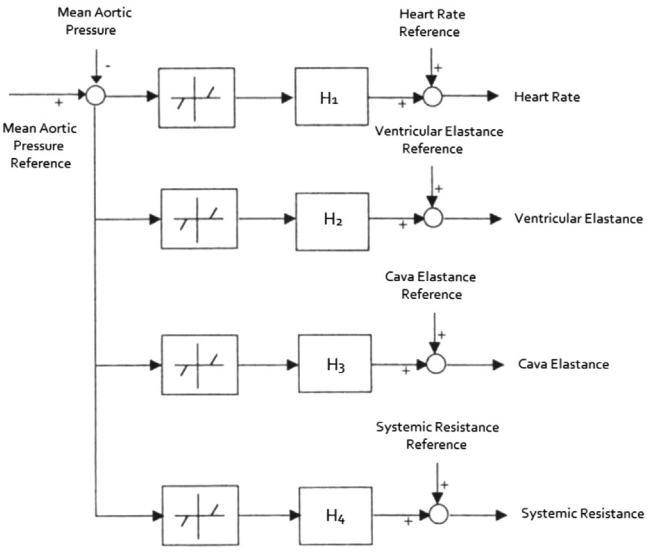

Fig. 2. Diagram of the baroreceptor regulatory system.