Mathematical Modeling of Cardiovascular System Dynamics Using a Lumped Parameter Method

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Abstract: This work reviews the main aspects of cardiovascular system dynamics with an emphasis on modeling hemodynamic characteristics by the use of a lumped parameter approach. The methodological and physiological aspects of the circulation dynamics are summarized with the help of existing mathematical models. The main characteristics of the hemodynamic elements, such as the heart and arterial and venous systems, are first described. Distributed models of an arterial network are introduced, and their characteristics are compared with those of lumped

parameter models. We also discuss the nonlinear characteristics of the pressure–volume relationship in veins. Then the control pathways that participate in feedback mechanisms (baroreceptors and cardiopulmonary receptors) are described to explain the interaction between hemodynamics and autonomic nerve control in the circulation. Based on a set-point model, the computational aspects of reflex control are explained. [The Japanese Journal of Physiology 54: 545–553, 2004]

Key words: lumped parameter model, dynamics of the cardiovascular system, autonomic nerve control.

Introduction

The cardiovascular system is responsible for supplying the tissues and organs of the body with oxygen and other nutrients required for their metabolic needs, and its proper functioning is critical for an individual's optimal performance. Cardiovascular disease is a major cause of death in humans. Many experimental studies have examined the mechanisms and therapies of cardiovascular diseases. Along with the experimental approach, mathematical modeling has become a popular way to analyze the cardiovascular system.

Many mathematical models of the cardiovascular system have been published since Grodins [1] made the first global dynamic model of one in 1959. There is a wide variety of such models, which depends on their purpose and the methodology used [2–10]. Researchers have approached the modeling problem

from several different perspectives. Some subjects that have been extensively studied include hemodynamic models of specific vascular beds, such as the coronary or cerebral circulation [11–15]; the distributed impedance of arterial and pulmonary stress [6, 7, 16, 17]; lumped models of the integrated cardiovascular system [5, 9, 18, 19]; and hemodynamic control system [8, 20].

This paper reviews the fundamental issues in the development of lumped models of the integrated circulatory system combined with short-term nerve control. The models, related with the response to thermal stress, are not considered here because of the complexity of the underlying mechanisms. Furthermore, local circulations, such as coronary, cerebral, and renal circulation, are not discussed here. We emphasize the fundamentals and recent progress in models of the overall cardiovascular system, using the lumped

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parameter method combined with an autonomous nerve system for controlling heart mechanics and vessel hemodynamics.

Lumped Parametric Approximation of The Hemodynamic System

A model-based understanding of the fundamentals of blood flow dynamics, or *hemodynamics*, is important for the diagnosis and management of diseases of the cardiovascular system, including coronary artery and heart muscle dysfunction, valvular disorders, and pulmonary disease. Models of the cardiovascular system will help in understanding these conditions, ultimately leading to improved treatment. Of several modeling approaches, the lumped parameter model has become a popular way to analyze the hemodynamics of the cardiovascular system.

In general, cardiovascular system models consist of two major parts: the hemodynamic system and the autonomic nerve control, as shown in Fig. 1. The hemodynamics of vessels can be represented by the relationship between blood pressure and blood flow rate in the cardiovascular system. In the lumped model, the hemodynamic elements of the cardiovascular system are expressed as a series of equivalent elements in an electric circuit, as shown in Fig. 2. The application of Kirchhoff's law to each node in the lumped parameter hemodynamic model leads to the following differential equation for mass conservation.

$$\frac{dV}{dt} = Q_{in} - Q_{out} \quad (1)$$

where

$$Q = (P_i - P_o)/R \quad (2)$$

Fig. 2. Electrical analog of vascular hemodynamic elements. (a) Hemodynamic elements of a blood vessel. (b) Equivalent electric circuit.

$$P = V/C \quad (3)$$

In these equations, V is the volume of a compartment, Q is the flow rate, P is the pressure, and C is the capacitance. A new volume can be calculated from the flow rates derived by using Eq. 2. After obtaining the volume, the pressures at the nodes are calculated by using Eq. 3. The application of this formula to the other nodes enables us to obtain all the lumped information of the cardiovascular hemodynamics. In the remainder of this chapter, we briefly review hemodynamic modeling of circulation elements, using the lumped parameter approach.

Heart modeling. The ventricle in the cardiovascular system can be approximated as a chamber with

Fig. 1. Schematic of the cardiovascular system.

an entrance and an exit valve, whose compliance changes as a function of time. The compliance can be replaced by a capacitor in an electric analog. This approach is called the variable capacitor model. In 1982, Campbell *et al.* [21] developed a five-compartment model of the cardiovascular system with capacitances that vary with time, as proposed by Sunagawa and Sagawa [22]. This method has been used in most of the published cardiovascular system models [8, 22–24] because it is relatively simple and easily incorporates experimental results concerning the pressure–volume relation of the ventricle. In this method, the left ventricular capacitance varies between a minimum value during systole and a maximum value during diastole, using predetermined functions that are taken from elastance curves obtained in animal experiments [25].

In terms of the variable capacitor model, both ventricles are characterized by time-dependent compliances that vary between a minimum end-systolic value and a maximum diastolic one according to a predefined function. Estimates of the left ventricular maximum diastolic compliance, $C_{l,diast}$, are frequently based on estimates of the left ventricular end-diastolic elastance, $E_{l,diast}$ ($E_{l,diast} = 1/C_{l,diast}$). The latter is reported to range from 0.15 to 0.6 mmHg/ml for normal subjects [26]. If directly translated into $C_{l,diast}$, these values suggest a maximum diastolic left ventricular capacitance of 1.7 to 6.7 ml/mmHg. The right ventricular maximum diastolic capacitance, $C_{r,diast}$, is approximately twice the left ventricular value [27]. The left ventricular end-systolic elastance, $E_{l,sys}$, is

reported to be 2.0 ± 0.7 mmHg/ml [28]. When translated into $C_{l,sys}$, a value close to 0.5 ml/mmHg seems reasonable [26]. The right ventricular end-systolic capacitance, $C_{r,sys}$, ranges from 0.35 to 1.6 ml/mmHg [27]. The pumping action of the ventricles is realized by varying the ventricular capacitances between $C_{r,diast}$ and $C_{r,sys}$, a $C_{l,diast}$ and $C_{l,sys}$ [28]. During systole, the right and left ventricular elastances, $E_r(t)$ and $E_l(t)$, change from their respective minimum diastolic value to their end-systolic value according to a half-sine function. During early diastolic relaxation, they change from their respective end-systolic values to their minimum diastolic values according to a half-cosine function. During the remaining diastolic time, the elastances stay at their minimum diastolic values. The ventricular compliances are computed by the use of $C(t) = 1/E(t)$. An example of the left ventricular elastance as a function of time is depicted in Fig. 3 [23] and the data are compared with the experiment [28].

In consideration of the overall cardiovascular system, atrial contraction is not important at normal heart rates, whereas it is critical for adequate ventricular filling at high rates during exercise. Except for studies of the hemodynamic response to exercise, a relatively simple approximation is assumed for atrial function in cardiovascular modeling. In some papers, the atria are not represented explicitly; their function is partially absorbed into the function of the adjacent compartments [23, 24]. Ursino *et al.* [29–31] assumed noncontracting atria that were approximated simply by using a constant capacitor in their model.

Fig. 3. Left ventricular elastance vs. time. T_s means a systole time duration, whereas T_D represents a diastole time duration. The data generated from the variable capacitor model are compared with the experiment of Serizaki *et al.* [28].

Arterial network. In the lumped parameter model, the average pressure and flow rate are modeled as the electric potential and current, respectively. An arterial vessel is described by using its impedance, which is represented by an appropriate combination of resistors, capacitors, and inductors. The resistors are used to model viscous dissipation, and the capacitors account for artery compliance: the ability to accumulate and release blood by elastic deformation. The inductors are used to model convective inertia terms (Fig. 2).

There are two popular types of models for representing arterial networks in models of the cardiovascular system: lumped parameter models and distributed models. Some models are based on lumped parameter representations of the arterial networks [32–38], and others model vessel hemodynamics by using the fluid dynamic equations that govern flow through a distributed, compliant network [39–42]. Lumped parameter models are generally successful in illuminating the complex interaction of the major hemodynamic elements and the control system. However, their inability to represent the spatial distribution of hemodynamic elements is a severe limitation of their use in clinical studies.

Guyton *et al.* [36] developed a refined lumped parameter model of the cardiovascular system that embodies the behavior of the interacting cardiovascular, renal, and respiratory systems, including hormones and blood chemistry, using over 350 com-

partments. Avolio [3] proposed a lumped parameter model in which a 128-segment arterial network was solved computationally. Stettler *et al.* [43] developed a distributed representation of the arterial system. Unlike the lumped approximation for the arterial system, they solved the fluid mechanics equations for one-dimensional momentum and continuity by using the finite difference method and the method of characteristics (Fig. 4). They also included the effects of wall viscoelasticity and periodic wall shear. Xiao *et al.* [44] presented a model-based assessment of cardiovascular health by using a noninvasive method of evaluating several of these parameters, including systemic vascular resistance, maximum left ventricular elasticity, end diastolic volume, and cardiac output. The method is based on a distributed arterial model of the human cardiovascular system (28 arterial segments) to generate a solution library. They also used this to simulate the hemodynamics created by enhanced external counterpulsation, which is used to aid a failing heart by sequentially inflating cuffs on the lower extremity, out-of-phase with the left ventricle.

Systemic microcirculation. The term “microcirculation” includes the arterioles, precapillary sphincters, capillaries, and postcapillary venules. It is often assumed that the major resistive component in the systemic circulation is at the level of the microcirculation. In general, the dimension of the resistance is expressed in “peripheral resistance units (PRU: mmHg s/ml).” The total peripheral resistance of a

Fig. 4. An example of the distributed representation of the arterial network in the upper body.

human is close to 1 PRU, which is given as the cardiac output divided by the pressure difference between arteries and veins.

The degree of complexity of microcirculation modeling is dictated by the nature of the questions being asked and the region of the study's focus. For example, some models assume that the microcirculation is a resistor [24, 33] whose value is nearly 1 PRU, and others use a multibranched approximation for the microcirculation [31, 32]. The microcirculation is especially important in hemodialysis simulation [45–47] and microgravity modeling of the circulation [23, 48].

Melchior *et al.* [25] and Ursino *et al.* [29] presented a two-branch model in which the microcirculation compartment is divided into two pathways: lower limb and the remaining compartment except this. By contrast, Heldt *et al.* [23] used a four-branch model of the microcirculation to simulate orthostatic intolerance. They modeled arteriolar resistance to produce a total peripheral resistance of 1.0 PRU based on estimates of the distribution of cardiac output (CO) to the four circulatory branches (upper body [23% of CO], kidney [22% of CO], splanchnic circulation [30% of CO], and lower body [25% of CO]).

In the hemodialysis simulations using a lumped model done by Ursino's group [45–47], mass transfer in the blood-tissue-dialysate system was simulated with a model having three compartments: intracellular, interstitial, and plasma compartments. Fluid exchange between the intracellular and interstitial compartments depends on the osmotic concentration, whereas the hydraulic and osmotic pressure gradients at the capillary compartment determine fluid exchange between the interstitial fluid and plasma. The blood volume change during hemodialysis activates the autonomous nerve control mechanism of the cardiopulmonary reflex resulting from the variation of the returned blood volume to the right atrium.

Venous network and pulmonary circulation.

Capillaries unite to form veins, which convey blood back to the heart. To model the venous system with a lumped parameter model, resistance and capacitance values must be approximated. Compared with the systemic microcirculation, the resistance to blood flow in a vein is very low. In a complex model, Beneken [49] used individual peripheral venous resistance values that produced an overall venous resistance of 0.08 PRU. However, the venous transmural pressure in parts of the dependent vasculature can reach levels at which the nonlinear nature of the venous pressure–volume relation becomes important [50]. In particular, the lower limb, splanchnic, and

abdominal venous compartments show nonlinear pressure–volume relations. The following equation is one example of a nonlinear relation proposed by Melchior *et al.* [24]:

$$\Delta V = \frac{2\Delta V_{\max}}{\pi} \arctan\left(\frac{\pi C_0}{2\Delta V_{\max}} \Delta P_{\text{tran}}\right) \quad (4)$$

where ΔV is the change in compartment volume because of a change in transmural pressure, ΔP_{tran} . $\Delta V_{\max}$ is the maximal change in compartment volume, and C_0 is the compartment compliance at baseline transmural pressure. A schematic diagram of this relation is depicted in Fig. 5. An abrupt decrease in venous volume in the curve means vessel collapsing, and this phenomenon has been computed by Luo and Pedley [51] and Shim and Kamm [52].

As far as we know, no distributed model for the venous network has been proposed. However, it is worth noting that a distributed venous model may be more important in studies of venous-related diseases than a distributed arterial model because of the critical role of blood volume shifts between different vascular compartments on the venous side.

The pulmonary vasculature has the comparatively easy task of forcing blood through the low-resistance lung vasculature and returning it to the left heart. In nature, an accurate model of the pulmonary system requires a nonlinear “vascular waterfall” resistance and a nonlinear pulmonary capacitance [53]. Linear models are generally chosen to produce acceptable behavior for the integrated system.

Fig. 5. Pressure–volume relation in veins.

Short-Term Nerve Control of the Cardiovascular System

The hemodynamic properties of the cardiovascular system are modulated by a network of homeostasis-maintaining feedback mechanisms. This feedback control system must account for the major reflex mechanisms that govern the short-term behavior of the cardiovascular system, i.e., the two major neurally mediated cardiovascular reflexes: the arterial baroreflex and the cardiopulmonary reflex. This review does not consider long-term controls that are concerned with fluid and electrolyte regulation, such as the renin-angiotensin-aldosterone system, arterial natriuretic peptide, or ADH. Under certain conditions there may be important interactions between chemoreceptors and the baroreceptor reflex, but this is not considered here. A schematic representation of short-term regulation is depicted in Fig. 6. This figure shows the autonomous nerve control with the baroreceptor reflex and the cardiopulmonary control systems. Locally sensed blood pressures at carotid artery (P_A) and central vein (P_V) are relayed to the autonomic nervous system (ANS) where error signals (P_A^{eff} , P_V^{eff}) are generated by subtracting predefined set-point values (P_A^{ref} , P_V^{ref}) from the afferent pressure signals (P_A , P_V). These error signals subsequently dictate the efferent activity of the reflex model via parasympathetic and sympathetic arcs, such that the error signals in the following computational steps approach zero.

Baroreceptor reflex control. The baroreflex system consists of the carotid and aortic baroreceptors, which have different sensitivities [54]. However, no published papers include both receptors simultaneously using the lumped parameter approach. These receptors transfer a signal to the autonomic nervous system. A fast parasympathetic reflex via the vagus nerve tightly controls heart rate through the sinoatrial (SA) node, and slower sympathetic fibers modulate the strength of ventricular contraction and peripheral vascular tone besides making a slow contribution to the heart rate.

Many papers have implemented baroreflex control. DeBoer *et al.* [54] proposed the set-point model of the arterial baroreflex. The short-term control mechanism implemented by Heldt *et al.* [23] and Shim *et al.* [24] is based on a set-point model that aims at maintaining a constant mean arterial blood pressure by adjusting the heart rate, peripheral resistance, venous tone, and right and left end-systolic cardiac capacitance dynamically (Fig. 6).

Cardiopulmonary reflex control. Cardiopulmonary receptors, which are in the atria, ventricles, and pulmonary vasculature, provide the controller with information about blood volume. Their effector mechanisms include varying arteriolar and venous tone, but with anatomic patterns that differ from the arterial baroreceptors. Melchior *et al.* [55] first introduced modeling of the cardiopulmonary reflex to simulate orthostatic intolerance. This model, combined

Fig. 6. Control mechanisms, including two pathways.

with that of the arterial baroreflex, was modified by Ursino *et al.* [56] to mathematically investigate physiological factors involved in hemodialysis hypotension. Heldt *et al.* [29] integrated the arterial baroreflex and cardiopulmonary reflex loop in their lumped parameter model. They considered the interaction between them based on the experimental observation that central hypovolemia leads to an increase in the heart rate gain of the arterial baroreflex.

Conclusion

In this paper we reviewed the main aspects of cardiovascular system dynamics with an emphasis on modeling hemodynamic characteristics by using a lumped parameter approach. The hemodynamic elements, such as the heart and arterial and venous systems, were described. We also discussed the nonlinear characteristics of the pressure-volume relationship in veins. The control pathways that participate in feedback mechanisms (baroreceptors and cardiopulmonary receptors) were described to explain the interaction between hemodynamics and autonomic nerve control in the circulation.

We believe that simulation technology combined with powerful computing resources can make major contributions to assessing the blood hemodynamics in the circulation. Furthermore, experimental results can be interpreted more effectively with the aid of a computational model that simulates the critical components and behaviors of the cardiovascular system. Experiments are used to refine models and specify their parameters. Conversely, models illuminate and enhance the interpretation of the experimental results. We view experiments and computational models as highly synergistic because the value of one is greatly enhanced by the existence of the other. It could be argued that these are not merely advantages, but that they are *essential* aspects of the study of blood hemodynamics associated with cardiovascular diseases.

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