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A multiple-input multiple-output system for modeling the cardiac dynamics

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Abstract—**We describe the dynamics of the cardiovascular system by finding the input-output relationships in the state space of a functional cardiac model, based on state equations and observability criteria of control theory. The unit step response of the multiple-input multiple-output system model illustrates the damping effect of the arterial wall to the pulsatility of the heart. Our results show that hypertensive patients exhibit a lower inertia of the blood flow.**

I. Introduction

Mathematical modeling is now widely applied in physiology and medicine to support the life scientist and clinical worker. A model is, by definition, an approximation of a system in terms of its representation [1]. The vascular system is a widely studied physiological system. Its hemodynamic characteristics, such as total peripheral resistance, total arterial compliance and characteristic impedance of the proximal aorta allows us to understand the cardiovascular system [2]. Although mathematical modeling and parameter estimation may help understanding the performance of the system, the strong interactions between the characteristics of the vascular system make it difficult for a deeper understanding. A well known model to operate with the vascular characteristics is the Windkessel model.

The Windkessel model, developed by Otto Frank, expresses heart and systemic arterial system as a closed hydraulic circuit comprising a water pump connected to a chamber. The circuit is filled with water except for a pocket of air in the chamber. Water is pumped into the chamber, and both it compresses the air in the pocket and pushes water out of the chamber, back to the pump. The elasticity and extensibility of the main artery is simulated by the compressibility of the air in the pocket, as blood is pumped into it by the heart ventricle. This effect is commonly referred to as *arterial compliance,* capacitor C. The term compliance is the parameter that specifies the elastic nature of the blood vessels. It is defined as the incremental change in volume that would result from an incremental change in pressure.

The resistance water encounters while leaving the Windkessel and flowing back to the pump, simulates the resistance to flow encountered by the blood as it flows through the arterial tree from the major arteries, to minor arteries, to arterioles, and to capillaries, due to decreasing vessel diameter. This resistance to flow, R, is known as *peripheral resistance* [3], [4].

We consider the four-element Windkesse1 model, first proposed by Burathi and Gnudi in 1982 [5]. This model is shown schematically in Fig. 1 and it consists of parallel connection of resistor and capacitor. Resistor R_p represents total peripheral resistance and capacitor C stands for compliance of vessels. Another resistive element between the pump and the air-chamber, R_c, simulates the resistance to blood flow due to the aortic or pulmonary valve. L is an inertial element in parallel with the characteristic resistance R_c. With this arrangement, the model can account for the inertia of the whole arterial system at low frequencies and at medium and high frequencies permits the characteristic resistance to come into play [6].

Other authors have modeled the cardiovascular system based on either the two, three or four-element Windkessel model, to estimate parameters [2],[7], to simulate the waveform of the pressure signal [8], or to study some specific characteristics, [9-12].

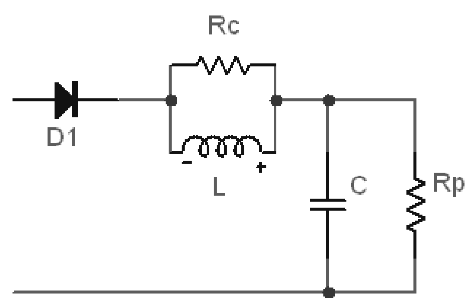

Fig. 1. Four-element Windkessel model

Our goal is to describe the dynamics of the cardiovascular system by finding the input-output relationships in the state space, assuming the heart as a stable biological system with feedback [13],[14].

In this paper we use observability criteria and state equations to simultaneously calculate multiple relationships that partly characterize the cardiac dynamics.

II. Methods

A. Data

We used public data from MIMIC II (Multiparameter Intelligent Monitoring in Intensive Care) Clinical Database, made available by Physionet [15]. Each record in the MIMIC II Clinical Database contains information about a single patient, who had been admitted to an ICU. The database also includes thousands of records of continuous high-resolution physiologic waveforms and minute-by-minute numeric time series of physiologic measurements. We considered only those records in the database matching waveform and clinical data. Some records were discarded due to lacking of clinical information, in particular of stroke volume data, needed to calculate arterial compliance using the area method as explained later.

Table I lists data from the MIMIC II database. Columns 2 and 3 show systolic and diastolic pressures respectively. In column 4 the calculated compliance for each record is listed.

Values in column 5 indicate the differential pressure (i.e. SP-DP), a variable which is associated to the inertia of the system.

TABLE I
CALCULATED COMPLIANCE AND OBSERVABILITY DETERMINANT

Signal	**SP mmHg**	**DP mmHg**	**C x 10^{-4} cm^3/ mmHg**	**SP-DP mmHg**	**Det (Obs)**
a40002	110.89	78.63	1.01	32.26	0.95
a40006	124.4	56	3.76	68.4	0.09
a40050	106.8	53.52	2.30	53.28	0.2
a40096	102.64	62.46	3.15	40.18	0.12
a40277	94	67.02	1.52	26.98	0.43
a40329	133.4	41.8	1.66	91.6	0.36
a40384	110	47.8	0.73	62.2	1.84
a40424	100	49.65	4.94	50.35	0.07
a40493	94.56	42	1.32	52.56	0.57
a40551	116,04	57,12	1,88	58.92	0.29
a40717	125.44	53.89	2.42	71.55	0.18
a40764	101.92	54.96	1.12	46.96	0.78
a40921	138.1	80.9	1.51	57.2	0.44
a40928	98	41.12	1.35	56.88	0.54
a40937	115.44	53.84	1.31	61.6	0.58
a41137	139.55	78.22	2.02	61.33	0.25
a41694	108.32	40.04	1.29	68.28	0.59
a41770	93.28	57.12	7.09	36.16	0.06

B. The area method to calculate compliance

We use the area method to estimate compliance. It is based on a linear relation between pressure and volume [16], taking into account the area under the pressure curve above a constant level. The method makes use of the equation

$$C = \frac{SV}{K\left(P_s^* - P_d\right)}$$

where

$$K = \left(A_s + A_d\right) / A_d$$

is an area index, expressing the ratio of the total area under the aortic pressure curve divided by the diastolic area. The area A_s goes from the start of the cycle up to the time of the dicrotic notch of the aortic pressure curve. A_d goes to end of diastole. *SV* represents the *Stroke Volume*. P_s^* is the pressure at the instant of the dicrotic notch and P_d stands for diastolic pressure.

C. Modeling in the state-space

As the operation of the cardiac system involves many variables such as pressure, blood density, compliance, arterial wall resistance, among others, it would be best modeled by a MIMO system. We designed such model by connecting two SISO (single-input single-output) systems in parallel. The input matrix represents two variables: compliance and inertia of blood flow.

The transfer functions for the four-element Windkessel model, with 2 inputs and 2 outputs are:

$$\begin{aligned} & s^2 E_{o1}(s) + sE_{o1}(s)\frac{1}{\tau} + E_{o1}(s)\frac{1}{C} = E_i(s)\frac{1}{C} \\ & s^2 L E_{o2}(s) + sE_{o2}(s)\tau + E_{o2}(s) = E_i(s) \end{aligned} \quad (1)$$

where τ is R_pC.
From (1), the state equations of the model are defined by:

$$\begin{aligned} & \ddot{e}_{o1} + \frac{1}{\tau}\dot{e}_{o1} + \frac{1}{C}e_{o1} = \frac{1}{C}e_{i1} \\ & \ddot{e}_{o2} + \frac{\tau}{L}\dot{e}_{o2} + \frac{1}{L}e_{o2} = \frac{1}{L}e_{i2} \end{aligned} \quad (2)$$

The input, output and state variables of the system are:

$$\begin{aligned} & x_1 = e_{o1} \;\; ; \quad e_{i1} = u_1 \\ & x_2 = \dot{e}_{o1} = \dot{x}_1 \\ & \dot{x}_2 = -\frac{1}{C}x_1 - \frac{1}{\tau}x_2 + \frac{1}{C}u_1 \end{aligned} \quad (3)$$

$$\begin{aligned} & x_3 = e_{o2}; \quad e_{i2} = u_2 \\ & x_4 = \dot{e}_{o2} = \dot{x}_3 \\ & \dot{x}_4 = -\frac{1}{L}x_3 - \frac{\tau}{L}x_4 + \frac{1}{L}u_2 \end{aligned} \quad (4)$$

$$\begin{aligned} & y_1 = e_{o1} = x_1 \\ & y_2 = e_{o2} = x_3 \end{aligned} \quad (5)$$

In matrix notation:

$$\begin{aligned}\dot{\mathbf{x}} &= \mathbf{Ax}+\mathbf{Bu}\\ \mathbf{y} &= \mathbf{Cx}\end{aligned} \qquad (6)$$

where $\dot{\mathbf{x}}$ is the state vector, $\mathbf{y}$ is the output vector, $\mathbf{A}$ is the state matrix, $\mathbf{B}$ is the input matrix, $\mathbf{C}$ is the output matrix and $\mathbf{u}$ is the input vector .

Finally,

$$\begin{bmatrix}\dot{x}_1\\ \dot{x}_2\\ \dot{x}_3\\ \dot{x}_4\end{bmatrix}=\begin{bmatrix}0 & 1 & 0 & 0\\ -\frac{1}{C} & -\frac{1}{\tau} & 0 & 0\\ 0 & 0 & 0 & 1\\ 0 & 0 & -\frac{1}{L} & -\frac{\tau}{L}\end{bmatrix}\begin{bmatrix}x_1\\ x_2\\ x_3\\ x_4\end{bmatrix}+\begin{bmatrix}0 & 1 & 0 & 0\\ \frac{1}{C} & 0 & 0 & 0\\ 1 & 0 & 0 & 0\\ 0 & \frac{1}{L} & 0 & 0\end{bmatrix}\begin{bmatrix}u_1\\ u_2\\ u_3\\ u_4\end{bmatrix} \quad (7)$$

$$\begin{bmatrix}y_1\\ y_2\\ y_3\\ y_4\end{bmatrix}=\begin{bmatrix}1 & 0 & 0 & 0\\ 0 & 0 & 1 & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0\end{bmatrix}\begin{bmatrix}x_1\\ x_2\\ x_3\\ x_4\end{bmatrix}$$

where $u_3 = u_4 = 0$ and $y_3 = y_4 = 0$ to get a square matrix

D. *Observability of the system*

A system is fully observable if state $\mathbf{x}(t_0)$ is determined from the observation of $\mathbf{y}(t)$ for a finite time interval $t_0 \le t \le t_1$. Therefore a system is fully observable if all state transitions eventually affect all the elements of the output vector. The concept of observability is useful to solve the problem of recovering unmeasured state variables from measurable variables in the minimal possible time. Internal states can be inferred from external outputs.

For a system to be observable, the matrix of observability given by:

$$\mathscr{O} = \begin{bmatrix}C\\ CA\\ \ldots\\ CA^{n-1}\end{bmatrix}_{nmxn} \qquad (8)$$

should have a non zero determinant.

To verify if a system is observable, we calculate the determinant of the observability matrix, one for each patient. There is a relationship between the value of such determinant and the calculated values of compliance.

III. Results and Discussion

Results of the analysis of the observability of the system are listed in column 6 of Table I. We found non zero determinants for all 18 analyzed cases.

There is a linear relationship between compliance and determinant of the observability matrix. For high values of compliance, the determinant approaches zero, and viceversa. This indicates that for highly compliant systems, the model tends to be non observable.

We could calculate the relationships between all inputs and outputs due to the observability of our system. As an example, we show the transfer matrix for patient signal a40764 (position 12 in the table). Each element of the matrix is a transfer function indicating the relationships between inputs and outputs for that particular patient.

If

$$G_{11} = \frac{Y_1(s)}{U_1(s)};$$

$$G_{12} = \frac{Y_1(s)}{U_2(s)};$$

$$G_{21} = \frac{Y_2(s)}{U_1(s)};$$

$$G_{22} = \frac{Y_2(s)}{U_2(s)}$$

then

$$\begin{bmatrix}\mathbf{Y}_1(s)\\ \mathbf{Y}_2(s)\end{bmatrix}=\begin{bmatrix}\mathbf{G}_{11}(s) & \mathbf{G}_{12}(s)\\ \mathbf{G}_{21}(s) & \mathbf{G}_{22}(s)\end{bmatrix}\begin{bmatrix}\mathbf{U}_1(s)\\ \mathbf{U}_2(s)\end{bmatrix}$$

$$\mathbf{G}_{11}=\frac{0.8926s^2+0.0139s+0.0190}{s^4+1.3854s^3+0.9352s^2+0.0430s+0.0190}$$

$$\mathbf{G}_{12}=\frac{s^3+1.3854s^2+0.9139s+0.0139}{s^4+1.3854s^3+0.9352s^2+0.0430s+0.0190}$$

$$\mathbf{G}_{21}=\frac{s^3+1.3854s^2+0.0426s+0.0292}{s^4+1.3854s^3+0.9352s^2+0.0430s+0.0190}$$

$$\mathbf{G}_{22}=\frac{0.0213s^2+0.0292s+0.0190}{s^4+1.3854s^3+0.9352s^2+0.0430s+0.0190}$$

Figure 2 illustrates how inputs and outputs relationships are built.

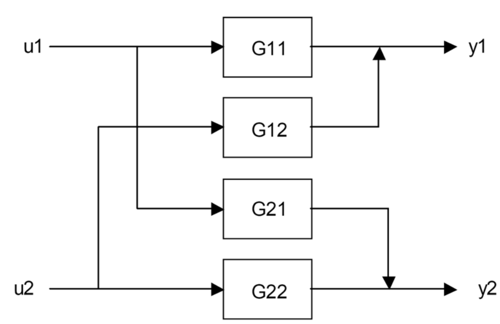

Fig. 2. Multiple transfer functions

Figure 3 shows the model response for a hypertensive patient (Record #a40717, No. 11 in Table I). Fig. 3(a) illustrates the variation of compliance in time for systolic pressure, while 3(b) represents the variation of compliance for diastolic pressure. Fig. 3(c) and Fig. 3(d) show the inertia of blood flow in time for systolic and diastolic pressures respectively.

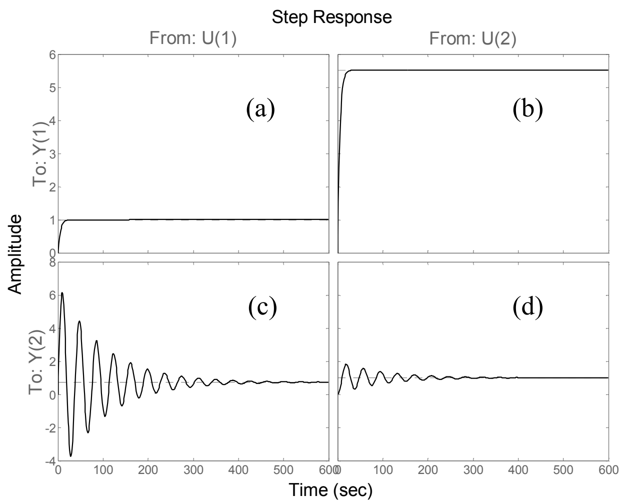

Fig. 3. Response for a hypertensive patient

In Fig. 3(c) the recovery time of the arterial wall as shown by the inertia of the blood flow is approximately 1 s, longer than the recovery time modeled for normotensive patients. The compliance represents the increase in blood volume in a vessel when the pressure in the same vessel is also increased. As it is known, patients with established hypertension show reduced distensibility and compliance in comparison to normotensive subjects, which supports our results [13],[17].

IV. Conclusion

Modeling the cardiac system with modern control theory tools allows the analysis of cardiovascular dynamics using state equations.

The goal of our paper was to understand the relationship of arterial compliance and inertia of blood flow with systolic and diastolic pressures, two clinical variables which are easily and non invasively captured in the hospital setting.

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