

Simulating ventricular elastance with a heart-arterial interaction model

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Mathematical models are necessary to understand the cardiovascular system and can assist in clinical conditions. The purpose of this paper is to describe a simple model based on the interaction of the ventricle with the arterial system that is able to simulate ventricular properties, such as ventricular elastance or blood pressure, using arterial pressure as an input. To achieve this aim, an already validated heart-arterial interaction model is adapted. It consists in the coupling of a Windkessel model for the arterial system with the time-varying elastance concept for the ventricular function. During the ejection phase ventricular elastance can be calculated from arterial pressure using differential equations. For the rest of the cardiac cycle the elastance curve needs to be extended appropriately. The model is tested using an invasively measured pressure data set for simulation. Measured aortic pressure is used to compute ventricular elastance, which is then used as an input to the original model and the resulting ventricular pressure curve is compared to the measurement. The simulation results show overall a good agreement with the measured data and therefore suggest that the model could be used to assess ventricular properties.

1 Introduction

For the early diagnosis and treatment of cardiovascular diseases a comprehensive knowledge of the cardiovascular system is essential. Various mathematical models for simulating the heart and arterial system have been developed in order to contribute to its understanding and even assist clinical diagnosis [1]. For clinical applications complex models are only of limited use, as the assessment of the required parameters can be very difficult [2]. Thus, for this purpose simple models whose parameters have a straightforward physiological interpretation are necessary.

A very well-known and validated class of simple lumped-parameter models of the arterial system are the so-called Windkessel models. Their name derives

from the assumption that the large, compliant arteries act as a Windkessel where blood is stored during systole in analogy to an old-fashioned hand-pumped fire engine [3]. Numerous extensions of the original model consisting of a compliance and a resistance element have been developed by introducing new elements [4]. A way to describe ventricular activities was elaborated by Suga et al. in form of the elastance model [5]. Elastance is defined as the ratio of ventricular blood pressure to volume and thus provides a measure for the stiffness of the cardiac muscle.

Models for the heart and the arterial system like the ones introduced above are often considered separately. However, blood pressure and flow result from the interaction between the ejecting ventricle and the arterial system. Therefore models describing the coupling of heart and arteries have been established. An ex-

ample for such a heart-arterial interaction model was proposed by Segers et al. [6]. Their simulations are based on the assumption that important ventricular properties such as ventricular elastance are known. In clinical practice though, the assessment of ventricular properties is very difficult and expensive. More frequently, aortic blood pressure and flow are measured non-invasively. For this reason, the aim of this work is to adapt the heart-arterial interaction model in a way to derive properties of the left ventricle, namely elastance, blood pressure and volume, from aortic pressure measurements. In this paper, model approaches that accomplish this task are presented. In order to test the possible applicability of these models, simulations and measured data are compared.

2 Methods

The modeling approach is based on a coupling of the time-varying elastance concept describing the function of the left ventricle with the classical three- or four-element Windkessel model representing the arterial system. The time-varying elastance $E(t)$ is assumed to relate ventricular blood volume V_v to ventricular blood pressure P_v by

$$E(t) = \frac{P_v(t)}{V_v(t) - V_0}, \quad (1)$$

where V_0 is an experimentally determined correction volume [5]. It has been shown by Senzaki et al. that the elastance curves when normalized both by amplitude and time to peak amplitude are of nearly constant shape in human hearts [7]. Thus presuming this normalized shape as given, E is determined by four parameters: minimal and maximal value E_{min} and E_{max} , heart rate and time to reach maximal elastance. In [6] this approach for modeling the heart was taken to find model equations that use elastance as an input.

Windkessel models are lumped-parameter models describing the hemodynamics of the arterial system [3]. In this work a three- and a four-element model (WK3 and WK4) are used, consisting of the total peripheral resistance R , the total arterial compliance C , the characteristic impedance of the aorta Z_c and (in case of the four-element model) the total inertia of the arterial system L .

Segers et al. introduced and validated the heart-arterial interaction model with a four-element Windkessel illustrated in figure 1 [6]. The cardiac valves are modeled as perfectly closing devices allowing only forward flow and acting as simple resistances R_{A-V} for the mitral valve and R_{V-art} for the aortic valve when opened. The preload or filling rate of the heart is represented by the venous filling pressure P_{venous} .

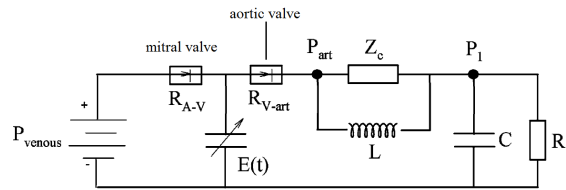


Figure 1: Electrical analog representation of the heart-arterial interaction model with WK4 (adapted from [6]).

The combination of Windkessel and elastance equations yields a system of three ordinary differential equations for the unknown ventricular blood volume V_v , Windkessel pressure P_1 and aortal pressure P_{art} :

$$\begin{aligned} \frac{dV_v}{dt} &= \frac{P_{venous} - E(V_v - V_0)}{R_{A-V}} - \frac{E(V_v - V_0) - P_{art}}{R_{V-art}} \\ \frac{dP_1}{dt} &= \frac{1}{C} \frac{E(V_v - V_0) - P_{art}}{R_{V-art}} - \frac{P_1}{RC} \\ \frac{dP_{art}}{dt} &= \left(1 + \frac{Z_c}{R_{V-art}}\right)^{-1} \left[\frac{Z_c}{R_{V-art}} \left(\frac{dE}{dt} (V_v - V_0) \right. \right. \\ &\quad \left. \left. + E \frac{dV_v}{dt} \right) + \frac{dP_1}{dt} + \frac{Z_c}{L} (P_1 - P_{art}) \right]. \end{aligned} \quad (2)$$

These equations are solved throughout the whole cardiac cycle with R_{A-V} and R_{V-art} changing from infinity to an appropriate finite value according to the sign of $P_{venous} - P_v$ and $P_v - P_{art}$, respectively. Ventricular pressure P_v and aortic blood flow Q_{art} can be calculated using formula (1) and $\frac{dV_v}{dt} = -Q_{art}$.

In order to solve the model equations (2), the time-varying elastance function has to be known. However, in practice it is very difficult to assess the parameters defining the function $E(t)$, but comparatively easy to measure the aortic blood pressure P_{art} . Therefore the model was modified in a way to simulate E using measured P_{art} -curves. It must be pointed out that only during the ejection phase, when the aortic valve

is opened, an actual connection between the ventricle and the aorta exists. Hence only in this phase the elastance curve can really be calculated.

In order to find an equation for E during the ejection phase, $E(V_v - V_0)$ is replaced by P_v in the model (2). Rearranging the third equation, the new model with unknowns P_1 , P_v and V_v is given by

$$\begin{aligned} \frac{dV_v}{dt} &= -\frac{P_v - P_{art}}{R_{V-art}} \\ \frac{dP_1}{dt} &= \frac{1}{C} \frac{P_v - P_{art}}{R_{V-art}} - \frac{P_1}{RC} \\ \frac{dP_v}{dt} &= \frac{dP_{art}}{dt} + \frac{R_{V-art}}{Z_c} \left(\frac{dP_{art}}{dt} - \frac{1}{C} \frac{P_v - P_{art}}{R_{V-art}} \right. \\ &\quad \left. + \frac{P_1}{RC} - \frac{Z_c}{L} (P_1 - P_{art}) \right). \end{aligned} \quad (3)$$

E can then be calculated from formula (1). Note that this model also requires the time derivative of P_{art} which has to be approximated numerically.

For the rest of the cardiac cycle E needs to be extended in a suitable way. This was achieved by assuming that the elastance function is of a form similar to the one used by Danielsen et al. [8] but with an additional sinus term to obtain a faster increase of E in early systole. The elastance function used in this work (figure 2) is given by

$$E(t) = E_{min} \cdot (1 - \phi(t)) + E_{max} \cdot \phi(t), \quad (4)$$

where the function ϕ is defined as

$$\phi(t) = \begin{cases} a_\phi \sin\left(\frac{\pi t}{t_{ce}}\right) - b_\phi \sin\left(\frac{2\pi t}{t_{ce}}\right) & 0 \leq t < t_{ce} \\ +0.1 \cdot \sin\left(\frac{3\pi t}{t_{ce}}\right) & \\ 0 & t_{ce} \leq t \leq T \end{cases} \quad (5)$$

and t_{ce} denotes the time for the onset of constant elastance.

The values of E determined during the ejection phase are used to estimate the parameters a_ϕ , b_ϕ , E_{max} , E_{min} and t_{ce} in a way that the function given by (4) and (5)

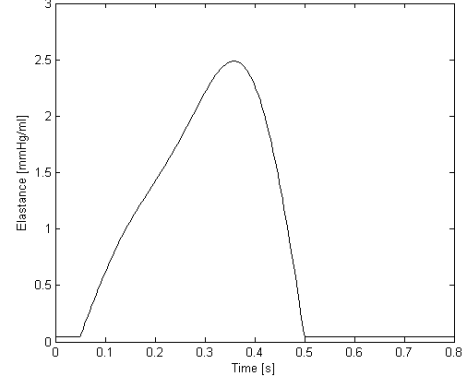


Figure 2: Time-varying elastance $E(t)$ given by (4) and (5) with $a_\phi = 0.9$, $b_\phi = 0.25$, $t_{ce} = 0.45$ s, $E_{max} = 2.49$ mmHg/ml, $E_{min} = 0.049$ mmHg/ml.

approximates the calculated curve E as well as possible during the ejection phase. As maximal elastance occurs during the ejection phase, E_{max} is determined by the calculated values. The other four parameters are each varied over an appropriate range of values to minimize the difference between the analytical function and the simulated values.

In a similar way, model equations for a coupling of the elastance concept and the three-element Windkessel model can be deduced (figure 3).

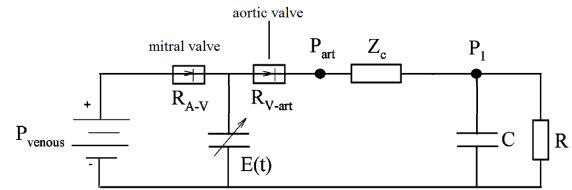


Figure 3: Electrical analog representation of the heart-arterial interaction model with WK3 (adapted from [6]).

The use of the three-element Windkessel leads to a system of only two differential equations for P_1 and V_v . The equation for V_v follows from $\frac{dV_v}{dt} = -Q_{art}$ and the fact that the blood flow through the aortic valve Q_{art} equals the flow through the resistance Z_c :

$$\frac{dV_v}{dt} = -Q_{art} = -Q_{Z_c} = \frac{P_1 - P_{art}}{Z_c}. \quad (6)$$

An equation for P_1 results from the equality $Q_{Z_c} =$

$Q_C + Q_R$ where the flow through R is given by $Q_R = \frac{P_1}{R}$ and the flow through C by $Q_C = C \frac{dP_1}{dt}$. Using $Q_{Z_c} = \frac{P_{art} - P_1}{Z_c}$ yields

$$\frac{dP_1}{dt} = \frac{P_{art} - P_1}{CZ_c} - \frac{P_1}{RC}. \quad (7)$$

Having solved these two equations, the equality $Q_{Z_c} = Q_{art}$ can be used to obtain

$$\frac{E(V_v - V_0) - P_{art}}{R_{V-art}} = \frac{P_{art} - P_1}{Z_c}.$$

Consequently, it is possible to calculate E from the measured aortic pressure P_{art} and the solutions V_v and P_1 from equations (6) and (7) by the formula

$$E = \frac{1}{V_v - V_0} \left(\frac{R_{V-art}}{Z_c} (P_{art} - P_1) + P_{art} \right). \quad (8)$$

3 Results

In order to test the previously described model, a measured aortic and left ventricular pressure data set was used for a simulation. The measured pressure curves are shown in figure 4. Pressure was measured invasively applying a 5F Millar SPC-454D catheter (see [9] for details). The study was approved by the regional ethics committee, and all of the participants gave written informed consent.

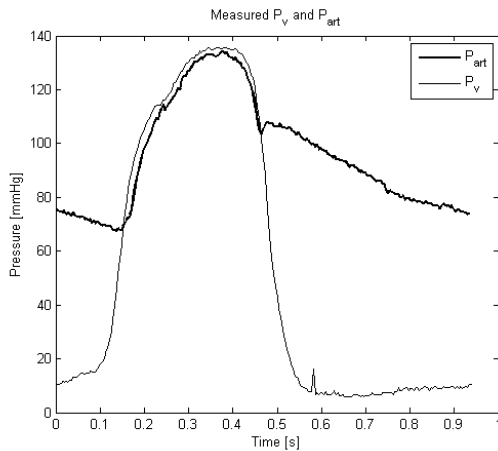


Figure 4: Measured aortic and ventricular pressure curves.

The measured aortic pressure curve was taken as an input for the model (3) with WK4 and the model (6)-(8) with WK3 to determine two sets of parameters for the elastance function (4)-(5). Then these elastance parameter sets for WK4 and WK3 were again used as an input for the corresponding original models represented in figure 1 and 3 in order to compute ventricular and aortic pressure and volume. The resulting simulated ventricular pressure curves were compared to the measured data.

In addition to the aortic pressure, the model for calculating the elastance curve and the original model of Segers et al. need some more parameters, namely the Windkessel parameters R , C , Z_c and L , the duration of one heartbeat T , the filling pressure P_{venous} , the enddiastolic volume EDV , the correction volume V_0 and the valve resistances R_{V-art} and R_{A-v} . The Windkessel parameters were estimated empirically in a way to fit the aortic pressure curve. The values used for this simulation are given in table 1. T was deduced from the P_{art} -curve as $T = 0.94$ s. As no ventricular volume data was available, EDV and V_0 were given appropriate values. For this simulation $EDV = 120$ ml and $V_0 = -10$ ml were chosen. The venous filling pressure, which is only used for simulating the original model, was calculated from the relation $E_{min} = \frac{P_{venous}}{EDV - V_0}$ with the minimal elastance value found before. The valve resistances were set to $R_{V-art} = R_{A-v} = 0.007$ mmHg/(ml/s). The parameter values used here are in the same range as those specified in [10].

	WK4	WK3
R [mmHg/(ml/s)]	0.9	0.9
C [ml/mmHg]	0.8	1.0
Z_c [mmHg/(ml/s)]	0.09	0.08
L [mmHg/(ml/s ²)]	0.002	-

Tabelle 1: Values for the Windkessel parameters.

Figure 5 shows the elastance curves simulated with the parameters given above for the WK4 model (3) in the upper panel and the WK3 model (6)-(8) in the lower panel. The elastance values calculated from the differential equations for the ejection phase are illustrated (asterisks) as well as the approximating functions of the form (4) (solid line).

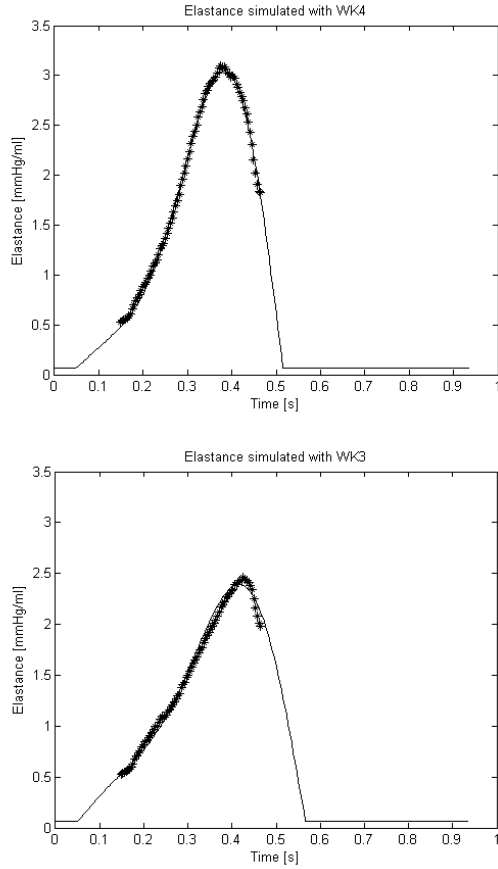


Figure 5: Elastance curves simulated with WK4 (upper panel) and WK3 (lower panel). The asterisks denote the simulated values during ejection phase, the approximating elastance function of form (4) is given by the solid line.

Figure 6 shows the simulation results of the original models using the corresponding elastance parameter sets found before. The simulation with the WK4 model given by equations (2) is shown in the upper panel, the WK3 model results can be seen in the lower panel.

Finally, in figure 7 the outcome of the simulations with WK4 and WK3 and the real ventricular pressure data are compared.

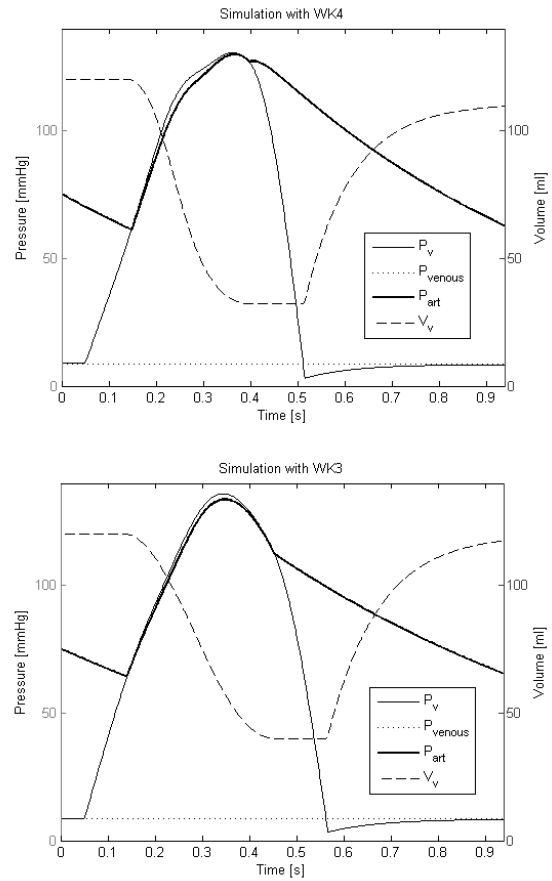


Figure 6: Simulation of the original model with WK4 (upper panel) and WK3 (lower panel).

4 Discussion

The main objective of this work was to find a simple model based on the interaction of ventricle and arteries that is able to simulate properties of the heart using arterial pressure as an input. The simulation results given in figures 5-7 indeed suggest that the heart-arterial interaction models represented in figure 1 and 3 achieve this goal.

A first observation taken from figure 5 is that the elastance values calculated for the ejection phase are in the expected range of values for human hearts and resemble the form found in measurements [7]. Furthermore it can be seen that the functions given in (4) and (5) are suitable for approximating these values and provide an extension to the whole cardiac cycle that resembles

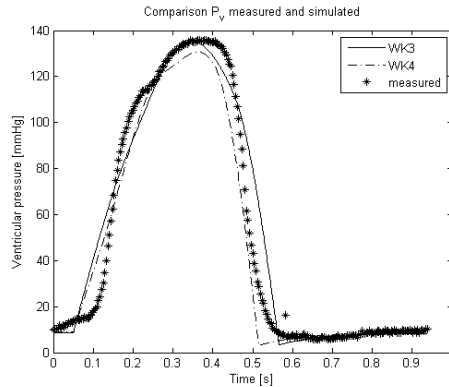


Figure 7: Comparison between measured ventricular pressure and P_v simulated with WK4 and WK3.

the curves found in [7].

Comparing the results for the four-element Windkessel to those obtained with the three-element model in figure 5, it is evident that both models qualitatively yield very similar elastance functions. The maximal elastance E_{max} calculated with the WK4 model is higher than the maximal value retrieved from the WK3 simulation. Also, the time to reach this maximal value is shorter in the WK4 model than in the WK3 version.

Considering the simulation results for P_{art} , P_v and V_v obtained through simulating the original models using the previously calculated elastance parameters (figure 6), one notable difference is that in the WK4 simulation the aortic valve closes much earlier than in the WK3 simulation and the real data. However, unlike the WK3 model, the four-element Windkessel is able to model the short increase in aortic pressure in early diastole that is also seen in the measured P_{art} curve in figure 4, whereas use of the WK3 model leads to a simple exponential decay in aortic pressure during diastole.

As can be seen from figure 7, there is a good agreement between measured and simulated ventricular pressure. The shape of all curves is similar and important values like minimal and maximal pressure hardly differ. During the isovolumic contraction phase though, the simulated pressure does not increase as fast as the measured pressure, and at the beginning of the filling phase simulated pressure decreases a bit too far. Although the WK4 model yields higher elastance

values than the WK3 model, there is not as much difference in the resulting ventricular pressure curves.

Although the model yields promising simulation results, several limitations need to be acknowledged. First, in this work the model was only applied to one specific data set. Of course, to thoroughly validate the proposed model, testing with a larger cohort of patient data is necessary. Also the aortic and ventricular pressure curves used for the simulation were measured at the same patient but not at the same time. Another source of weakness is that several of the necessary parameters were given appropriate values instead of being measured or determined algorithmically. The findings are also limited by the lack of information on ventricular blood volume, which would be necessary to directly compare simulated elastance curves to measurements. Naturally, measuring errors may occur when using catheters, which means that simulation results cannot be compared to real values, only to these measured values. However, in the study that was used here, pressure-tip catheters were applied, which currently provide one of the most accurate measuring methods for blood pressure [11]. One of the most important advantages of the model is the small number of parameters required and their straightforward physiological interpretation. On the other hand, the low number of model parameters at the same time provides a limitation, as already pointed out for the original model in [6].

In conclusion, a simple and physiologically relevant heart-arterial interaction model was elaborated and the simulation results support the idea that this model can be applied to assess ventricular properties. However, further research and testing with a larger cohort with additional measurements is required to decide whether the model has practical relevance.

As a perspective for possible future research, the heart-arterial interaction model could be combined with other modeling techniques to use non-invasively measured pressure curves as an input. Aortic pressure curves can be determined from peripheral measurements by using transfer functions, for example with the algorithm used in [9]. Coupling such an algorithm to this model could make it possible to assess important ventricular parameters only by carrying out a simple brachial cuff based measurement. In this way the model could support the analysis of cardiovascular function in clinical conditions.

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