Simulating Aortic Blood Flow and Pressure by an Optimal Control Model

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Abstract. Parameters derived from aortic pressure and flow waves are considered to be important indicators of cardiovascular risk. To reduce the measurement effort, validated methods already exist to transfer non-invasively assessed peripheral blood pressure curves to central ones. In this work, an optimal control model is introduced, which could potentially be used to simulate the corresponding ejection from the heart. It is based on the well-established three-element Windkessel model of the arterial system, coupled with an optimality criterion. The resulting optimal control problem was solved in part symbolically, in part numerically and simulation experiments were performed to investigate the capability of the model to generate pathophysiological flow and pressure patterns with meaningful parameter values. Moreover, the sensitivity of the model to variations in the parameters, that were considered relevant for the use as a blood flow model, was analysed. The results show that it is indeed possible to simulate realistic flow and pressure waves for parameters within the pathophysiological range of humans. Moreover, the sensitivity analysis indicates that parameter identification based on a pressure measurement might be possible. Overall, the model shows a big potential for the simulation of blood flow based on pressure alone.

Introduction

The hemodynamics in the human body is determined by the characteristics of the heart and the vascular system as well as by their interplay. The corresponding state variables, blood pressure and flow, are therefore supposed to hold important information about the status of the cardiovascular system of a specific person. Parameters derived from one or both of these two quantities are used for the stratification of cardiovascular risk and have been shown to have predictive power for the occurrence of adverse events [1].

However, measuring aortic pressure and flow requires elaborate equipment and trained operators and represents, in the case of invasive measurements, an additional risk for the patient. To overcome this limitation, methods have been developed to estimate the aortic pressure waveform from non-invasive peripheral readings [2,3]. Part of these methods has been validated for various cardiac conditions and is now commercially available for the use in everyday (clinical) life [4-7]. Central pressure parameters derived from these synthesized curves have proven their value in a multitude of studies [1].

Regarding the flow waves, different attempts have been made to provide an approximation using solely information from the corresponding pressure signal [8-10]. In the 1970ies, an approach based on the assumption of minimal cardiac cycle work was proposed [11,12]. The main idea is to combine a so called Windkessel (WK) model of the arterial system with an optimality criterion. For a given parameterisation of the WK model and a suitable choice of constraints, the resulting optimization problem then simultaneously yields optimal patterns of flow and pressure [13]. By comparing the latter to a measured pressure curve, a fitting procedure can be used to identify the parameters in the WK model and thus, finally, a flow curve is obtained. This approach has been investigated extensively in the 1970ies and 80is [14-17] using different optimality criteria and WK models. A blood flow model of this type is also used nowadays in a commercially available device [18].

The aim of this work is to examine an optimal control model based on an optimality criterion proposed by Hämäläinen et al. [19] using a slightly different WK model as well as different boundary conditions. Simulation experiments were performed and the ability of the model to imitate physiological as well as pathological flow and pressure patterns was investigated. Furthermore, the sensitivity of the model to variations in the parameters, that are considered relevant for the use as a blood flow model, was analysed.

1 Methods

The optimization model presented in this work is based on the well-established 3-element Windkessel (WK) model that describes the dynamic relation between pressure and flow when the system is in steady state, and the idea that the heart works in an optimal manner. Combination of the WK model and the optimality criterion results in an optimal control problem which has to be solved appropriately. Therefore, suitable boundary conditions have to be formulated and adequate methods have to be chosen to subsequently solve the problem numerically.

1.1 Modelling

Aortic pressure p and flow q are assumed to be related according to the so called 3-element Windkessel model

$$p(t) = Z_c \cdot q(t) + p_{wk}(t) + P_\infty \tag{1}$$

$$\dot{p}_{wk}(t) = -\frac{1}{RC} p_{wk}(t) + \frac{1}{C} q(t) \tag{2}$$

whereby the dot represents the time derivative. The peripheral resistance R describes the resistance opposed to the flow by the vascular system, which is mostly caused by the small arteries and arterioles. The arterial compliance C specifies the distensibility of the large elastic arteries, in particular the aorta, and the characteristic impedance Z_c takes into account the compliance and inertance of the very proximal aorta [20]. P_∞ is an asymptotic pressure level that represents the pressure that is not caused by the ejection of the heart but is maintained by the vascular system. It is often set to zero for simplicity [20]. p_{wk} is an auxiliary quantity called the Windkessel pressure.

An optimization problem proposed by Hämäläinen et al. [19] was chosen for this work (t_s denotes the ejection duration): Find (p, q) such that

$$J = \int_0^{t_s} \alpha p(t) q(t) + \dot{q}\,(t)^2 \mathrm{d}t \to \min \tag{3}$$

under the constraint that a given stroke volume

$$SV = \int_0^{t_s} q(t) \mathrm{d}t \tag{4}$$

has to be reached.

The first term of the integral (3) represents the hydraulic work done by the heart per beat, times a nonnegative weighting factor α. Thus, one tries to find those patterns of pressure and flow that minimize the energy used by the heart to generate a given stroke volume. The second term in (3) is a structural penalty term that penalizes peaks in the acceleration of blood, which are considered to lower the efficiency of the cardiac contraction [19].

In order to formulate an optimal control problem, equation (1) is used to eliminate p from equation (3) and the acceleration $\dot{q}$ is set to be the control, which is denoted by u. Furthermore, an additional equation for the left ventricular volume V is included in order to enable the specification of the stroke volume SV as a boundary condition. In systole, the volume of blood contained in the left ventricle changes solely due to the ejection of blood into the arterial system and hence, the derivative of V is given by $-q(t)$. The optimal control problem then reads:

Minimize

$$J(u) = \int_0^{t_s} \alpha (Z_c q + p_{wk} + P_\infty) q + u^2 \mathrm{d}t \tag{5}$$

under

$$\begin{pmatrix} \dot{V}(t) \\ \dot{q}(t) \\ \dot{p}_{wk}(t) \end{pmatrix} = \begin{pmatrix} -q(t) \\ u(t) \\ -\frac{1}{RC} p_{wk}(t) + \frac{1}{C} q(t) \end{pmatrix} \tag{6}$$

$$\begin{matrix} V(0) = V_0 & V(t_s) = V_0 - SV \\ q(0) = 0 & q(t_s) = 0 \\ p_{wk}(0) = P_0 - P_\infty & p_{wk}(t_s) = (P_0 - P_\infty) e^{\frac{T - t_s}{RC}} \end{matrix} \tag{7}$$

V_0 denotes the left ventricular end-diastolic volume, which can be chosen arbitrarily since the absolute values of V do not affect p_{wk} or q. At the end of systole, this initial volume has been reduced by SV, i.e. $V(t_s) = V_0 - SV$. During diastole, the aortic valve is closed and therefore flow from the heart is assumed to be zero during this phase, which yields the boundary conditions for q. Those for p_{wk} result from the assumption of the system being in a steady state, i.e. p_{wk} has to be a periodic function.

More precisely, $q(0) = 0$ yields $p_{wk}(0) = P_0 - P_\infty$ according to equation (1). From equation (2) it follows that p_{wk} describes an exponential decay in diastole, when $q \equiv 0$. Together with the assumption of periodicity, i.e. $p_{wk}(0) = p_{wk}(T)$, for T denoting the duration of the heartbeat, the diastolic WK pressure is thus given by

$$p_{wk}(t) = (P_0 - P_\infty)e^{\frac{T-t}{RC}}, \ \ \mathrm{t_s \le t \le T} \tag{8}$$

which finally yields the boundary condition stated in (7).

The optimal control problem (5)-(7) can be solved with Pontryagin's maximum principle [21] which results in a system of 6 linear ordinary differential equations (ODE) for the optimal solution: 3 for the state variables V, q, p_{wk} and 3 for the costate variables λ_1, λ_2 and λ_3.

$$\begin{aligned}
\dot{V}(t) &= -q(t)\\
\dot{q}(t) &= \frac{1}{2}\lambda_2(t)\\
\dot{p_{wk}}(t) &= -\frac{1}{RC}p_{wk}(t) + \frac{1}{C}q(t)\\
\dot{\lambda_1}(t) &= 0\\
\dot{\lambda_2}(t) &= \alpha(2Z_c q(t) + p_{wk}(t) + P_\infty) + \lambda_1(t)\\
&\qquad\qquad - \frac{1}{C}\lambda_3(t)\\
\dot{\lambda_3}(t) &= \alpha q(t) + \frac{1}{RC}\lambda_3(t)
\end{aligned} \tag{9}$$

This system has 6 degrees of freedom. Thus, together with the boundary conditions specified in (7), the solution of the optimal control problem is, if it exists, uniquely described.

1.2 Implementation

A numerical solution of the system given in (9) satisfying the boundary conditions (7) cannot be found straight forward with common ODE solvers, since these require initial values for all variables. An iterative procedure like the shooting method would be needed that adjusts the unknown initial values of the costates until (7) is satisfied. However, this again requires an adequate initial guess of $\lambda_i(0)$ for $i = \{1,2,3\}$, which is difficult since the costates do not represent physiological quantities and thus their magnitude is hard to estimate.

Therefore, another approach was used in this work. The system of ODEs (9) with the initial values $V(0), q(0)$ and $p_{wk}(0)$, i.e. the left hand side in (7), was symbolically solved using Maple 15 (Maplesoft, a division of Waterloo Maple Inc., Waterloo, Ontario).

The solutions obtained for V, q and p_{wk} thus depend on the time t, the ejection duration t_s and the length of the heartbeat T, the parameters $V_0, P_0, P_\infty, R, C, Z_c$ and α as well as three unknown constants $c := (C_1, C_2, C_3)$, which represent the remaining degrees of freedom.

In a next step, a system of linear equations $Ac = b$ for the unknowns was built up using the right hand side of (7), whereby the matrix A as well as the vector b depend on $t_s, T, P_0, P_\infty, R, C, Z_c$ and α. Finally, the expressions for $q(t), p_{wk}(t)$, A and b were simplified and automatically translated to Matlab code using the "CodeGeneration" package in Maple.

All further computations and simulation experiments were performed by using Matlab R2011b (The MathWorks, Inc., Natick, Massachusetts, United States). To generate pressure and flow for a given parameter set, first, the system of linear equations is solved to obtain C_1, C_2 and C_3. From these, $q(t)$ and $p_{wk}(t)$ are evaluated during systole and finally $p(t)$ is obtained from equation (1). During diastole, $p_{wk}(t)$ is computed according to (8) and since it holds that $p(t) = p_{wk}(t) + P_\infty$ during this phase, $p(t)$ can be determined for the whole cardiac cycle.

1.3 Simulation experiments

In order to examine the capability of the model to represent different physiological as well as pathological conditions, simulation experiments were performed. In a first step, the possible shape variations were investigated for parameterisations within the pathophysiological range of humans found in literature [17,22].

Then, the sensitivity of the model to changes in the model parameters was assessed. Since the final goal of this approach is to provide an estimate of the flow curve for a given pressure signal, the initial pressure P_0, the duration of the heartbeat T as well as the mean pressure mBP were supposed to be given. Furthermore, the time constant RC of the modelled exponential pressure decay (8) as well as P_∞ and the ejection duration can be estimated from the pressure wave [23,24] and were thus also assumed to be known. Therefore, only R, C, Z_c and α were varied and the corresponding SV was computed from the following equation which can be easily derived from the Windkessel model (1), (2) and the definition of the total peripheral resistance: $TPR := mBP \cdot T/SV$.

$$SV = \frac{(mBP - P_\infty) \cdot T}{R + Z_c} \tag{10}$$

2 Results

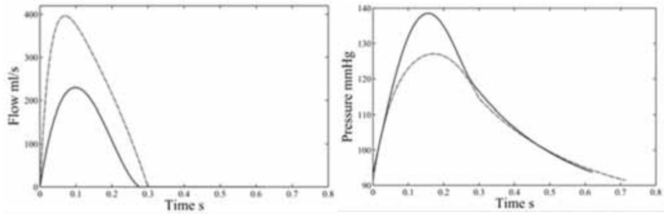

Figure 1. Comparison of qualitatively and quantitatively different, simulated flow and pressure patterns corresponding to the parameterisation of case 1 (dashed line) and case 2 (solid line) given in table 1.

Figure 1 shows 2 pairs of pressure and flow curves obtained with the parameterisation given in table 1. For both, pressure and flow, substantial differences in the shapes can be seen. The parameters chosen for case 1 are in a physiological range for a healthy individual, whereas those for case 2 imitate a pathological arterial stiffness. The corresponding pressure and flow waves reflect these characteristics.

For the sensitivity analysis, the parameterisation of case 1 was taken as default and R,C,Z_c and α were varied, see figure 2. The diastolic part of the pressure signals is the same for all parameters because the time constant of the decay remained unchanged. Moreover, since mean pressure is fixed, the variations generally have a stronger effect on the flow than on the pressure curves.

Figure 2A shows the effect of changes in R and C while keeping their product RC fixed and adapting the stroke volume according to (10). In the pressure signal, small changes in the upstroke, the height of the maximum as well as its position can be observed. The flow curves are mainly affected by the decrease in stroke volume resulting from the increase in resistance. However, for very elastic arteries, i.e. C high, and little resistance, also the wave shape is altered.

Simulation runs for different values of the characteristic impedance Z_c are depicted in figure 2B. When Z_c increases, the maximum pressure is shifted to the right and the decline of the flow curve changes from convex to concave.

Finally, simulation results for variations in α are presented in figure 2C. The higher α becomes, the earlier maximum flow is reached. Also, the decline of the flow wave is affected in a similar way as before for varying Z_c. The pressure wave exhibits a flatter shape for higher values of α.

Parameter	Case 1	Case 2	Unit		
R	0.204	0.410	mmHg*s/ml		
C	1.50	0.67	ml/mmHg		
Z_c	0.04	0.09	mmHg*s/ml		
α	25000	500	-		
P_∞	83.4	83.4	mmHg		
P_0	91.4	93.5	mmHg		
mBP	108.8	113.6	mmHg		
t_s	300	276	ms		
T			714	625	ms
SV			73.5	37.8	ml
TPR			1.0571	1.879	mmHg*s/ml

Table 1. Parameterisation simulating a healthy (case 1) and a pathological (case 2) case.

3 Discussion

The aim of this work was to investigate the capability of the introduced optimal control model to generate pathophysiological flow and pressure patterns with meaningful parameter values. Furthermore, we wanted to examine its potential to be used to simulate blood flow for a given pressure signal.

The parameters C, TPR and Z_c chosen for case 1 are within the range reported in literature for healthy individuals [22] and also the pressure and flow waves resemble typical contours as given for example in [1].

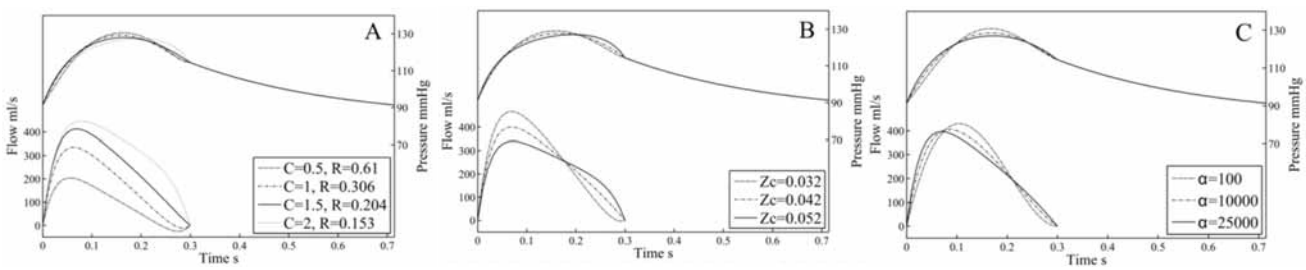

Figure 2. Sensitivity of the model to variations in R and C for fixed RC (A), in Z_c (B) and in α (C).

In case 2, the lower value of arterial compliance, a direct index of arterial stiffness, and the higher value of characteristic impedance, an indirect index of arterial stiffness, imitate stiffer arteries compared to case 1 [25]. The furthermore elevated resistance is typical for subjects with hypertension [1]. As would be expected based on these parameters, the pressure indeed rises higher than for case 2 even though the stroke volume is lower. These examples indicate that (1) it is possible to generate realistic flow and pressure patterns with the optimal control model and (2) the different model parameters affect the simulated patterns in accordance with their physiological meaning.

In order to use this model to simulate blood flow for a given pressure curve, the model parameters have to be identified by comparing the modelled pressure to a measurement (e.g. minimizing the squared error between them). For this purpose, it is desirable to reduce the number of unknown parameters, since the complexity of the model identification increases with the number of parameters. As it is assumed that the pressure pattern is known anyways, it seems logical to derive as much information as possible beforehand. Therefore, we assumed the initial pressure level P_0, mean pressure mBP as well as the timing information T and t_s to be given. The first three can be extracted directly from the recorded signal, the latter can be estimated from it [24]. Furthermore, the diastolic part of the pressure curve can be used to determine P_∞ and RC [23]. Thus, altogether, P_0, mBP, P_∞, RC, T and t_s can be assumed to be known and only the remaining parameters R, C, Z_c, SV and α have to found. Because RC is fixed and SV can be calculated according to (10), this set of parameters is further reduced to R (or C), Z_c and α. Therefore, we studied the sensitivity of the model only with regards to these parameters.

The results of the sensitivity analysis show that changing these parameters does affect important characteristics of the shape of the simulated pressure wave, like its upstroke or the position of its maximum. Thus, although the quantitative changes were overall rather subtle, parameter identification from a pressure recording might be feasible. However, since the effect of lowering Z_c resembles that of increasing R, providing good first estimates for the fitting procedure might be a crucial point.

The weighting factor α strongly affected the position of maximum flow. For healthy individuals, it seems convincing from an evolutionary point of view to assume that the heart works in such a manner that the energy expenditure is minimized [26]. Applied to the optimality criterion given in (3), this corresponds to high values of α. In this case, the simulated flow patterns show an early maximum resembling those reported for healthy hearts [1]. Lower values of α indicate that less emphasis is led on the minimization of stroke work in (3), which could imply that the heart cannot work optimally any more. The obtained ejection patterns reach their maximum later in systole and also the shape of the decline is changed, which is indeed characteristic for failing hearts [1].

The optimal control model used in this investigation is based on an optimality criterion by Hämäläinen et al. [19]. However, in contrast to [19], we included an asymptotic pressure level P_∞ in the WK model. Moreover, we used different boundary conditions (BC) for the WK pressure p_{wk}. Hämäläinen et al. tried 6 different options for fixed t_s, namely specifying both or only one value of $p_{wk}(0)$ and $p_{wk}(t_s)$, their difference, their sum as well as using purely periodic BC. Their model reacted very sensitively to changes in the BC, which the authors stated as major drawback. It has to be kept in mind though, that the BC have to meet the assumptions of the WK model and thus, not all choices of BC are valid. For example, for fixing both values $p_{wk}(0)$ and $p_{wk}(t_s)$, the periodicity, i.e. the assumption of steady state, is not fulfilled. The same holds for specifying the difference or the sum of $p_{wk}(0)$ and $p_{wk}(t_s)$. Therefore, it seems logical that the choice of BC strongly affects the model itself. In our approach, the value of $p_{wk}(t_s)$ depends on P_0 as well as on R and C and thus, the periodicity is fulfilled for any value of R and C.

Hämäläinen et al. also reported a hypersensitivity of their models to variations in single parameters. However, satisfying an optimality criterion is a very strong requirement and both, the parameter values and the BC form the optimal solution. In other words, BC and model parameters are not independent from each other. It therefore seems logical that changing one parameter independently possibly destroys this balance.

Our results furthermore show that by using all information available from a pressure signal and by considering the dependency between R, Z_c and SV (10) induced by the WK model, a wide range of parameter values produces realistic results.

4 Conclusion

The results show that it is indeed possible to generate flow curves with this approach that resemble physiological ones. Furthermore, the identification of the model parameters from a given pressure curve seems feasible. However, further research is needed to verify these considerations.

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