Analytical Solution to a Minimal Cardiovascular Model

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Abstract

Lumped-parameter models of the cardiovascular system have been used extensively in the past, especially when coupled to time-varying elastance (or compliance) representations of ventricular contraction. In this paper, we use a physiologically motivated approximation to the time-varying compliance waveform to derive analytical solutions to the short-term (intra-beat) and long-term (inter-beat) evolution of a minimal cardiovascular model. We show that this approximation turns a non-linear, periodically varying model into one that is periodically-varying and linear for physiologically reasonable initial conditions. The solution to the equations of motion takes the form of an affine transformation of the initial conditions. The methodology outlined in this paper is applicable to larger versions of the type of models considered here.

1. Introduction

Recently, several authors have shown interest in exploring and analyzing minimal lumped-parameter cardiovascular models with the potential to serve as aids in the clinical decision making process [1, 2]. The topological simplicity of such models begs the question whether analytical methods can be used to arrive at solutions of their governing equations. Such analytical solutions are highly desirable as they convey tremendous insight into the structure of the model and its dynamic behavior. For example, one can study the solution's dependence on model parameters and can explicitly compute sensitivities required for model fitting to experimental data. Furthermore, analytical solutions usually allow for simulations at speeds significantly greater than what is required for numerical simulations.

The goal of this paper is to derive an analytical solution of the intra-beat and the inter-beat evolution of a minimal model of the cardiovascular system. By invoking a physiologically-motivated approximation of the time-varying ventricular compliance, we turn a non-linear time-varying model into one that is linear and periodically varying. The resultant analytical solutions can be used as the basis for cycle-averaging (as pursued in [3]) or find utility in clinical decision support (as suggested in [2, 1]). The methodology presented below can be applied directly to larger models of the cardiovascular system and is therefore not limited to the specific topology considered here.

2. Model description

We adopted the minimal model presented in [3] as the basis for our work. It consists of a central venous compartment, a single cardiac compartment, and a single arterial compartment that are connected in series and in closed-loop (see Figure 1). The parameter assignments for the model are largely taken from Davis and Mark [4].

The arterial and the venous compartments are described by passive, linear, time-invariant circuit elements. The cardiac compartment is both non-linear (due to the diodes) and time-varying (due to the time-varying capacitor). The pumping action of the heart is represented by a time-varying elastance (the reciprocal of compliance).

Figure 2 shows the normalized time-varying elastance waveform for the human left ventricle as adapted from Senzaki and co-workers [5] (left panel). To arrive at the time-varying compliance waveform, $C(t)$, shown as the solid line in the right panel of Figure 2, we scaled the inverse of the time-varying elastance to vary between realistic systolic (low capacitance) and diastolic (high capacitance) values.

The resultant state evolution equations can be implemented on a computer and solved numerically once an

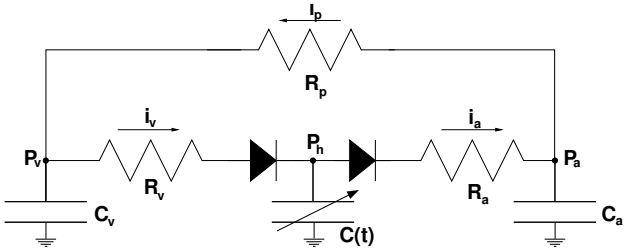

Figure 1. Circuit diagram of the pulsatile hemodynamic model. P_h, P_a, and P_v are the pressures in the cardiac, the arterial, and the venous compartment, respectively. $C(t)$ is the time-varying cardiac compliance.

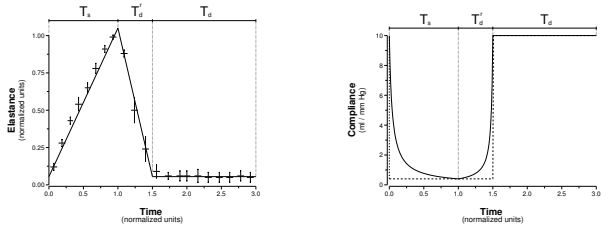

Figure 2. Time-varying ventricular elastance (left); time-varying ventricular compliance (right; solid line) and piecewise constant compliance (right; dashed line).

appropriate set of initial conditions have been supplied. We will refer to the model described thus far as the *time-varying capacitance model*.

To solve for the evolution of the model analytically, we will make a simplifying assumption, namely that the time-varying capacitance of the ventricular compartment is *piecewise constant* (as suggested by the dashed line in the right panel of Figure 2):

$$C(t) = \begin{cases} C_s, & \text{for} \quad 0 \le t \le T_s + T_d^r \\ C_d, & \text{for} \quad T_s + T_d^r < t \le T \end{cases}$$

We thus move from a ventricular model based on a periodically time-varying capacitance to one that is switching periodically between two capacitance values. We will refer to the model incorporating the piecewise constant capacitance approximation as the *switched capacitance model*. At any given moment, the switched capacitance model is in one of two possible configurations: a systolic (ventricular ejection) configuration shown in Figure 3 or a diastolic (ventricular filling) configuration shown in Figure 4. This simplification turns the non-linear, time-varying model into one that is T-periodically varying and effectively linear.

Since the switched capacitance model is effectively linear and T-periodic, one could directly apply results from Floquet theory (see, for example, [6]) to arrive at the evolution equations of the system. In the derivations below, however, we opted for a more straight-forward solution of the differential equations as this process suggests certain natural approximations.

3. Intra-beat evolution

3.1. Systolic phase

Physiologically reasonable initial conditions for the systolic configuration of the model are given by $P_h > P_a > P_v$. Solving for the node equations and the flow equations, we arrive at the following set of differential equations:

$$\begin{aligned} C_v R_p \dot{P}_v &= P_a - P_v \\ C_a \dot{P}_a &= -P_a \left(\tfrac{C_a + C_s}{R_a C_s} + \tfrac{1}{R_p} \right) - P_v \left(\tfrac{C_v}{R_a C_s} - \tfrac{1}{R_p} \right) + \tfrac{Q}{R_a C_s} \end{aligned}$$

where, in order to eliminate the ventricular pressure P_h, we made use of the fact that total charge, Q, in the circuit is conserved

$$Q = C(t) P_h + C_a P_a + C_v P_v = const.$$

When introducing the time constants

$$\tau_{pv} \equiv R_p C_v \quad \text{and} \quad \tau_{as} \equiv R_a \frac{C_a C_s}{C_a + C_s}$$

the dimensionless smallness parameters

$$\delta_s \equiv \frac{R_a C_s}{R_p (C_s + C_a)} \quad \text{and} \quad \gamma_s \equiv \frac{C_s + C_a}{C_v}$$

and the systolic equilibrium potential

$$\bar{P}_s \equiv \frac{Q}{C_v + C_s + C_a}$$

we obtain a homogenous set of state equations by introducing state variables that measure the deviation from the systolic equilibrium potential, namely

$$p_{as} \equiv P_a - \bar{P}_s \quad \text{and} \quad p_{vs} \equiv P_v - \bar{P}_s.$$

The set of state evolution equations thus reduces to

$$\begin{aligned} \tau_{pv} \tfrac{d}{dt} p_{vs} &= -p_{vs} + p_{as} \\ \tau_{as} \tfrac{d}{dt} p_{as} &= -p_{vs} \tfrac{1}{\gamma_s} (1 - \delta_s \gamma_s) - p_{as} (1 + \delta_s) \end{aligned} \tag{1}$$

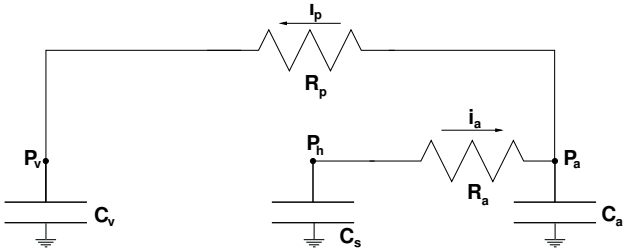

Figure 3. Circuit configuration during ventricular systole.

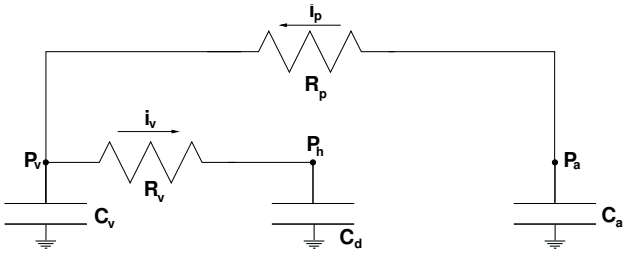

Figure 4. Circuit configuration during ventricular diastole.

(If one were interested in an approximate analytical solution to the switched capacitance model, one would drop the terms containing δ_s in the parentheses of Equation 1 as they are small compared to unity.)

This homogeneous set of first order differential equations can be solved using standard methods. The general solution is given by

$$P_v(t) = \bar{P}_s + Ae^{\lambda_{s1}t} + Be^{\lambda_{s2}t}$$
$$P_a(t) = \bar{P}_s + A(1+\tau_{pv}\lambda_{s1})e^{\lambda_{s1}t} + B(1+\tau_{pv}\lambda_{s2})e^{\lambda_{s2}t}$$

where the time constants λ_{s1} and λ_{s2} are functions of the time constants τ_{pv} and τ_{as}, and the smallness parameters γ_s and δ_s. The constants A and B are determined by the initial conditions.

In vectorized notation, in which bold face identifies vector-valued variables, the solution takes the form

$$\mathbf{P}_s(t) = \bar{\mathbf{P}}_s + M_s(t)\left[\begin{array}{c} A \\ B \end{array}\right],$$

where

$$\mathbf{P}_s(t) \equiv \left[\begin{array}{c} P_v(t) \\ P_a(t) \end{array}\right], \quad \bar{\mathbf{P}}_s \equiv \left[\begin{array}{c} \bar{P}_s \\ \bar{P}_s \end{array}\right],$$

and

$$M_s(t) \equiv \left[\begin{array}{cc} e^{\lambda_{s1}t} & e^{\lambda_{s2}t} \\ (1+\tau_{pv}\lambda_{s1})e^{\lambda_{s1}t} & (1+\tau_{pv}\lambda_{s2})e^{\lambda_{s2}t} \end{array}\right]$$

3.2. Diastolic phase

We proceed in complete analogy to the previous section in order to solve the state evolution equations during the diastolic phase of the cardiac cycle. Introducing the time constants

$$\tau_{pa} \equiv R_p C_a \quad \text{and} \quad \tau_{vd} \equiv R_v \frac{C_v C_d}{C_v + C_d}$$

and the dimensionless smallness parameters

$$\delta_d \equiv \frac{R_p C_a - R_v C_d}{R_p(C_v + C_d)} \quad \text{and} \quad \gamma_d \equiv \frac{R_v C_d}{R_p(C_v + C_d)}$$

along with the diastolic equilibrium potential

$$\bar{P}_d = \frac{Q}{C_d + C_a + C_v},$$

we can write the state evolution equations in the following form:

$$\tau_{vd}\frac{d}{dt}p_{vd} = -(1+\gamma_d)p_{vd} - \delta_d p_{ad}$$
$$\tau_{pa}\frac{d}{dt}p_{ad} = p_{vd} - p_{ad}$$

where we have introduced the state variables p_{vd} and p_{ad} that measure deviations from the steady-state potential $\bar{P}_d$.

The general solution of this set of homogeneous, first order differential equations can be expressed in vectorized form as:

$$\mathbf{P}_d(t) = \bar{\mathbf{P}}_d + M_d(t)\left[\begin{array}{c} C \\ D \end{array}\right],$$

where

$$\mathbf{P}_d(t) \equiv \left[\begin{array}{c} P_v(t) \\ P_a(t) \end{array}\right], \quad \bar{\mathbf{P}}_d \equiv \left[\begin{array}{c} \bar{P}_d \\ \bar{P}_d \end{array}\right],$$

and

$$M_d(t) \equiv \left[\begin{array}{cc} (1+\tau_{pa}\lambda_{d1})e^{\lambda_{d1}t} & (1+\tau_{pa}\lambda_{d2})e^{\lambda_{d2}t} \\ e^{\lambda_{d1}t} & e^{\lambda_{d2}t} \end{array}\right].$$

The time constants λ_{d1} and λ_{d2} are functions of the time constants τ_{vd} and τ_{pa} and the diastolic smallness parameters δ_d and γ_d.

4. Inter-beat evolution

Without loss of generality, we assume that the cardiac cycle starts in systole. Introducing

$$E_s \equiv M_s(T_s + T_d^r)M_s^{-1}(0) \quad \text{and} \quad \tilde{\mathbf{P}}_s \equiv (1 - E_s)\bar{\mathbf{P}}_s$$

we can express the pressures at the end of the systolic phase of the cardiac cycle according to

$$\mathbf{P}_s(T_s + T_d^r) = \tilde{\mathbf{P}}_s + E_s\mathbf{P}_s(0).$$

Similarly, if we introduce

$$E_d \equiv M_d(T_d)M_d^{-1}(0) \quad \text{and} \quad \tilde{\mathbf{P}}_d \equiv (1 - E_d)\bar{\mathbf{P}}_d$$

we can express the pressures at the end of the diastolic phase of the cardiac cycle according to

$$\mathbf{P}_d(T_d) = \tilde{\mathbf{P}}_d + E_d\mathbf{P}_d(0).$$

Since the initial state of the diastolic period equals the final state of the preceding systolic period

$$\mathbf{P}_d(0) = \mathbf{P}_s(T_s + T_d^r)$$

one can express the solution at the end of the entire cardiac cycle as an affine transformation of the initial state at the beginning of systole

$$\begin{aligned} \mathbf{P}_d(T_d) &= \tilde{\mathbf{P}}_d + E_d \cdot \mathbf{P}_s(T_s + T_d^r) \\ &= \tilde{\mathbf{P}}_d + E_d \cdot [\tilde{\mathbf{P}}_s + E_s\mathbf{P}_s(0)] \end{aligned} \tag{2}$$

Setting

$$\tilde{\mathbf{P}} \equiv \tilde{\mathbf{P}}_d + E_d\tilde{\mathbf{P}}_s \qquad \text{and} \qquad E_T \equiv E_d E_s$$

Equation 2 simplifies to

$$\mathbf{P}_d(T_d) = \tilde{\mathbf{P}} + E_T \cdot \mathbf{P}_s(0). \tag{3}$$

Equation 3 can be regarded as an evolution equation for a time step of one cardiac period, T. Using the fact that the pressures at the beginning of a systolic phase are equal to the pressures at the end of the preceding diastolic phase, one can relate the state of the system at the end of $(n+1)$ cycles to the state of the system at the end of the nth cycle according to

$$\mathbf{P}_d[n+1] = \tilde{\mathbf{P}} + E_T \mathbf{P}_d[n]$$

where the square brackets indicate time evolution in units of entire cardiac cycles. Repeatedly substituting this expression into itself, we obtain

$$\begin{aligned} \mathbf{P}_d[n+1] &= \tilde{\mathbf{P}} + E_T \mathbf{P}_d[n] \\ &= (1+E_T)\tilde{\mathbf{P}} + E_T^2 \mathbf{P}_d[n-1] \\ &\vdots \\ &= (1+E_T+\cdots+E_T^n)\tilde{\mathbf{P}} + E_T^{n+1}\mathbf{P}_d[0]. \end{aligned}$$

Summing up the geometric progression, we obtain

$$\begin{aligned} \mathbf{P}_d[n+1] &= \frac{1-E_T^{n+1}}{1-E_T}\tilde{\mathbf{P}} + E_T^{n+1}\mathbf{P}_d[0] \\ &= \frac{1}{1-E_T}\tilde{\mathbf{P}} + E_T^{n+1}\left(\mathbf{P}_d[0] - \frac{1}{1-E_T}\tilde{\mathbf{P}}\right) \end{aligned}$$

where, in both expressions, the term $1/(1-E_T)$ is to be interpreted as the matrix inverse $(I-E_T)^{-1}$. The first term in the previous equation represents the steady periodic mode. (One can readily see that the second term vanishes identically, if the initial state is taken to be the steady periodic mode.) The second term describes transitional dynamics that will eventually die out as the eigenvalues of the matrix E_T can be shown to be less than unity.

5. Results

When comparing the beat-to-beat dynamic behavior of the time-varying capacitance model to the inter-cycle evolution of the analytical solution to the switched capacitance model, we observed a maximum relative error of about 8%. This error was encountered for systolic arterial blood pressure. All other clinically relevant cardiovascular variables (such as stroke volume, ventricular end-diastolic volume, venous pressure, mean and diastolic arterial blood pressures) were all within 4% of their reference values derived from the time-varying capacitance model. Furthermore, these relative errors did not change significantly when physiologically important parameters of the model were perturbed over wide ranges. Thus, the relative errors encountered when using the analytical solution can be considered as constant bias.

6. Conclusion

Using a physiologically-based approximation of the time-varying ventricular compliance, we were able to linearize a previously non-linear, time-varying minimal cardiovascular model and found analytical solutions to its intra-beat and the inter-beat evolution. The inter-beat solution captures the dynamics of the non-linear, time-varying model quite well. The methodology presented is directly applicable to larger versions of the cardiovascular model. We believe that studying the analytical solutions will help our understanding of the behavior of the cardiovascular system and might aid in using these kinds of models in clinical decision support.

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