2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

A Lumped Parameter Model for Cardiac Output Estimation Using Arterial Blood Pressure Waveform

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***Abstract*— This paper investigates a subject-specific lumped parameter cardiovascular model for estimating Cardiac Output (CO) using the radial Arterial Blood Pressure (ABP) waveform. The model integrates a simplified model of the left ventricle along with a linear third order model of the arterial tree and generates reasonably accurate ABP waveforms along with the Dicrotic Notch (DN). Non-linear least square optimization technique is used to obtain uncalibrated estimates of cardiovascular parameters. Thermodilution CO measurements have been used to evaluate the CO estimation accuracy. The model achieves less than 15% normalized error across 10 subjects with different shapes of ABP waveform.**

I. INTRODUCTION

Arterial Blood Pressure (ABP) waveform has been a popular physiological signal used for assessing the hemodynamic status and cardiovascular health of an individual, especially in critical care units. It is created as a result of the complex dynamic interaction between the heart and the systemic vascular bed and can be used to provide information on both these components of our Cardiovascular System (CVS).

Several pulse contour methods (PCMs) have used the ABP waveform to estimate CVS parameters like Stroke Volume (SV), Cardiac Output (CO) and Total Peripheral Resistance (TPR). Extensive reviews of minimally invasive CO estimation methods have been done in [1], [2] and [3]. Some of these methods use 2-element lumped parameter models with linear and/or non-linear elements where as some others are based on the area under the systolic region of the ABP waveform. Few techniques compute the instantaneous pulsatile aortic blood flow waveform from the ABP signal and compute CO as the time-averaged flow over a cardiac cycle. As per the study done in [2], CO estimation based on Liljestrand and Zander estimator [4] performed better and had an error of 0.79L/min with calibration. In a separate study done in [1], Wesseling's Corrected Impedance method [5] achieved a Normalized Root Mean Square Error (NRMSE) of 12.3% without calibration.

Diastolic Pulse Contour Analysis method has been another popular technique used for CVS parameter estimation where in the diastolic decay portion of the ABP waveform is fitted to a modified third order lumped parameter model [6] with 4 elements. In this model, the arterial compliance is split up into two components, larger proximal compliance of the elastic arteries and the smaller distal compliance of the muscular arteries. Both are separated by an inductor representing the blood intertance.

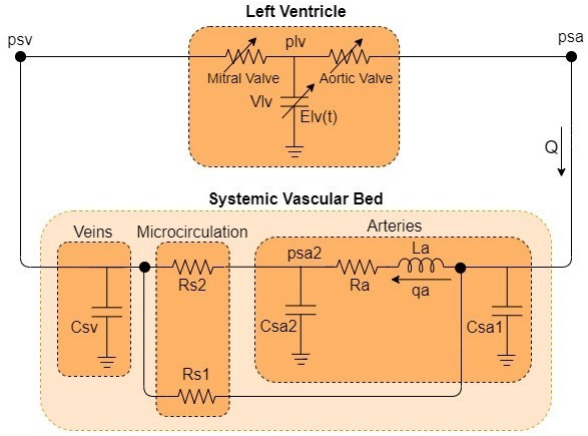

Fig. 1. 5th order CVS model.

A subject-specific pulsatile lumped parameter CVS model is investigated in this paper, for estimating Cardiac Output (CO) from the minimally-invasive ABP waveform measurements at the radial artery. The model is capable of generating the morphology of the ABP waveform accurately including the Dicrotic Notch (DN). Levenberg-Marquardt algorithm has been used to solve the non-linear least square optimization problem and obtain uncalibrated estimates of CVS parameters. Thermodilution CO data, measured simultaneously with the ABP waveform, has been used to evaluate the estimation accuracy. The model has been evaluated for three different shapes of the ABP waveform, across 10 subjects with a single CO measurement per subject, and achieves less than 15% NRMSE in all the cases.

II. METHODOLOGY

A. Proposed Model

The proposed 5th order lumped parameter model for this study is shown in Fig. 1. The 3rd order model in [7] has been modified to generate the morphology of the ABP waveform more accurately. The systemic arterial compliance is split into $Csa1$ and $Csa2$, where *smaller compliance* $Csa1$ consists of the compliance starting from the ascending aorta upto the radial artery and the *larger compliance* $Csa2$ consists of the remaining arterial compliance. Hence, $Csa1$ includes the aortic arch and its left/right limb branches i.e. brachiocephalic, subclavian, axillary, brachial and radial arteries and the voltage at that node is used for matching with the radial ABP measurements. Ra and La is the resistance and inductance of systemic arteries, respectively. $Rs1$ is the

peripheral resistance downstream of radial artery and $Rs2$ is the remaining systemic peripheral resistance. Systemic Veins, right heart, pulmonary vascular bed, and left atrium are lumped into the compliance element Csv.

The heart valves are modeled as pressure-dependent resistors that permit flow only in the forward direction [8]. The resistors are modeled as smooth sigmoidal functions given by (1). A large resistance R_{cl} represents a closed valve i.e. the flow through the valve is blocked, whereas a small resistance R_{op} represents an open valve. If the pressure gradient across the valve, $\Delta P_{valve}, > 0$ then $R_{valve} = R_{op}$ i.e. the valve is open and if $\Delta P_{valve} < 0$ then R_{valve} becomes R_{cl} and the valve closes.

$$R_{valve} = R_{cl} - \frac{R_{cl} - R_{op}}{1 + e^{-20(\Delta P_{valve})}} \tag{1}$$

Left Ventricle (LV) is modeled as a single variable capacitor driven by a time-varying elastance function. One of the ways of modeling the normalized elastance function for LV, $E_{lv}(t)$, is given by (2), where E_{max} and E_{min} are end-systolic and end-diastolic elastance, respectively, T is cardiac cycle length, T_M is systole duration and T_r is duration of early relaxation phase in diastole. The left ventricular pressure $plv(t)$ is approximated by (3), where $Vlv(t)$ is LV volume and Vd is LV volume when transmural pressure is zero. Both equations (2) and (3) are popular approximations and have been used in various CVS models [8],[9].

$$E_{lv}(t) = \begin{cases} E_{min} + \frac{1}{2}(E_{max} - E_{min})[1 - cos(\frac{\pi t}{T_M})] \\ \qquad \text{for,} \quad 0 \leq t \leq T_M \\ E_{min} + \frac{1}{2}(E_{max} - E_{min})[1 + cos(\frac{\pi (t - T_M)}{T_r})] \\ \qquad \text{for,} \quad T_M \leq t \leq T_M + T_r \\ E_{min} \qquad \text{for,} \quad T_M + T_r \leq t \leq T \end{cases} \tag{2}$$

$$plv(t) = E_{lv}(t)(Vlv(t) - V_d) \tag{3}$$

Systole duration, T_M, is the time duration from the beginning of the cardiac cycle till End of Systole time (T_{EOS}). In case of aortic ABP, the incisura is prominent and indicates EOS. But as the ABP wave travels down to the radial artery, due to high-frequency attenuation and wave reflections, the incisura is masked and replaced by DN, which is not a good indicator of EOS either. In this study, EOS is estimated as the first point, after the negative peak of the 1st derivative of the ABP signal, at which the sign of the 3rd derivative of the ABP signal changes from positive to negative [10].

B. Dataset

ABP data used for this analysis has been obtained from the Multi-parameter Intelligent Monitoring for Intensive Care III (MIMIC-III) database on Physionet [11], [12]. Such subjects are identified for whom simultaneously sampled ABP waveforms, Cardiac Output (CO) measurements and clinical meta-data details (age, height, weight) are available. ABP waveform has been collected in a minimally invasive fashion at the radial artery with a sampling frequency of 125 Hz and CO has been collected using invasive thermodilution technique. Since the CO measurements are intermittent, ABP measurements are taken from the same time window for which the CO measurement is available.

C. Sensitivity Analysis & Parameter Estimation

Sensitivity analysis is performed to reduce the number of parameters to be estimated and increase the confidence in the estimated parameter values. The model parameters are perturbed about a local operating point and the matrix of first-order partial derivatives, also known as the Jacobian Matrix, is computed using finite-difference approximation method. In order to compare the sensitivities, the partial derivatives are normalized by the nominal outputs and the nominal parameter values such that they become non-dimensional. The obtained sensitivities are ranked and a subset of the parameter set, which are observed to influence the variability of the model output considerably, are selected for estimation. The following set of parameters are found to be sensitive and are selected for optimization for all subjects: $\theta = \{E_{max}, E_{min}, Rs2, Csa1, Csa2, Ra\}$.

The cost function to be minimized by the parameter estimation algorithm uses a least square formulation and is a sum of the squares of the error between the model outputs and the measurement data. In order to reduce the estimation complexity, the model output vector doesn't consist of all the points of the ABP waveform and instead, consists of only a few features extracted from the ABP waveform, like the SBP and DBP [8], [13]. DN is another characteristic feature of the ABP waveform which is caused by a combination of reflected pressure waves. Since the amplitude of the reflected waves depends on systemic vascular resistance (SVR), the morphology of the DN also depends on SVR and Mean Arterial Pressure (MAP). The ABP waveform can be classified into Class I, II, III and IV, based on the shape of the DN [14]. Class I waveform has a distinct DN with a peak and a trough which has been included in the cost function for optimizing Class I waveform. Class II waveforms have not been evaluated in this study.

$$\begin{aligned} J_1 &= \frac{1}{M}\left[\sum_{i=1}^{i=M}\left(\frac{SBP_{est}(i) - SBP_{meas}(i)}{SBP_{meas}(i)}\right)^2\right] \\ &+ \frac{1}{M}\left[\sum_{i=1}^{i=M}\left(\frac{DBP_{est}(i) - DBP_{meas}(i)}{DBP_{meas}(i)}\right)^2\right] \\ J_2 &= \frac{1}{M}\left[\sum_{i=1}^{i=M}\left(\frac{SBP_{est}(i) - SBP_{meas}(i)}{SBP_{meas}(i)}\right)^2\right] \\ &+ \frac{1}{M}\left[\sum_{i=1}^{i=M}\left(\frac{DBP_{est}(i) - DBP_{meas}(i)}{DBP_{meas}(i)}\right)^2\right] \\ &+ \frac{1}{M}\left[\sum_{i=1}^{i=M}\left(\frac{DNpk_{est}(i) - DNpk_{meas}(i)}{DNpk_{meas}(i)}\right)^2\right] \\ &+ \frac{1}{M}\left[\sum_{i=1}^{i=M}\left(\frac{DNtr_{est}(i) - DNtr_{meas}(i)}{DNtr_{meas}(i)}\right)^2\right] \end{aligned} \tag{4}$$

Hence, there are two different cost functions, J_1 and J_2, which are listed in (4), where M indicates the number of cardiac cycles used for estimation and i is the index to the cardiac cycle. $DNpk(i)$ and $DNtr(i)$ are the peak and trough values, respectively, of the DN of the i^{th} cardiac cycle of Class-I ABP waveforms. J_2 cost function is used in case of Class I ABP and J_1 cost function is used in case of Class III and class IV ABP.

Since the model output is a nonlinear function of the parameters, nonlinear optimization technique has been used to minimize the least squares residual. Also, since the cost function is easily differentiable, gradient based Levenberg-Marquardt (LM) algorithm is used to solve the minimization problem by using the gradient of the cost function to find the point of minimum cost. The LM technique is iterative and has been shown to converge even when the initial parameter values are far from the optimal solution, although it converges rapidly if the initial parameter estimates are close to the optimal solution [15], [8].

D. Initialization of Parameters and State Variables

CO estimated from the subject's meta-data ($COmeta$) is used to initialize the state variables and nominal parameters of the model. It is estimated as per Eq. (5) where $height$ is in cm, $weight$ is in kg, BSA is body surface area in m^2, ET is Ejection Time in ms, HR is heart rate in bpm and Age is in $years$ [6].

$$\begin{aligned} BSA &= \sqrt{height * weight/3600} \\ SV &= -6.6 + 0.25 * (ET - 35) - 0.62 * HR \\ &\quad + 40.4 * BSA - 0.51 * Age \\ COmeta &= HR * SV \end{aligned} \tag{5}$$

Table I and Table II contain the initial values of the state variables and the nominal values of the parameters of the model, respectively. Both have been initialized based on the broad methodology outlined in [8], which uses the blood volume distribution and blood flow distribution in various compartments as outlined in [16]. V_T is the total volume of blood which is assumed to circulate through the body in one minute and is assumed to be the same as CO estimated using meta-data i.e. $COmeta$. F_T is the total volumetric flow rate in ml/s and is assumed to be equal to $V_T/60$. For initializing qa, $Rs1$ and $Rs2$, it is assumed that 10% of F_T flows through the arms i.e. through $Rs1$ and remaining 90% of F_T flows through Ra and $Rs2$. The systemic artery compliances, $Cs1$ and $Cs2$, are initialized as ratio of stressed volume to mean pressure at their respective nodes. The systemic arterial network and the systemic venous network are assumed to contain 13% of V_T and 72% of V_T, respectively. Since the $Cs1$ compartment is assumed to consist of the compliance starting from the ascending aorta upto the radial artery, it is assumed to contain 3% of V_T and $Cs2$ compartment contains the remaining 10%. Stressed Volume is assumed to be 25% for $Cs1$ compartment, 19% for $Cs2$ compartment and 5% for Csv compartment.

Peak of the elastance function, E_{max}, happens at T_{EOS} i.e. the end of systole and is initialized as $pEOS/(50 - V_d)$, where end-systolic volume is assumed to be 50mL. E_{min} is initialized as $4/(120 - V_d)$, where end-diastolic pressure is assumed to be 4mmHg and end-diastolic volume is assumed to be 120mL.

TABLE I
INITIAL VALUES OF CVS MODEL STATE VARIABLES

State	Physiological Meaning	Initial Value	Unit
psa	Arterial pressure@$Csa1$	$mean(ABP_{meas})$	mmHg
$psa2$	Arterial pressure@$Csa2$	$0.95 * psa$	mmHg
psv	Systemic venous pressure	3.5	mmHg
Vlv	Left ventricular volume	60	ml
qa	Flow between Csa1 & Csa2	$0.9 * F_T$	ml/s

Nominal values for Ra and La depend on class of the ABP waveform. La is set to .0045, .006 and .0035 for Class 1, Class III and Class IV ABP, respectively. Ra is in the range 0.04 to 0.12, 0.12 to 0.2 and 0.1 to 0.14 for Class 1, Class III and Class IV ABP, respectively. Optimum value for Ra is the one with the lowest waveform NRMSE.

TABLE II
NOMINAL VALUES OF CVS MODEL PARAMETERS

Parameter	Physiological Meaning	Nominal Value
E_{max}	Maximum elastance	$\frac{pEOS}{50-10}$
E_{min}	Minimum elastance	$\frac{4}{120-10}$
T_r	Elastance Relaxation time	$T_M/2$
T_M	Time for Max Elastance	T_{EOS}
V_d	Unstressed LV Volume	10
R_{cl}	Closed Valve R	20
$R_{mv,op}$	Open Mitral Valve Res.	0.007
$R_{av,op}$	Open Aortic Valve Res.	0.001
$Rs2$	Peripheral resistance 2	$\frac{psa2-psv}{qa}$
$Csa1$	Systemic artery compliance	$\frac{0.25*0.03*V_T}{psa}$
$Csa2$	Systemic artery compliance	$\frac{0.19*0.1*V_T}{psa2}$
Csv	Systemic venous compliance	$\frac{0.05*0.72*V_T}{psv}$
Ra	Arterial resistance	$0.04 - 0.14$
La	Arterial inductance	.0045/.0035/.006
$Rs1$	Peripheral resistance 1	$9 * (Rs2 + Ra)$

III. SIMULATION RESULTS

Normalized Root-Mean-Square Error (NRMSE) is used as the goodness-of-fit metric to determine how well the estimated ABP waveform matches the ABP measurements. It is given by (6), where N is the number of samples used to assess the fit.

$$NRMSE = \sqrt{\frac{1}{N}\sum_{i=1}^{i=N}\left(\frac{ABP_{est}(i) - ABP_{meas}(i)}{ABP_{meas}(i)}\right)^2} \tag{6}$$

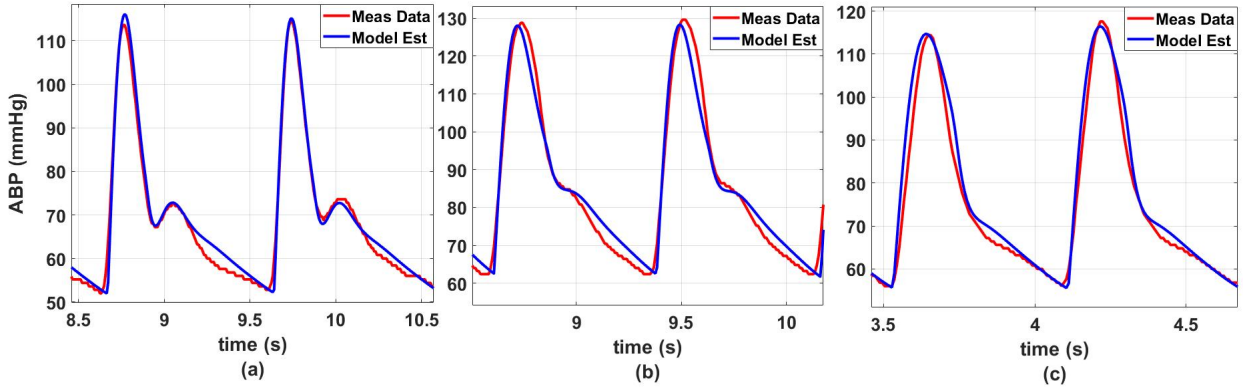

Fig. 2. (a) Class I, (b) Class III and (c) Class IV waveform.

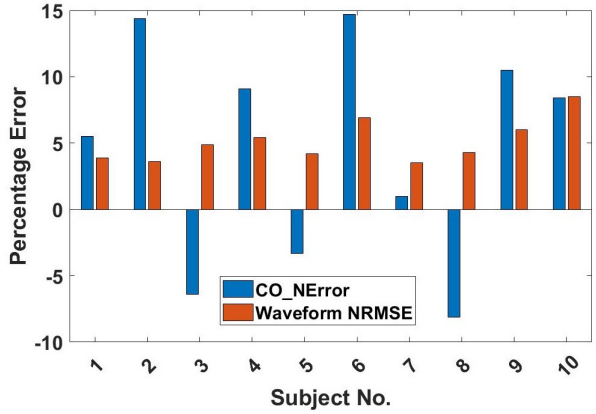

Fig. 3. CO and Waveform % Estimation Error. Subjects 1 to 6 have Class I, 7 & 8 have Class III and 9 & 10 have Class IV ABP waveforms.

Another performance metric used is the normalized error in estimating CO and is computed using (7). CO is estimated as the average current flowing out of aortic valve during systole. For each subject, 10 cardiac cycles of ABP data is selected for parameter estimation. The ABP data is in a small window around the time instant for which thermodilution CO measurement is available for that subject.

$$CO\_NError = \frac{CO_{est} - CO_{meas}}{CO_{meas}} \tag{7}$$

Figure 2 indicates that the 5th order model can generate the shape of the DN and the morphology of the ABP waveform reasonably well for all classes. Figure 3 shows the CO estimation performance for the investigated model for 10 subjects with different classes of ABP waveforms. As shown, the proposed technique achieves waveform NRMSE of less than 8.5% and CO estimation error of less than 15% for all subjects.

IV. CONCLUSION

This paper explores a subject-specific pulsatile lumped parameter model for estimating CO using the radial ABP waveform. The model is evaluated against thermodilution CO measurements and achieves less than 15% normalized error in all the cases. This preliminary study includes only 10 subjects with one CO measurement and a more extensive study with larger data set will be conducted in future. Reliability of this model in tracking relative changes in CO will also be investigated in future.

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