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Finite-time joint estimation of the arterial blood flow and the arterial Windkessel parameters using modulating functions ⋆

Mohamed A. Bahloul * **Taous-Meriem Laleg Kirati.** *

* *Computer Electrical and Mathematical Science and Engineering (CEMSE) Division, King Abdullah University of Science and Technology (KAUST), 23955-6900 Thuwal, Kingdom of Saudi Arabia (e-mail: mohamad.bahloul,taousmeriem.laleg@kaust.edu.sa).*

Abstract: Studying the arterial hemodynamic response plays a crucial role in the understanding and the treatment of cardiovascular diseases. Due to the difficulty of measuring the arterial blood flow, its estimation through a particular arterial vessel, using non-invasive arterial pressure waveform measurements, has always been an important topic in physiology. For instance, knowing the blood flow in a specific site of the arterial network helps in the detection of arterial stenosis. It may also help in the diagnosis of heart valve's diseases. In this paper, an algorithm based on modulating functions is proposed to estimate the arterial blood flow as well as to calibrate the conventional Windkessel model using arterial blood pressure signals measured in a particular site of the arterial system. The algorithm is presented and illustrated through several numerical tests.

Keywords: Finite-time estimation, modulating functions, Windkessel model, blood flow

1. INTRODUCTION

Cardiovascular diseases (CVDs) are the primary cause of death worldwide, with a reported fatality rate of over 17 million (31 % of all global deaths) in 2015, Ruan et al. (2018). In general, CVDs affect the blood flow, either by narrowing or blocking the blood vessels causing arterial stenosis that can generate heart attacks, or by damaging the heart valves, which control the flow of blood into and out of the heart. In the view of this, the investigation of the blood flow through the arterial network, has always been an imperative subject matter in both physiology and biomedical engineering. It is commonly known that perceiving and analysing the blood flow waveform in a specific site of an artery, provide relevant information about the physiological state of the cardiovascular system. However, the existing tools for the non-invasive measurement of the blood flow are either complex to use, uncomfortable, expensive or do not provide reliable measurements as they may need additional pre-processing, Fossan et al. (2018); Ledezma (2012); Bidhult et al. (2019).

Mathematical modeling of the arterial hemodynamics has been subject of intensive studies, Lazakidou (2011). The models usually describe the blood flow dynamics and are characterized by parameters that have physiological attributes. These models vary in term of dimensionality, from 0-Dimension (0D), which are given by time dependent ordinary differential equations (ODE) and usually referred to as lumped parametric models, to 3-Dimension (3D) models, which take into account the spatial variability and are described by partial differential equations (PDE), Bahloul and Laleg-Kirati (2018); Grinberg et al. (2009). As the model's dimensionality increases, its accuracy increases as well as its complexity.

Many studies showed the potential of 0D models in representing the overall behavior of the arterial network with a reduced number of characteristic parameters that have a physical relevance, Zhou et al. (2019). As a lumped parameter model, the well-known Windkessel model (WK) has been considered, for a long time in this regard. Originally formulated by Frank in 1899, the conventional WK model, known as two-element Windkessel (WK2), considers the whole arterial network as an elastic reservoir that receives as input the blood flow, from the heart. This elastic reservoir ensures the continuous flow through the arterial system even after the closure of the valves in the diastolic phase. As depicted in figure 1, the electrical analogue of WK2 consists of a capacitor (C) connected in parallel to a resistor (R_p) representing the total arterial compliance and peripheral resistance, respectively, Westerhof et al. (2019). Over the last decade, the potential use of the WK model in clinical routine has been investigated. For instance, it can serve as a tool to estimate physiological parameters which are not possible to evaluate and quantify directly, in a non invasive way, such as the arterial compliance or the local arterial stiffness.

Several estimation algorithms have been proposed in the literature, Kind et al. (2010), for the identification of the Windkessel model's parameters. These algorithms are based on iterative numerical optimization methods, with a recursive trust region, which minimize an error between the real and predicted data, in both time or/and frequency

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domains. Although, these approaches are reliable, they are computationally expensive and often depend on the initialization. They are also not robust against noise. Additionally, these algorithms require both blood pressure and blood flow signals. Even if the blood pressure waveform is widely accessible, there are still several limitations in measuring blood flow signal. Indeed, blood pressure sensors are easier to set up and more readily available in both popular and clinical practices than blood flow sensors. Therefore, there is a growing interest in developing new estimation tools that can estimate jointly and accurately the model's parameters and the blood flow from non invasive available measurements of the arterial blood pressure.

In this paper, we propose a finite-time estimation method based on the so-called modulating functions (MF) to estimate jointly the blood flow in a specific site of the arterial network and the two-element Windkessel model's parameters. The concept of modulating functions is not new, dating from its first introduction by Shinbrot, Shinbrot (1957), in 1957. MF based-estimation is a non-asymptotic method that has been successfully used in parameters' identification for both integer order systems Co and Ydstie (1990); Balestrino et al. (2000); Guo et al. (2014) and fractional order systems Liu et al. (2013); Wei et al. (2019). MF based estimation methods offer several advantages Belkhatir and Laleg-Kirati (2017); Belkhatir et al. (2018); Asiri (2017). For example, it is computationally less costly compared to optimization based methods and do not require initial conditions. In addition, it is robust against noise and numerically more stable as the numerical computation of noisy measurements' derivatives is avoided.

The rest of this paper is organized as follows. Section 2 introduces some preliminary results on the mathematical formulation of the arterial Windkessel model and modulating functions. Modulation function based-algorithm for the joint estimation of the arterial blood flow and WK2 parameters is proposed in Section 3. Some numerical examples that illustrate the performance of the proposed algorithm are provided in Section 4 along with a discussion of the results. Finally, the conclusion and future work are given in section 5.

2. PRELIMINARIES

2.1 Windkessel Model

The concept of Windkessel representation was borrowed from electrical circuit analogy, where the electrical voltage corresponds to the arterial blood pressure and the current corresponds to the blood flow through the arteries. With reference to Fig. 1, we present in this part the mathematical formulation of Frank's Windkessel as follow:

On the basis of the conservation mass, the input arterial blood flow, $Q_a(t)$, pumped from the left ventricle of the heart to the arterial vascular bed can be expressed as:

$$Q_a(t) = Q_{stored}(t) + Q_{out}(t), \tag{1}$$

where $Q_{stored}(t)$ is the blood stored in the arterial tree and $Q_{out}(t)$ corresponds to the flow out of the arterial system. Q_{out} is supposed to be proportional to the aortic blood pressure $P_a(t)$, that is:

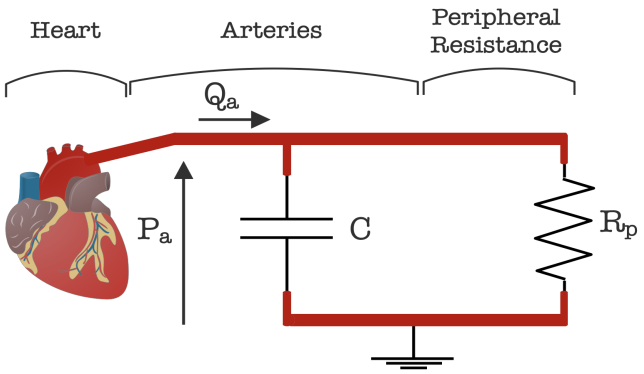

Fig. 1. Schematic representation of the electrical analog of the two element Windkessel model. It consists of a capacitor (C), connected in parallel to a resistor (R_p) accounting for the total arterial compliance and the total peripheral resistance, respectively.

$$Q_{out}(t) = \frac{1}{R_p} P_a(t), \tag{2}$$

where R_p is the total peripheral resistance. Regarding to $Q_{stored}(t)$, it is defined as the rate of flow by taking the first derivative of the blood volume $V(t)$ equation for the time, that is:

$$Q_{stored}(t) = \frac{dV(t)}{dt} \tag{3}$$

$$Q_{stored}(t) = \underbrace{\frac{dV(t)}{dP_a(t)}}_{C} \frac{dP_a(t)}{dt} = C\frac{dP_a(t)}{dt} \tag{4}$$

where $C = \frac{dV(t)}{dP_a(t)}$ is a proportionality constant accounting for the total arterial compliance. Substituting (2) and (4) into (1) yield:

$$Q_{in}(t) = C\frac{dP_a(t)}{dt} + \frac{1}{R_p} P_a(t). \tag{5}$$

Equation (5) can be written as:

$$F_{in}(t) = \tau\frac{dP_a(t)}{dt} + P_a(t), \tag{6}$$

where $F_{in}(t) = R_p Q_{in}(t)$ and the time constant τ equals to the product R_pC.

2.2 Modulating functions

Definition, *Preisig and Rippin (1993):* Let $[0,T] \subset \mathbb{R}$, $n \in \mathbb{N}^*$, $m \in \mathbb{N}$ with $m \leqslant n-1$, and ϕ_m be a function defined on $[0,T]$ between which ϕ_m depends on m. The function ϕ_m is called $(n,m)^{th}$ order (generalized) modulating function on $[0,T]$, if it satisfies the following properties: for $p = 0, 1, 2, \ldots, n-1$,

$(P1)$ $\phi_m(t) \in C^n([0,T])$

$(P2)$ $\phi_m^{(p)}(0) = 0$,

$(P3)$ $\phi_m^{(p)}(T) = 0$,

where $T > 0$ and p refers to the order of the derivative and $C^n([0,T])$ $(n \in \mathbb{N}^*)$ denotes the space of n times continuously differentiable functions over $[0,T]$.

In the following, we recall the integration by part formula which is essential in the application of the modulating functions to parameters identification

Lemma: Let $f, g \in C^n(\mathbb{R})$, where $n \in \mathbb{N}^*$. Then, for any interval $[0,T] \cup \mathbb{R}$, we have:

$$\int_0^T f(t)\ g^{(n)}(t)dt = (-1)^n \int_0^T f^{(n)}(t)\ g(t)dt + \underbrace{\sum_{k=0}^{n-1}(-1)^k \left[f^{(k)}(t)\ g^{(n-1-k)}(t)\right]_{t=0}^{t=T}}_{S} \quad (7)$$

In the case where f is a MF, the term S in (7) is equal to 0. Hence, the MF will allow the transfer of the differentiation of the input or/and output to the differentiation of the MF which can be done analytically and thus will avoid numerical un-stability.

2.3 Modulating functions based-estimation method

The MF based method is a non-asymptotic estimation approach where the basic idea is to transform the estimation problem for a differential equation into a solution problem of a set of algebraic integral equations. Thanks to its properties, MF based estimation approach is considered to be very fast and easy to implement. In addition, by dint of the integration by part criteria (Lemma) along with modulating function properties (P2-P3 in the definition) the MF based method is robust with respect to corrupting noises. In the following, we present the main steps of a MF based method.

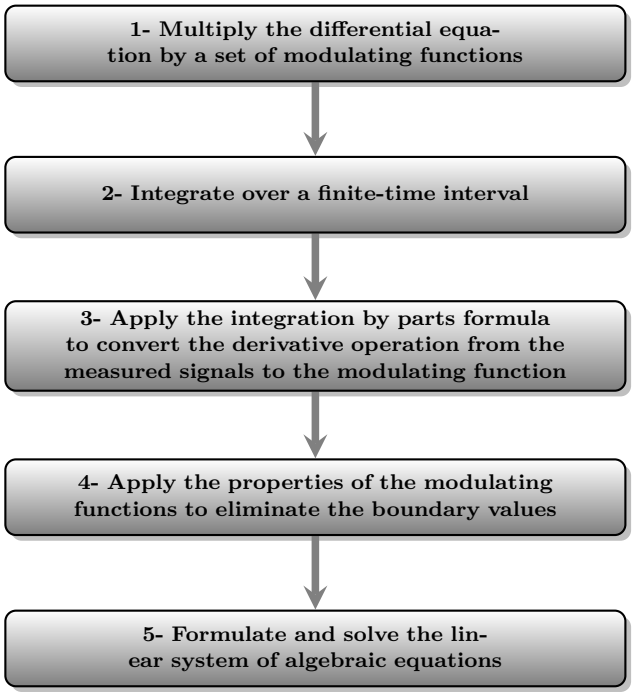

Fig. 2. Modulating function-based estimation method's procedure

3. JOINT ESTIMATION OF THE ARTERIAL BLOOD FLOW AND WINDKESSEL MODEL'S PARAMETERS

After defining the MF-based estimation procedure and its properties, in this section, we show the application of this approach to system (6) for the sake of estimating the input $F_{in}(t)$ along with the time constant τ, from the measured output given by the arterial blood pressure waveform, $P_a(t)$. Hence, the generic estimation problem can be formulated as follows:

$$\textbf{EP}\ \begin{cases} \textit{Given the ODE (6), the output signal } P_a(t) \\ \textit{for } t \in [0,T], \textit{ jointly find estimates } (\hat{F}_{in}(t), \hat{\tau}) \\ \textit{for the unknown input signal and time constant.} \end{cases}$$

As the main concept of the MF based method is to write the differential equation as a set of algebraic integral equations, as an elementary step, we need to decompose the input signal $F_{in}(t)$ in the space spanned by a set of known basis functions $\{\beta_i(t)\}_{i=1}^V$, as follow:

$$F_{in}(t) = \sum_{i=1}^{V} \xi_i \beta_i(t), \quad (8)$$

where $\{\xi_i\}_{i=1}^V$, $V \in \mathbb{N}^*$, will be considered the unknown projection parameters. Accordingly, (6) can be written as:

$$\sum_{i=1}^{V} \xi_i \beta_i(t) = \tau \dot{P}_a(t) + P_a(t), \quad (9)$$

$\dot{P}_a$ denotes the derivative of $P_a(t)$ with respect to time. Based on this projection, the estimation problem can be formulated as follows:

$$\textbf{EP}^*\ \begin{cases} \textit{Given the ODE (9) and the output signal } P_a(t) \textit{ for} \\ t \in [0,T], \textit{ jointly find estimates } (\{\hat{\xi}_i(t)\}_{i=1}^V, \hat{\tau}) \textit{ for} \\ \textit{the unknown projection weights and time constant.} \end{cases}$$

In what follows, the different steps of the proposed algorithm are presented to solve EP^*, and hence EP:

Step 1: Multiply (9) by a set of modulating functions ϕ_m, for $m = 1, ..., M.$:

$$\phi_m(t) \sum_{i=1}^{V} \xi \beta_i(t) = \phi_m(t)\tau \dot{P}_a(t) + \phi_m(t) P_a(t) \quad (10)$$

Step 2: Integrate over the time interval [0,T]:

$$\sum_{i=1}^{V} \xi_i \int_0^T \phi_m(t)\beta_i(t)dt = \tau \int_0^T \phi_m(t)\dot{P}_a(t)dt + \int_0^T \phi_m(t)P_a(t)dt \quad (11)$$

It is worth to note that one of the main offered advantages by the MF-based method is that the integral in this step has an effect to dampen and filter the noise of the measured signals.

Step 3: Applying formula (7) given in the Lemma, we obtain:

$$\sum_{i=1}^{V} \xi_i \int_0^T \phi_m(t)\beta_i(t)dt - \tau\left[S_T - S_0 - \int_0^T P_a(t)\dot{\phi}_m(t)dt\right] = \int_0^T \phi_m(t)P_a(t)dt, \quad (12)$$

where $S_0 = \phi_m(0)P_a(0)$ and $S_T = \phi_m(T)P_a(T)$ contain all the boundary values that are equal to 0 based on (P1-P3).

Step 4: Eliminate the null boundary values and form the linear system:

$$\sum_{i=1}^{V} \xi_i \int_0^T \phi_m(t)\beta_i(t)dt + \tau \int_0^T P_a(t)\dot{\phi}_m(t)dt = \int_0^T \phi_m(t)P_a(t)dt \tag{13}$$

Equation (13) can be written as a linear system, that is:

$$\sum_{i=1}^{N} \theta_i A_{mi} = b_m, \qquad m = 1\ ,..,\ M, \tag{14}$$

and its compact form is as follow:

$$A\theta = b, \tag{15}$$

where $A \in \mathbb{R}^{M\times N}$, $N = V + 1$ and b $\in \mathbb{R}^M$. The vector $\theta \in \mathbb{R}^N$ comprises the projections weight along with the characteristic time constant parameter τ, that is:

$$\theta = (\xi_1\ \xi_2\ ...\ \xi_V\ \tau)^T \tag{16}$$

where $(.)^T$ denotes the transpose of a row vector.

The constitution of the components of A and b are given in Algorithm 1.

Algorithm 1 Construction algorithm of A and b

for m = 1:1:M **do**

% Forming A

for j = 1:1:N-1 **do**

$$A(m,i) = \int_0^T \phi_m(t)\beta_i(t)dt$$

end for

$$A(m,N) = \int_0^T \dot{\phi}_m(t)P_a(t)dt$$

% Forming b

$$b(m,1) = \int_0^T \phi_m(t)P_a(t)dt$$

end for

Step 5: Solving the linear problem: For a given blood pressure signal $P_a(t)$, a set of M modulating functions and a set of V basis functions to project the input signal F_{in}, the estimate of parameters' vector $\hat{\theta} = (\hat{\xi_1}\ \hat{\xi_2}\ ...\ \hat{\xi_V}\ \hat{\tau})^T$ is computed by solving the following linear system of equations:

$$A\hat{\theta} = b, \tag{17}$$

Remark: There exist several types of modulating functions in the literature, such as polynomial and spline MFs, Fedele and Coluccio (2010), Asiri (2017). The number of modulating functions (M) depends on the number of unknown parameters (N). The minimum number of MF is equal to N. However it has been noticed that increasing M may help improve the estimation and especially in presence of noise . In this study, we chose $M \geq 2N$.

4. RESULTS AND DISCUSSION

The proposed algorithm has been tested using in-silico data set which has been generated from a validated one-dimensional numerical model of the arterial network, by Willemet et al. (2015). This database consists of hemodynamic signals (e.g. pressure, flow and distension waveforms) at all arterial locations. It presents arterial hemodynamic of virtual healthy adult subjects in which the cardiac and arterial parameters vary within physiological ranges. This in-silico data set is able to mimic the major hemodynamic properties sensed *in–vivo*. For this study, we selected 3 virtual subjects with different arterial characteristics, as shown in table 1. In the last column of table 1, we present the true constant time τ that will be subject to estimation along with the input F_{in}. The explored hemodynamic signals are measured at the level of the ascending aorta. The proposed algorithm has been implemented in Matlab and applied in both noise-free and noisy cases. In the noise corrupted case, white Gaussian random noise with zero mean has been added to the output signal $P_a(t)$ with different levels (1%, 3%, 5%, 10%). Then, the effectiveness and robustness of the method is evaluated by calculating the relative error (RE %) between the true parameter (τ) and the estimated one ($\hat{\tau}$), and the real input (Fin) and its estimate ($\hat{F_{in}}$) as follows:

$$\begin{cases} RE_{parameter} = \frac{\|\tau-\hat{\tau}\|_2}{\|\tau\|_2} \times 100\% \\ RE_{input} = \frac{\left\|F_{in}-\hat{F}_{in}\right\|_2}{\|F_{in}\|_2} \times 100\% \end{cases} \tag{17}$$

The following modulating function has been used:

$$\phi_m(t) = t^{M+\bar{q}+1-m}(T-t)^{\bar{q}+m} \tag{18}$$

where $m = 1,\ 2,\ ...\ , M$ with M is the total number of modulating functions and $\bar{q} \in \mathbb{R}^+$ is a degree of freedom parameter, Belkhatir and Laleg-Kirati (2018).

Fig. 3 shows the reconstruction results of the input blood flow in the absence of noise using a Jacobi polynomial projection basis, for the three Subjects. For these estimations, we took ($M = 14$, $\bar{q} = 1.3$) for Subjects 1 & 2, and ($M = 17$,$\bar{q} = 0.65$) for Subject 3. $V = 7$ projection basis functions have been considered for subjects 1 & 2, and ($V = 8$) for subject 3. We observe from the reconstruction and absolute error plots for subjects 1 and 2 which have

Table 1. Arterial characteristics of three virtual subjects. T_c corresponds the cardiac period, SV is the stroke volume, SP is the systolic blood pressure value, DP is the diastolic blood pressure value and τ is the time constant.

Parameter / Subject	T_c [sec]	SV [ml]	SP [mmHg]	DP [mmHg]	τ
Subject 1	0.83	66.40	98.04	67.22	1.26
Subject 2	0.83	83.00	105.07	78.52	1.53
Subject 3	0.95	99.60	103.93	69.25	1.38

Table 2. Relative error (%) of the estimated parameter and blood flow input for three different virtual subjects.

RE (%) / Subject	$\frac{\|\tau-\hat{\tau}\|_2}{\|\tau\|_2}\times 100$	$\frac{\left\|F_{in}-\hat{F}_{in}\right\|_2}{\|F_{in}\|_2}\times 100$
Subject 1	24.63	14.00
Subject 2	3.17	16.15
Subject 3	14.37	13.75

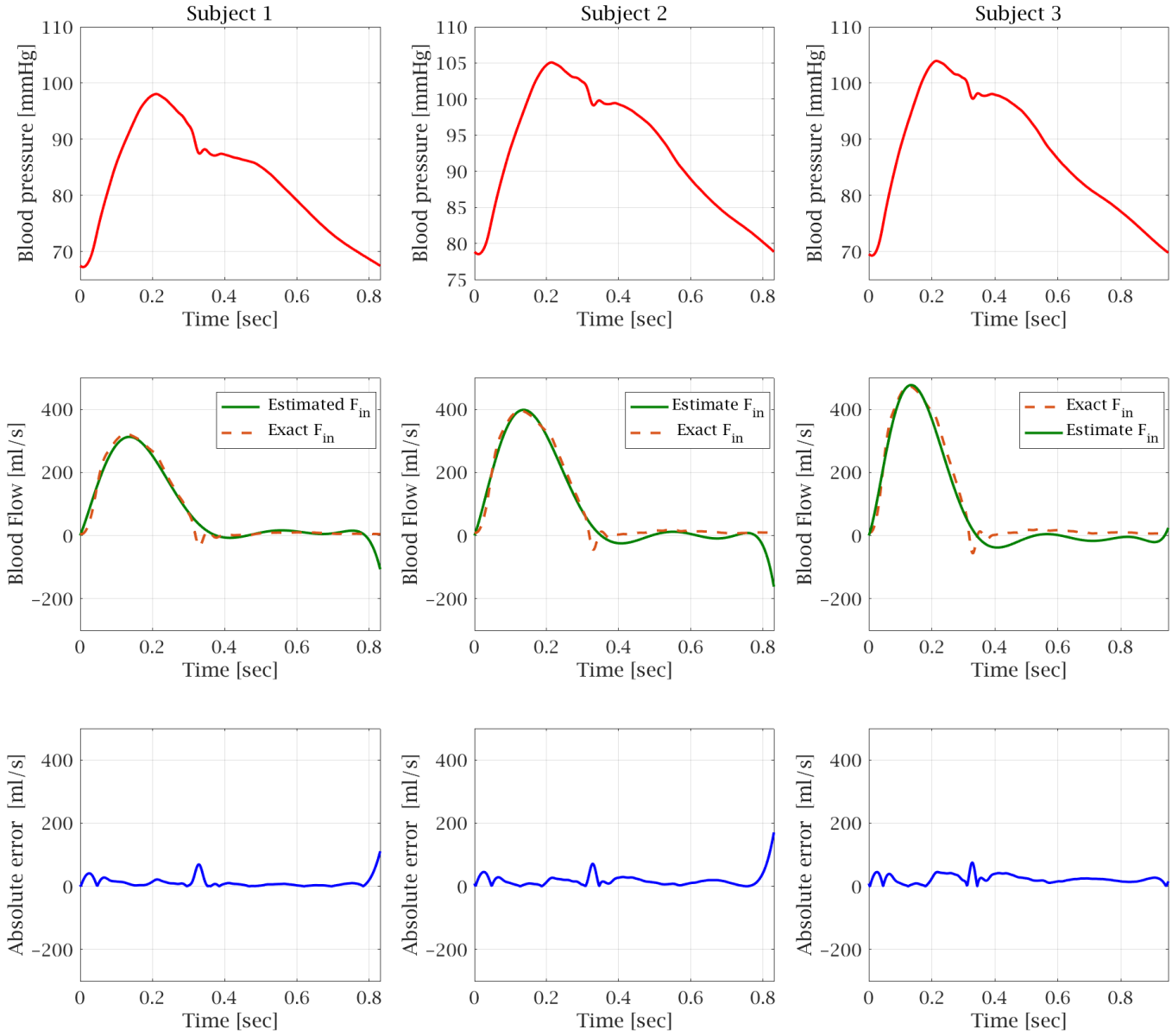

Fig. 3. Estimated input blood flow F_{in} in noise-free by blood pressure for three different subjects using Jacobi polynomial basis with unknown time constant parameters τ.

cardiac periods equal to 0.83 sec, that the estimation results are affected at the boundary, unlike subject 3 with a cardiac period equals to 0.95 sec where this effect is attenuated. The relative errors for both parameter and input estimations are reported in Table 2. It is clear, from these results, that the algorithm gives the best parameter estimation performance in the case of subject 2, but at the expense of the input estimation accuracy. Unlike, subject 3 presents the best performance in term of input estimation.

Fig. 4 shows the reconstruction result along with the absolute error of multi-cycles blood flow input. Since the results are similar for all the subjects, we present only the reconstruction plot of subject 1. For this simulation, we took $M = 223$ and $\bar{q} = 4$. For the projection basis, we used 43 cubic b-splines functions. It is clear from this plot that the estimation result is less accurate in the first two cycles, then it converges along the remaining cycles. Based on our extensive numerical investigations, we noticed that as much as we increase the number of cycle, the algorithm requires more basis functions as well as MFs, to converge.

Table 3. Relative error (%) of estimated parameter and and blood flow input for corrupted output by different noise level (up to 10%)

RE (%) / Noise level	$\frac{\|\tau-\hat{\tau}\|_2}{\|\tau\|_2} \times 100$	$\frac{\|F_{in}-\hat{F}_{in}\|_2}{\|F_{in}\|_2} \times 100$
0% noise	24.63	13.75
1% noise	18.11	14.50
3% noise	3.62	19.01
5% noise	8.69	25.80
10% noise	24.63	36.89

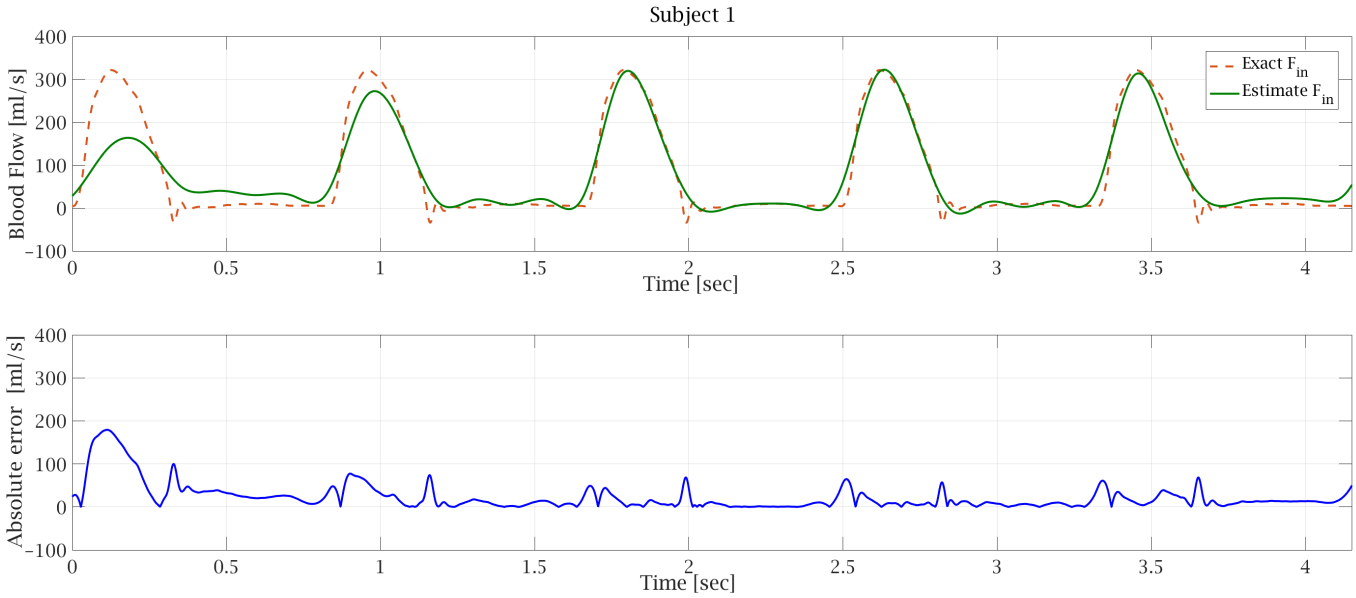

Fig. 4. Estimated multi-cycle input blood flow signal, in the absence of noise, using cubic b-splines basis.

In addition, whatever the number of estimated cycles, the first two cycles are always not well estimated.

Fig. 5 illustrates the effect of the noise level while the number of MFs is fixed to ($M = 14$) and the number of basis functions ($V = 7$), in the case of subject 1. We observe from this investigation that the estimation results are not accurate at the amplitude. In addition, if we increase the number of basis functions and MFs, the error might be cancelled.

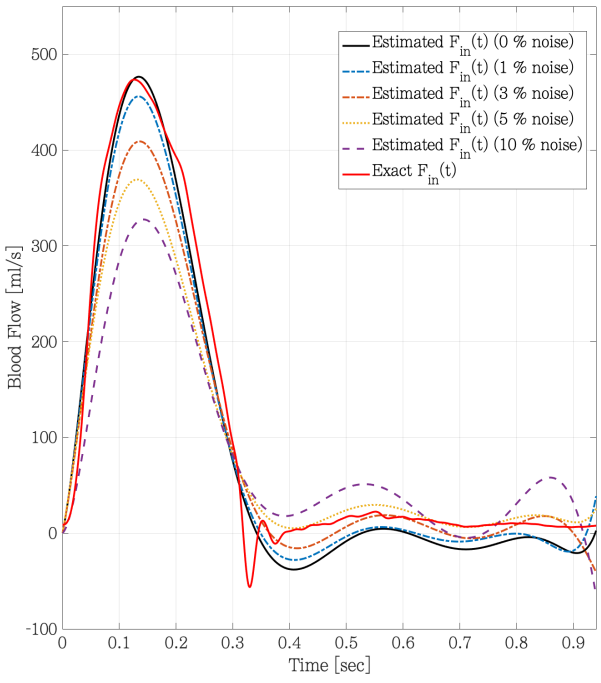

Fig. 5. Estimated blood flow input in noise-free (black) and noisy (1%, 3%, 5% and 10% noise level) cases by known blood pressure waveform.

Based on the above results and from the extensive numerical investigations that we conducted, it is worth to point the following observations:

- The total number of MFs affects the proposed algorithm performance. There exist a minimal number of MFs to get a good performance, then increasing M within a certain range will not affect the performance of the algorithm significantly. In the noisy case increasing M improves the estimation results.
- The choice of the projection basis and the number of functions affects the performance of the algorithm. We think that this choice depends on the prior knowledge of some properties of the estimated input such as smoothness and periodicity.

5. CONCLUSION

The estimation of the blood flow and arterial characteristic parameters is of great potential in the understanding and treatment of cardiovascular diseases. In this paper, we explore the use of identification-based modulating function methods for finite-time joint estimation of the arterial blood flow and the standard two element Windkessel model's parameters. The proposed algorithm can handle different input estimation scenarios such as one-cycle blood flow in both noise-free and noisy cases, and multi-cycle input. The extensive numerical investigations have resulted in useful observations and guidelines for potential and effective implementation of this algorithm.

In the future, further work should be conducted to refine more the tuning of the algorithm. Furthermore, we plan to investigate more on the numerical issues encountered in solving the linear problem within the last step of the algorithm. In fact, the condition number of the matrix inverse depends on the type and number of MFs which may lead to some numerical issues. In addition, in order to validate the proposed algorithm, we plan to use several sets of real hemodynamic data for both normal and abnormal subjects with different age, while analyzing and

comparing the results between the proposed algorithm and other different asymptotic and non-asymptotic estimation approaches. This phase should be conducted closely with experts in the cardiology field to interpret and better understand the obtained estimates.

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