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Estimation of three- and four-element windkessel parameters using subspace model identification

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Abstract

A windkessel model is widely used to operationalize vascular characteristics. In this paper we employ a non-iterative subspace model identification (SMI) algorithm to estimate parameters in a three- and four-element windkessel model by application of physical foreknowledge. Simulation data of the systemic circulation were used to investigate systematic and random errors in the parameter estimations. Results were compared to different methods as proposed in literature: one closed-loop and two iterative methods for the three-element model, and one iterative method for the four-element model. For the three-element model no significant systematic errors were observed using SMI. Concerning random errors, SMI appeared more robust in parameter estimations compared to the other methods (P<0.05 for a signal-to-noise ratio of 18 dB). For the four-element model, a significant systematic error in the estimate of the arterial inertance $L$ was observed (P=0.011). However, for all methods an increasing number of outliers in parameter estimates were observed at increased noise levels. These outliers were almost exclusive due to errors in estimates of $L$. In conclusion, with SMI physical parameters can mathematically be derived by application of physiological foreknowledge. For a three-element windkessel model, SMI appeared a very robust method to estimate parameters. However, application to a four-element windkessel model was less accurate because of low identifiability of $L$. Therefore, based on the simulation results, the use of the four-element windkessel model is questionable.

Key words: windkessel model ■ subspace model identification ■ peripheral resistance ■ arterial compliance ■ proximal arterial characteristic impedance ■ arterial inertance
Estimation of windkessel parameters using subspace model identification

Introduction

In the study of cardiovascular diseases much insight can be gained from hemodynamic characteristics of the vascular system, such as total peripheral resistance, total arterial compliance and characteristic impedance of the proximal aorta. Mathematical modeling and parameter estimation may help understanding the cardiovascular system, but is hampered by strong interactions between vascular characteristics. A well-known model to operationalize vascular characteristics is the windkessel model. Otto Frank has laid the basis for this model at the beginning of the twentieth century. He postulated that the aorta could be represented by a manometer with a lumped distensible section and a lumped peripheral resistance, or in electrical analogon, a combination of a capacitor and resistor in parallel\(^1\). In later research this classical two-element windkessel model has been extended with a third element to account for the impedance of the proximal part of the arterial bed\(^2\), and a fourth element to account for the inertia of the blood\(^3,4\).

The estimation of these parameters has been the subject of a number of studies over the past decades\(^3,5,6\). Mostly, *ad hoc* iterative techniques are used. However, iterative techniques have some typical disadvantages in common, such as no guaranteed convergence, local minima of the objective criterion and sensitivity to initial estimates. Subspace model identification (SMI) is a robust non-iterative method, with no non-linear optimization part involved. Furthermore, SMI can realize a state-space model from input-output data solely and only requires an estimate of the system order. The latter (i.e., the number of dynamical windkessel elements) can be determined through inspection of dominant singular values. Thus, from a numerical point of view SMI is very attractive for model identification purposes. However, when physical model parameters are of interest, SMI is usually not applicable.

The aim of this study was to investigate if SMI could be used to estimate parameters in three- and four-element windkessel models. Simulation data were used to investigate systematic errors in the parameter estimations by comparing the estimated values with the simulated values. Random errors were investigated in repeated simulations with different noise realizations.
Windkessel model

The three-element windkessel model (see Figure 1) has been used extensively to study the overall characteristics of the systemic and pulmonary arterial system\(^2\)-\(^{11}\). The model parameters are \(Z_0\), \(R\), \(C_a\) respectively, accounting for the characteristic impedance of the proximal part of the arterial bed (aorta, pulmonary artery), arterial inertance, peripheral resistance and total arterial compliance.

Stergiopulos et al.\(^3\) showed that a three-element windkessel model overestimates total arterial compliance and underestimates the characteristic impedance. To overcome this problem, an inertial term \(L\) was placed in parallel with the characteristic impedance to form the four-element windkessel model, as was previous introduced by Burattini and Gnudi\(^4\) (see Figure 1). It was found that ascending aortic pressure could be predicted more accurate from aortic flow in seven dogs using this four-element model.

In this paper we assume linear pressure-independent parameters. Since the three-element windkessel model consists of only one dynamic element, one state is needed to describe the dynamics. Assuming the flow through the aorta or pulmonary artery \(F_a(t)\) as an input, the state equations follow from the three-element windkessel model in Figure 1 using basic network theory:

\[
\frac{dP_p(t)}{dt} = -\frac{1}{RC_a} P_p(t) + \frac{1}{C_a} F_a(t) \tag{1}
\]

\[
P_p(t) = P_p(t) + Z_0 F_a(t), \tag{2}
\]

with state \(P_p(t)\) denoting pressure over the arterial compliance.

The four-element windkessel model consists of two dynamic elements. Hence, we need two states to describe the dynamics. The state vector consists of states \(F_L(t)\) and \(P_p(t)\), with \(F_L(t)\) denoting flow through the total arterial inertance. Again, assuming \(F_a(t)\) as an input, the state equations follow from the four-element windkessel model in Figure 1.

![Figure 1 - Three (A) and four (B) element windkessel model. Parameters are \(Z_0\), \(C_a\) and \(R\), and for the four-element windkessel model, \(L\), accounting for respectively the characteristic impedance of the proximal part of the arterial bed, peripheral resistance, total arterial compliance and arterial inertance.](image-url)
In state space notation they read:

\[
\begin{bmatrix}
\frac{dF_i(t)}{dt} \\
\frac{dP_j(t)}{dt}
\end{bmatrix} =
\begin{bmatrix}
-Z_0 \\
0
\end{bmatrix}
\begin{bmatrix}
F_i(t) \\
F_j(t)
\end{bmatrix} +
\begin{bmatrix}
\frac{Z_0}{L} \\
\frac{1}{C_s}
\end{bmatrix}
\begin{bmatrix}
F_j(t) \\
P_j(t)
\end{bmatrix}
\]

(3)

\[
P_i(t) =
\begin{bmatrix}
-Z_0 \\
1
\end{bmatrix}
\begin{bmatrix}
F_i(t) \\
F_j(t)
\end{bmatrix} +
\begin{bmatrix}
\frac{Z_0}{L} \\
\frac{1}{C_s}
\end{bmatrix}
\begin{bmatrix}
F_j(t) \\
P_j(t)
\end{bmatrix}
\]

(4)

The identification objective is to compute the state-space matrices, denoted as \(A, B, C\) and \(D\), from pressure \(P_a(t)\) and flow \(F_a(t)\) using SMI and to derive windkessel parameter values from these.

**Subspace model identification**

In this paper we employ the ordinary MOESP algorithm, stated by Verhaegen and Dewilde\(^\text{12}\). This algorithm realizes a state-space model from input-output data solely. The algorithm requires an estimate of the underlying system order \(n\) from outside, only. Next steps include the construction of Hankel matrices of the input and output data, data compression via RQ factorization, the computation of an SVD and solving for the system matrices. More about the MOESP implementation can be found in\(^\text{12-14}\).

State-space matrices are calculated as full state-space matrices in a certain optimally conditioned basis that is uniquely determined. This implies that the subspace algorithm delivers us the (discrete) system matrices up to a similarity transformation matrix \(T_d\) (an exception holds for \(D_d\)):

\[
\begin{align*}
A_{dT} & = T_d^{-1} A_d T_d, \\
B_{dT} & = T_d^{-1} B_d, \\
C_{dT} & = C_d T_d, \\
D_{dT} & = D_d,
\end{align*}
\]

(5)

with \(A_d, B_d, C_d\) and \(D_d\) the discrete system matrices.

In the next paragraph we show how to derive the windkessel parameters from \(A_{dT}, B_{dT}, C_{dT}\) and \(D_{dT}\). An estimate of the system order can be determined by singular values if we can distinguish disturbed singular values of the system from singular values due to noise\(^\text{15}\). Hence, the ability to determine the model order depends on the gap between a set of dominant singular values that correspond to the dynamics of the system and a set of small values due to noise. The three- and four-element windkessel models correspond to respectively a first and second order system.
Obtaining parameter values

The subspace algorithm delivers us discrete-time matrices. Prior to the determination of the windkessel parameter, indices should thus be converted to continuous-time. This conversion was performed using a zero-order-hold method. The continuous-time matrices are denoted as $A$, $B$, $C$, $D$, and $T$.

**Three-element windkessel model**

From (1) and (2) we have the (continuous) state-space matrices:

$$
A = -\frac{1}{RC_s}, \quad B = \frac{1}{C_s}, \\
C = 1, \quad D = Z_0.
$$

After converting the discrete subspace matrices to continuous-time, $D_T$ provides us an estimate of $Z_0$ directly. $A_T$ contains the eigenvalue of the system that equals the estimate of $A$ by definition and thus provides $1/RC_s$. $B$ and $C$ are subject to a transformation matrix $T$. Since we know $C$ in advance, the estimate of $B$ can be calculated by $\hat{B} = C_T B_T = \hat{C} \hat{B}$, where $\hat{C}$ is the estimate of $C$.

**Four-element windkessel model**

The (continuous-time) state-space matrices for the four-element windkessel model are:

$$
A = \begin{bmatrix}
-Z_0/L & 0 \\
0 & -1/RC_s
\end{bmatrix}, \quad B = \begin{bmatrix}
Z_0/L \\
1/C_s
\end{bmatrix}, \\
C = \begin{bmatrix}
-Z_0 \\
1
\end{bmatrix}, \quad D = \begin{bmatrix}
Z_0
\end{bmatrix}.
$$

As for the three-element windkessel model, the discrete-time subspace matrices are converted to continuous-time. Again, $D_T$ delivers us the estimate of $Z_0$. $A$ is a diagonal matrix and thus we are able to perform an eigenvalue decomposition on $A_T$ to obtain the diagonal elements or eigenvalues. The eigenvalue decomposition yields,

$$
A_T = T \hat{A} T^{-1},
$$

where $\hat{A}$ is the estimate of $A$, and $T$ the similarity transformation matrix that contains the eigenvectors of $A_T$. From $\hat{A}$ we obtain the estimates of $-Z_0/L$ and $1/RC_s$.

The estimation of the elements of $B$ and $C$ require some additional steps. Matrix division of $B_T$ and $C_T$ by $T$, computed from , is not possible since the derived $T$ is not the
true similarity, but *just* a transformation matrix (though they are dependent); this is due to another degree of freedom. Although the elements of $B$ and $C$ cannot be derived individually, the multiplication of these can. Consider:

$$B_r C_T = TBCT^{-1}$$

$$= \begin{bmatrix} t_1 & 0 \\ 0 & t_2 \end{bmatrix} \begin{bmatrix} \hat{b}_1 \\ \hat{b}_2 \end{bmatrix} \begin{bmatrix} \hat{c}_1 \\ \hat{c}_2 \end{bmatrix} \begin{bmatrix} t_1^{-1} & 0 \\ 0 & t_2^{-1} \end{bmatrix}$$

$$= \begin{bmatrix} \hat{b}_1 \hat{c}_1 & t_1 \hat{b}_1 \hat{c}_1 t_1^{-1} \\ t_2 \hat{b}_2 \hat{c}_2 t_2^{-1} & \hat{b}_2 \hat{c}_2 \end{bmatrix},$$

and observe that elements $(1,1)$ and $(2,2)$ of $B_r C_T$ are unaffected by $T$. $BC$ is given by:

$$BC = \begin{bmatrix} -\frac{Z_0^2}{L} & \frac{Z_0}{L} \\ \frac{Z_0}{C_s} & \frac{1}{C_s} \end{bmatrix}.$$

Hence, $B_r C_T$ deliver us estimates for $-Z_0^2 / L$ and $1/C_s$.

In summary, the structure of the windkessel model allows identification of the parameters independent of a transformation matrix:

$$\hat{D} = \hat{Z}_0$$

$$\hat{A}(1,1) = -\frac{\hat{Z}_0}{L}$$

$$\hat{A}(2,2) = -\frac{1}{R C_s}$$

$$B_r C_T (1,1) = -\frac{\hat{Z}_0^2}{L}$$

$$B_r C_T (2,2) = \frac{1}{C_s}.$$

Equations (9) are solved to obtain the windkessel parameters. In case of increased noise levels not all parameters may be uniquely derived. Therefore, these equations are solved in a non-linear least squares sense. Note that, although this is an iterative process the system identification itself is non-iterative.
The accuracy of the SMI techniques in estimating windkessel parameters were evaluated using simulation data. Data were computed as responses of the three- and four-element windkessel models (1)-(4) to a realistic periodic aortic flow curve which has been invasively measured in a healthy human (see Figure 2). To reach a steady state, 20 beats were simulated and only the last beat was taken to obtain an aortic pressure curve. Numerical integration was performed using the MATLAB ODE15S solver (R14SP1), supporting stiff differential equations and a variable order method. Venous pressure was assumed to be negligible so that aortic pressure represents the pressure difference across the systemic vascular bed. To investigate the robustness of SMI both flow and pressure data were contaminated with zero-mean white Gaussian noise. Signal-to-noise ratios (SNR) were defined by systolic signal power and specified noise power:

\[
\text{SNR} = 10 \cdot \log_{10} \left( \frac{\text{Power}_{\text{signal}}}{\text{Power}_{\text{noise}}} \right) = 10 \cdot \log_{10} \left( \frac{\text{RMS}_{\text{signal}}}{\text{RMS}_{\text{noise}}} \right)^2, \tag{10}
\]

with RMS the root mean square. It should be noted that SMI could also be used for model identification in the presence of colored noise. In this case, an instrumental variable matrix should be computed to obtain unbiased estimates.12

An important issue in model identification is the selection of the sampling frequency since it affects the estimation accuracy. Because heart period cannot be changed, only the sampling frequency can be optimized. Sampling with a too low frequency results in loss
of information, whereas a too high frequency, compared to the model time constants, is numerically unattractive since all poles will be clustered around point 1 in discrete time. The choice of the sampling frequency should thus be a trade-off between noise reduction (by lowering the sampling frequency) and relevance for the model dynamics\textsuperscript{16}. Based on empirical observations and time constants, a sampling frequency of 250 Hz was chosen. Validation of the estimated windkessel models was performed using the root-mean-square-error (RMSE), defined as:

\[
\text{RMSE} = \sqrt{\frac{1}{N} \sum_{k=1}^{N} (P_a(k) - \hat{P}_a(k))^2},
\]

where \(\hat{P}_a(k)\) denotes an estimated curve and \(P_a(k)\) a “true” curve. The goodness-of-fit was additionally assessed by the “variance accounted for” (VAF), defined as:

\[
\text{VAF}(P_a(k), \hat{P}_a(k)) = \left(1 - \frac{\frac{1}{N} \sum_{k=1}^{N} \|P_a(k) - \hat{P}_a(k)\|_2^2}{\frac{1}{N} \sum_{k=1}^{N} \|P_a(k)\|_2^2}\right) \times 100%.
\]

In this expression, a VAF of 100\% indicates a zero a perfect fit. For other predictions the VAF will be lower. Hence, the VAF can be used to evaluate the accuracy of a model to predict an output.

**Three-element windkessel model**

In order to explore systematic errors in the estimates of \(Z_0\), \(C_a\), and \(R\), these parameters were estimated from simulation data for which these parameters were alternately set at three levels (see Table 1). Parameter values for the systemic circulation were taken from literature, resembling physiology in normal as well as in pathological conditions (i.e. normotensive, hypotensive and hypertensive blood pressure)\textsuperscript{5,17}. Figure 2 shows examples

<table>
<thead>
<tr>
<th>Parameter</th>
<th>hypotensive</th>
<th>normotensive</th>
<th>hypertensive</th>
<th>dimension</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Z_0)</td>
<td>0.02</td>
<td>0.033</td>
<td>0.05</td>
<td>mmHg·s/ml</td>
</tr>
<tr>
<td>(C_a)</td>
<td>2</td>
<td>1.5</td>
<td>0.7</td>
<td>ml/mmHg</td>
</tr>
<tr>
<td>(R)</td>
<td>0.6</td>
<td>0.95</td>
<td>1.4</td>
<td>mmHg·s/ml</td>
</tr>
<tr>
<td>(L)</td>
<td>0.005</td>
<td>0.01</td>
<td>0.02</td>
<td>mmHg·s²/ml</td>
</tr>
</tbody>
</table>

 Each combination is simulated using the three- or four-element windkessel model. Parameter values are taken from literature, resembling physiology in normal as well as in pathological state\textsuperscript{5,17}. 151
of the responses of the windkessel model. Pressure-flow data were calculated for all possible combinations (i.e. $3^3=27$), contaminated with zero-mean white Gaussian noise sequences at an SNR of 30 dB (equal to a standard deviation of approximately 3.2 mmHg for pressure and 6 ml/s for flow when simulated with baseline parameters). For each parameter combination, 50 noise realizations were generated. Hence, the complete data set consisted of 1350 pairs of pressure-flow data (i.e. a full three factor design with three levels for each factor with 50 noise-realizations for each parameter combination). Figure 2 shows an example of simulated pressure and flow data with all three parameters set at its nominal values. Statistical analysis on estimation accuracy was evaluated by performing an analysis of variance (ANOVA). A three-way ANOVA was performed to study the effect of varying the three parameters.

To study the random errors in the estimates of $Z_0$, $C_a$ and $R$, these parameters were estimated from simulation data for different noise levels. Simulation data were calculated with nominal parameter values. Noise levels were set in the range 60 dB down to 6 dB with step size of 3 dB (corresponding to a noise standard deviation ranging between 0.2 and 25.5 mmHg for pressure and 0.6 and 47.8 ml/s for flow). For each level, SMI was applied to 50 noise realizations.

Four-element windkessel model

The four-element windkessel model consists of the parameters $Z_0$, $C_a$ and $R$, and $L$. As for the three-element windkessel model, parameters were alternately set at three levels (see Table 1), resulting in $3^4=81$ combinations. Also, for each parameter combination, 50 white noise-realizations with an SNR of 30 dB were simulated. Hence, the complete dataset consisted of 4050 pairs of pressure-flow data. The same analyses as for the three-element windkessel model were performed.

Comparison with other methods

The SMI approach for estimating three-element windkessel parameters was compared with three methods as proposed in literature. Among these were two iterative methods: one as proposed by Fogliardi et al.\textsuperscript{6}, further indicated as FOGL, and one maximum-likelihood estimator using a prediction-error minimization method (PEM)\textsuperscript{16}. In addition, a closed-loop expression as proposed by Cappello et al.\textsuperscript{5}, indicated as the energy balance method (EBM), was evaluated.

Initial parameters for the iterative methods FOGL and PEM were obtained from SMI and initial states were determined from the simulated pressure curves. EBM is a method based on conservation of mass and energy. Parameters are derived from total vascular resistance (i.e. $R + Z_0$), mean squared pressure and flow, and mean power. From the
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derived $R$, and $Z_0$, and from volume of the arterial compliance, $C_a$ is computed. For this method no initial values are required, although initial states should still be provided. These were determined from the simulated pressure curves.

Regarding the four-element windkessel model, the SMI approach was compared to PEM, but now applied to a four-element model.

All methods were applied on simulation data in the presence of zero-mean white Gaussian noise. As for the SMI methods, random errors of estimated parameters and the goodness of fit were evaluated.

Results

Three-element windkessel model

Using SMI there were no significant systematic errors in estimates of $Z_0$, $C_a$ and $R$ in comparison with true values: all parameters were estimated with an error less than 1% for 50 noise realization of 30 dB. In addition, the errors were not influenced by the levels of the parameters (no significant interaction, $P>0.05$). Table 2 shows random error in estimates of $Z_0$, $C_a$ and $R$ for SNR’s of 42, 30 and 18 dB. The table also shows random errors in the estimates obtained using EBM, FOGL and PEM. All methods were able to estimate $Z_0$ with no significant differences with respect to true values, except for EBM.

Table 2 – Comparison of estimated parameters in a three- and four-element windkessel model using different methods.

<table>
<thead>
<tr>
<th>SNR</th>
<th>True value</th>
<th>Three-element windkessel model</th>
<th>Four-element windkessel model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SMI</td>
<td>EBM</td>
</tr>
<tr>
<td>$Z_0$</td>
<td>42dB</td>
<td>0.033</td>
<td>0.033±0.001</td>
</tr>
<tr>
<td></td>
<td>30dB</td>
<td>0.033</td>
<td>0.033±0.003</td>
</tr>
<tr>
<td></td>
<td>18dB</td>
<td>0.033</td>
<td>0.032±0.011</td>
</tr>
<tr>
<td>$C_a$</td>
<td>42dB</td>
<td>1.5</td>
<td>1.54±0.03</td>
</tr>
<tr>
<td></td>
<td>30dB</td>
<td>1.5</td>
<td>1.56±0.12</td>
</tr>
<tr>
<td></td>
<td>18dB</td>
<td>1.5</td>
<td>1.63±0.47</td>
</tr>
<tr>
<td>$R$</td>
<td>42dB</td>
<td>0.95</td>
<td>0.95±0.02</td>
</tr>
<tr>
<td></td>
<td>30dB</td>
<td>0.95</td>
<td>0.94±0.06</td>
</tr>
<tr>
<td></td>
<td>18dB</td>
<td>0.95</td>
<td>0.97±0.23</td>
</tr>
<tr>
<td>$L$</td>
<td>42dB</td>
<td>0.01</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>30dB</td>
<td>0.01</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>18dB</td>
<td>0.01</td>
<td>-</td>
</tr>
</tbody>
</table>

†No realistic estimates are obtained (i.e. negative or >> of true value). SMI = subspace model identification; EBM = energy-balance method; FOGL = fogliadi; PEM = prediction error method.
which underestimated $Z_0$ at a noise level of 18 dB. Regarding $C_a$ large estimation errors were observed at a noise level of 18 dB for EBM, FOGL and PEM, while SMI was still able to estimate this parameter with reasonable accuracy. Regarding $R$ all methods were able to obtain estimates close to the true values, except PEM that could not provide realistic estimates at a noise level of 18 dB.

Figure 3 shows VAF and RMSE values of estimated pressure curves based on the estimated windkessel model obtained using all methods considered in this study.

### Four-element windkessel model

Application of SMI on a four-element model resulted in a significant number of outliers in the parameter estimations. If an outlier is defined using Chauvenet’s criterion (i.e. an outlier is assumed if the probability of an estimate multiplied by the total number of estimates is less than 0.5), there were on average 13 outliers in pressure-flow data simulated with all combinations of parameter values (i.e. 81 pairs of pressure-flow data) and a random white noise realization with an SNR of 30 dB. 10 of these outliers were due to inaccuracies in estimates of $L$, $Z_0$, $C_a$ and $R$ accounted respectively for 2, 1 and 0 outliers. Outliers were excluded in the analysis.

There was a significant systematic error in the estimate of $L$ in comparison with the true $L$ ($P = 0.011$). However, this error was not influenced by the levels of the other
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**Figure 4** - Singular values corresponding to data simulated with a three-element (A) and four-element windkessel model (B). Data corresponds to data in Figure 2. Singular values are shown for model order 1 to 5. When noise is added to simulated data (i.e. SNR 30 dB) the gap between dominant and non-dominant singular values decreases; noise free (open circles), noise added (dots).

windkessel parameters (no significant interaction, P>0.05). Furthermore, there was a significant interaction of parameter \( L \) on the estimate \( Z_0 \) (P=0.0045: with the true values of \( Z_0 \) set at its nominal value). For the other parameters, no significant systematic errors and no significant interactions were found (P>0.05).

Evaluation of random errors resulted in an increasing number of outliers for both SMI and PEM. At an SNR of 48 dB in 3% and 1% of simulation runs outliers were observed using SMI and PEM, respectively. These numbers increased to 13% and 16% at an SNR of 30 dB and to 34% and 36% at 18 dB. Table 2 shows estimated four-element windkessel parameters obtained using SMI and PEM after exclusion of outliers. With both methods, all parameters were fairly well estimated at an SNR of 48 dB. However, at an SNR of 30 dB large errors were found in estimates of \( L \). No realistic estimates of \( L \) were obtained at 18 dB. Also, at this noise level, the other parameters were badly estimated.

**Singular values**

In Figure 2 an example is shown of simulated pressure and flow curves using the four-element windkessel model. Figure 4 shows the first five singular values for these data. Also, singular values are shown for the case when white noise is added (SNR = 30 dB). Observe that for the four-element windkessel model, the gap between the second and third singular value reduces when noise is added to the data.
Discussion

In this study SMI techniques were evaluated to estimate three- and four windkessel parameters. For the windkessel models we assumed linear pressure-independent parameters. The SMI techniques were evaluated by application to simulation data, in which the true parameter values are known. To the best of our knowledge, this has been the first study in which SMI is applied on physiological data in order to estimate physiological parameters.

SMI is a technique for which a-priori knowledge of a parameterization is not required. Only the order of the system is required, which can be determined through inspection of dominant singular values. From a numerical point of view, one feature that makes the SMI approach so attractive is that it formulates the identification problem as a column space approximation problem followed by a set of linear least-squares problems. Hence, instead of using iterative optimization schemes, as are required in many windkessel estimation methods, basic numerical linear algebra tools are used. The non-iterative nature of the algorithms eliminates the possibility to converge to a local minimum. Furthermore, SMI does not require initial values for parameters and states, since these are estimated along with the identification of the system matrices.

State-space matrices are calculated as full state-space matrices in a certain optimally conditioned basis that is uniquely determined. This implies that the subspace algorithm delivers the system matrices up to a similarity transformation matrix. Therefore, SMI is usually not applicable if physical model parameters are of interest. However, we showed in this study that windkessel parameter could be estimated from subspace matrices by application of physiological foreknowledge.

Three-element windkessel model

With SMI, three-element windkessel parameters were estimated with high accuracy. On simulation data obtained with parameters within a physiological range, no systemic errors in the estimates were found. Concerning random errors, SMI performed better than EBM, FOGL and PEM with no significant random errors. For small SNR, EBM, FOGL and PEM became less stable, resulting in bad or unrealistic parameter estimates (see Table 2) and low VAF and RMSE values (see Figure 3). Thus, especially in situations with a low SNR, SMI is the preferred estimation method.

Four-element windkessel model

The four-element windkessel model, that extends the three-element windkessel model with an inertance $L$, has been the subject of a number of studies. From a phys-
ological point of view it has been shown that the four-element windkessel model resembles physiology better than the three-element windkessel model does. However, the estimation of the parameters appeared more problematic in comparison with the three-element model. Even if little noise was added to the data an increasing number of outliers arose for both SMI and PEM. These outliers were almost exclusively due to errors in the estimations of $L$. Despite this, VAF values were still high, suggesting that the influence of $L$ on pressure and flow is low (See Figure 3). Problems in estimating $L$ in experimental data have also been reported in previous research\textsuperscript{20,21}. However, no comparison could be made with physical values of $L$ since in these studies experimental data was used in which true values are unknown.

The bad identifiability of $L$ can be explained as follows. To estimate parameters sufficient exciting power is necessary which is dependent on sampling frequency and experiment duration. Considering pressure and flow curves, the required experiment duration is very small with respect to the time constants (i.e. the experiment duration is up to one heart period long). This results in insufficient excitation power that affects the estimation accuracy. Lack of excitation power was also illustrated by considering the singular values. In Figure 4 a gap between the second and third singular value of noise free data was observed, suggesting a second order system. However, this gap disappeared after addition of a small amount of noise. As a consequence, discrimination of model dynamics and noise is hardly possible, suggesting that the use of the four-element model is very limited, regardless of the estimation method.

Limitations

A limitation of this study is that no experimental data has been considered. Although the three- and four-element models have a validated physiological basis, modeling errors cannot be totally excluded. Therefore, no conclusions can be drawn about the performance of the estimation methods in the presence of modeling errors in addition to measurement errors. In addition, in this study we adopted the most commonly used geometric orientations of the windkessel models. Some authors have suggested other geometric orientations, especially for the four-element windkessel model\textsuperscript{24-27}. Although identification problems have been reported for these models as well\textsuperscript{3,21}, no information exists about accuracy of parameter estimates using these alternative models.

Conclusions

In this simulation-based study, we showed that with SMI physical parameters could be estimated by application of physiological foreknowledge. Application of SMI to estimate parameters in a three-element windkessel model resulted in high accurate estimates and
appeared to be a robust method compared to different conventional methods. A lower accuracy, however, is found when a four-element windkessel model is considered. This is caused by a lack of excitation power in pressure-flow curves, mainly resulting in estimation errors of arterial inertance. Therefore, based on the simulation results, the use of the four-element windkessel model is questionable.

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