Biomedical Signal Processing and Control 57 (2020) 101820

Contents lists available at ScienceDirect

Biomedical Signal Processing and Control

journal homepage: www.elsevier.com/locate/bspc

State-space analysis of fractional-order respiratory system models

Esra Saatci*, Ertugrul Saatci

Department of Electrical and Electronics Engineering, Istanbul Kultur University, Bakirkoy, Istanbul, Turkey

ARTICLE INFO

Article history:
Received 14 August 2019
Received in revised form
26 November 2019
Accepted 8 December 2019
Available online 21 December 2019

Keywords:
Fractional-order respiratory system models
State-space analysis
Stability analysis
Time-delay systems

ABSTRACT

Fractional Order Models (FOM) of the respiratory system have been used in the model-based analysis of the respiratory system. Although there are studies exploring the physiological correctness and fitting accuracy of the models, they are not analyzed in terms of interactions between parameters, time-varying dynamics and measurable signals. In this study we purpose to use state-space analysis to yield the time-varying nature of the system incorporated by the parameters, states and output. We tested the models for controllability, observability and stability characteristics while using the parameters found in the literature. Sufficient asymptotic stability bounds were driven by using stability theory of the discrete time-delay system. Results revealed that FOMs with estimated parameters offer systems with different characteristics. Thus, careful consideration must be given when interpreting estimated parameters in FOMs during respiratory tests.

1. Introduction

FOM of the respiratory system has attracted a great interest because functional and structural properties of the system can be obtained by a few physically motivated parameters. It has been shown that well known Maxwell and Kelvin-Voight models with integer order differential equations can not model the stress relaxation of the lung tissue [1], time varying ratio between transpulmonary pressure and total lung volume [2] and distributive self-similar structure of the system [3] very well. As it is the case for all respiratory system modelling approaches, respiratory system is excited by the combined sinusoidal pressure at low frequencies and FOM in frequency domain is fit to the measured impedance data. Frequency domain version of the FOM is called as Constant Phase Model (CPM) [4] which is used for the impedance modelling and system parameter estimation.

Both FOM and CPM have been evaluated and reviewed in the literature. The aim in the previous studies were to estimate the model parameters with lowest fitting error, to classify the diseased and healthy parameters and to investigate the power law property of the respiratory system [5], [6], [7], [8], [9]. In [10] authors analysed FOMs in terms of structural representation of the respiratory mechanics, whereas applications of the fractional calculus in the biological systems were investigated in [11]. In [12] statistical analysis is applied to calculate confidence intervals of the parameters' estimates. Parameters were estimated by least squares algorithm from impedance data and parameter variations were estimated by sample variances and sensitivity matrix. First, in [12], only one model was fit to the impedance data and combined errors were assumed to be Gaussian noise. More importantly, estimates of the parameters influenced the sensitivities in the proposed method and this made the results oblivious of model-parameter association. Therefore, we propose a comprehensive analysis, including establishing an association between information bearing parameters and dynamics of the system, performed on the already proposed and used FOMs of respiratory system. Here, our objective is to explore FOMs in control systems point of view and answer the following questions:

1. How unmeasurable dynamics in FOMs are related to the parameters?
2. Which of the FOMs are controllable and observable for the estimated parameter values in the literature?
3. Is the asymptotic stability an issue for the estimated parameter values in FOMs?

To answer the first question, we see respiratory system as a complex physical system which consists of mutual interconnections. Thus our starting point is to propose a state-space modelling framework where states prescribe a certain dynamical behavior. The key aspect here is that, in contrast to the CPMs, state-space model of FOMs neither depends on the frequency response of the system, nor is restricted to only parameter-system relationship.

* Corresponding author. Tel: +90 212 4984229.
E-mail addresses: esra.saatci@iku.edu.tr (E. Saatci), e.saatci@iku.edu.tr (E. Saatci).

https://doi.org/10.1016/j.bspc.2019.101820
1746-8094/

Table 1
Estimated Parameters and Values in FOMs [14].

Healthy	FOM1	FOM2	FOM3	FOM4
R	0.22	0.22	0.06	–
L	–	0.0007	0.029	0.0374
$1/C$	0	1.36	3.52	2.02
α	0	0	0.48	0.43
β	0.99	0.99	0	0.79
COPD	**FOM1**	**FOM2**	**FOM3**	**FOM4**
R	0.18	0.26	0.27	–
L	–	0.0009	0.0021	0.015
$1/C$	1.73	5.20	8.9	2.94
α	0	0	0.87	0.59
β	0.18	0.83	0	0.52

In contrast to earlier methods, this method leads to a set of natural state variables which are directly suitable for addressing the parameter-state-system relationships.

Controllability and observability analysis [13] is proposed to answer the second question. In this step, our aim is to investigate whether the parameter values estimated in the previous studies in FOMs lead to significant and meaningful dynamic behaviour in respiratory systems. At this stage, we should explain the meaning of controllable and observable models. If the model is not controllable and/or observable, either realization of the model is redundant, i.e. some states have no relationship to the input or output, or physical system is control deficient, i.e. dynamic variables are not fully controlled by physical actuators.

Finally, we proposed to explore the stability of FOMs by using well-known asymptotic Lyapunovs stability theorem for the last question. At this stage, discrete-time version of FOMs are utilized, thus the main source of inspiration is to explore the stability in discrete time-delay systems. The effort is made to address the derivation of the conditions that lead to stability in FOMs.

2. Methods

2.1. Constant Phase Models of Respiratory System

CPM of the respiratory system is expressed as a sum of resistive, inductive and capacitive terms as:

$$Z_{FOM}(s) = R + Ls^{\alpha} + \frac{1}{Cs^{\beta}} \tag{1}$$

where R represents all resistive pressure losses in the airways and lung parenchyme, L and C are the inertial effects of the airflow in low frequencies and the compliance of the lung respectively. $0 \leq \alpha, \beta \leq 1$ are fractional orders obtained from the fractional-order differential equations of the respiratory system and s is the Laplace variable.

Based on the estimated parameter values in the literature, four most commonly used version of (1) can be found in [14]. Table 1 summarizes the parameter values calculated by the real-time signals acquired from both healthy and Chronic Obstructive Pulmonary Disease (COPD) patients. The absence of some parameter values implies that the estimated value is too small, hence respective term can be eliminated from the model. Electrical analogy of these models can be all realized by domino ladder circuit as shown in Fig. 1, where transfer impedance is $Z(s) = Z_1(s) + \frac{1}{Y_1(s)}$ and $Z_1(s)$ is the sum of resistive and inertial fractional impedance and $Y_1(s)$ is the fractional admittance due to the elastic effects.

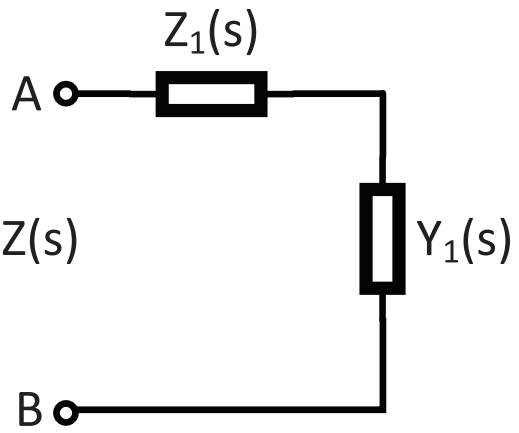

Fig. 1. Electrical analogy of constant phase model realized by domino ladder circuit.

Table 2
Matrices of State-Space Models

Models	FOM1	FOM2	FOM3	FOM4
$\mathbf{x}(t)$	$\begin{bmatrix} X_1(t) \\ X_2(t) \end{bmatrix}$	$\begin{bmatrix} X_1(t) \\ X_2(t) \end{bmatrix}$	$\begin{bmatrix} X_1(t) \\ X_2(t) \end{bmatrix}$	$\begin{bmatrix} X_1(t) \\ X_2(t) \end{bmatrix}$
$\mathbf{y}(t)$	$[Q(t)]$	$[Q(t)]$	$[Q(t)]$	$[Q(t)]$
$\mathbf{u}(t)$	$[P(t)]$	$[P(t)]$	$[P(t)]$	$[P(t)]$
$\mathbf{A}(\theta)$	$\begin{bmatrix} 0 & 1 \\ 0 & \frac{-1}{RC} \end{bmatrix}$	$\begin{bmatrix} 0 & 1 \\ \frac{-1}{LC} & \frac{-R}{L} \end{bmatrix}$	$\begin{bmatrix} 0 & 1 \\ \frac{-1}{LC} & \frac{-R}{L} \end{bmatrix}$	$\begin{bmatrix} 0 & 1 \\ \frac{-1}{LC} & 0 \end{bmatrix}$
$\mathbf{B}(\theta)$	$\begin{bmatrix} 0 \\ \frac{1}{RC} \end{bmatrix}$	$\begin{bmatrix} 0 \\ \frac{1}{LC} \end{bmatrix}$	$\begin{bmatrix} 0 \\ \frac{1}{LC} \end{bmatrix}$	$\begin{bmatrix} 0 \\ \frac{1}{LC} \end{bmatrix}$
$\mathbf{C}(\theta)$	$\begin{bmatrix} 0 & C \end{bmatrix}$	$\begin{bmatrix} 0 & C \end{bmatrix}$	$\begin{bmatrix} 0 & C \end{bmatrix}$	$\begin{bmatrix} 0 & C \end{bmatrix}$
$\mathbf{D}(\theta)$	$[0]$	$[0]$	$[0]$	$[0]$
γ	$\begin{bmatrix} \beta \\ \beta \end{bmatrix}$	$\begin{bmatrix} \beta \\ 1 \end{bmatrix}$	$\begin{bmatrix} 1 \\ \alpha \end{bmatrix}$	$\begin{bmatrix} \beta \\ \alpha \end{bmatrix}$

2.2. Continuous Time State-Space Model of the FOM

If respiratory system is assumed to be continuous time linear time invariant system, FOM of the respiratory system can be expressed in the state-space form as [15]:

$$\begin{aligned} \Delta_t^{\gamma} x(t) &= \mathbf{A}(\theta)\, x(t) + \mathbf{B}(\theta)\, u(t) \\ y(t) &= \mathbf{C}(\theta)\, x(t) + \mathbf{D}(\theta)\, u(t) \end{aligned} \tag{2}$$

where $\mathbf{x}(t) \in \mathbb{R}^n$, $\mathbf{y}(t) \in \mathbb{R}^m$ and $\mathbf{u}(t) \in \mathbb{R}^r$ are the state, output and input vectors respectively. $\mathbf{A}(\theta) \in \mathbb{R}^{n \times n}$ is the state transition matrix, $\mathbf{B}(\theta) \in \mathbb{R}^{n \times r}$ is the input matrix, $\mathbf{C}(\theta) \in \mathbb{R}^{m \times n}$ is the output matrix and $\mathbf{D}(\theta) \in \mathbb{R}^{m \times r}$ is the feed forward matrix. Model parameters, which are assumed to be time-invariant over the observation window, are expressed by a parameter vector $\theta \in \mathbb{R}^p$. $\gamma = \begin{bmatrix} \gamma_1 & \gamma_2 & \cdots & \gamma_n \end{bmatrix}^T$ denotes the fractional order vector and $\Delta_t^{\gamma} \mathbf{x}(t)$ is the γth order fractional derivative of the state vector $\mathbf{x}(t)$. Initial conditions in (2) are assumed to be zero. If $\gamma_1 = \gamma_2 = \cdots = \gamma_n = q$, the system is called as a commensurate order system [16]. In case of ordinary linear time invariant systems, fractional orders are all equal to one.

State-space model in (2) can be obtained from all versions of CPMs in (1) with parameters in Table 1. Application of derivations given in Appendix A lead to vectors and matrices $\mathbf{A}(\theta)$, $\mathbf{B}(\theta)$, $\mathbf{C}(\theta)$ and $\mathbf{D}(\theta)$ which are summarized in Table 2.

2.3. Discrete Time State-Space Models of the FOM

State-space analysis of non-commensurate FOM is performed on the discrete time state-space model of (2), because acquired res-

piratory signals are in discrete form. Grünwald-Letnikov definition of the fractional derivation is one of the approach to circumvent a problem of numerical calculations of the fractional derivations in (2). This approach allows us to compose discrete matrices from the matrices in (2) easily and "short memory" issues were already investigated in previous studies [16]. In this study, discretization steps of FOM by Grünwald-Letnikov definition of the fractional derivation, found in [16] is utilized to obtain time-delayed state-space model of the discrete time non-commensurate FOM:

$$\begin{aligned}\mathbf{x}(k+1) &= \mathbf{A}_0\left(\theta\right)\mathbf{x}(k) + \sum_{j=1}^{k}\mathbf{A}_j\mathbf{x}(k-j) + \mathbf{B}_d\left(\theta\right)\mathbf{u}(k)\\ \mathbf{y}(k) &= \mathbf{C}\left(\theta\right)\mathbf{x}(k) + \mathbf{D}\left(\theta\right)\mathbf{u}(k)\end{aligned} \tag{3}$$

where $k \in \mathbb{Z}^+ \cup \{0\}$ is a time index. State transition matrix $\mathbf{A}_j\left(\theta\right)$ can be obtained as follows:

Lets define $\bar{\mathbf{A}}\left(\theta\right)$ whose i^{th} row is calculated by

$$\left\{\bar{\mathbf{A}}\left(\theta\right)\right\}_{i,*} = \Delta_t^{\gamma_i}\left\{\mathbf{A}\left(\theta\right) - \mathbf{I}_n\right\}_{i,*}$$

where Δ_t is the discrete time step (we assumed $\Delta_t = 0.01s$ in the simulations) and $i \in \{1, 2, \ldots, n\}$ is the state number. $\mathbf{I}_n$ is $n \times n$ identity matrix. If a diagonal matrix is created by using non-integer diagonal combinations $\binom{\gamma_i}{j}$ as

$$\Upsilon_j = diag\left\{\binom{\gamma_1}{j}, \binom{\gamma_2}{j}, \cdots \binom{\gamma_n}{j}\right\} \tag{4}$$

where $\binom{\gamma}{j} = \begin{cases}\dfrac{\gamma(\gamma-1)\cdots(\gamma-j+1)}{j(j-1)\cdots 1} & j>0\\ 1 & j=0\end{cases}$, then discrete state transition matrix can be obtained as

$$\begin{aligned}\mathbf{A}_0\left(\theta\right) &= \bar{\mathbf{A}}\left(\theta\right) + \Upsilon_1\\ \mathbf{A}_j &= (-1)^j\Upsilon_{j+1}\end{aligned} \tag{5}$$

System defined in (3)–(5) is also a linear discrete time-delay system and in this work it is used for the controllability, observability and stability analysis. However first, one should define the solution of the system as a sum of natural and forced responses respectively. The complete solution is given as

$$\mathbf{x}(k) = \mathbf{G}_k\left(\theta\right)\mathbf{x}(0) + \sum_{j=0}^{k-1}\mathbf{G}_{k-1-j}\left(\theta\right)\mathbf{B}_d\left(\theta\right)\mathbf{u}(j) \tag{6}$$

where time varying transition matrix $\mathbf{G}_k\left(\theta\right)$ is given by

$$\begin{aligned}\mathbf{G}_0\left(\theta\right) &= \mathbf{I}_n\\ \mathbf{G}_k\left(\theta\right) &= \mathbf{A}_0\left(\theta\right)\mathbf{G}_{k-1}\left(\theta\right) + \sum_{j=1}^{k-1}\mathbf{A}_j\mathbf{G}_{k-1-j}\left(\theta\right)\end{aligned} \tag{7}$$

While proof of the solution given in (6) and (7) can be found in [16], the complications in the model and the solution should be explained here. Although respiratory signals are processed in a M point time window, the upper limit of the sums in (3) and (6) should be limited to the predefined value (K) due to the computational issues ($K<M$). Another important observation is that transition matrix $\mathbf{G}_k\left(\theta\right)$ in (7) is composed of powers of discrete state transition matrix $\mathbf{A}_j\left(\theta\right)$ in (5). This property of $\mathbf{G}_k\left(\theta\right)$ allows controllability and observability tests be computationally effective, because original controllability and observability tests incorporate matrix power of state transition matrix.

2.4. Controllability and Observability Analysis

Controllability and observability are two important analysis in the control systems to test the existence of the solutions for the given inputs. A system is said to be completely state controllable if for any k_i it is possible to construct a control vector $\mathbf{u}(k)$ which will transfer any given state $\mathbf{x}(k_i)$ to any final state $\mathbf{x}\left(k_f\right)$ in a finite time interval $k_i \le k \le k_f$ [17].

Theorem 1. *Discrete time non-commensurate fractional order system is completely state controllable if and only if there exits a finite time K such that the composite controllability matrix,* $\mathrm{P_K}\left(\theta\right) \in \mathbb{R}^{n\times Kr}$

$$\mathbf{P}_K\left(\theta\right) = \left[\mathbf{G}_0\left(\theta\right)\mathbf{B}_d\left(\theta\right) \quad \mathbf{G}_1\left(\theta\right)\mathbf{B}_d\left(\theta\right) \quad \cdots \quad \mathbf{G}_{K-1}\left(\theta\right)\mathbf{B}_d\left(\theta\right)\right]$$

is of rank n.

A system is said to be completely observable on $k_i \le k \le k_f$ if for every k_i and some k_f every state $\mathbf{x}(k_i)$ can be determined from the knowledge of $\mathbf{y}(k)$ on $k_i \le k \le k_f$ [17].

Theorem 2. *Discrete time non-commensurate fractional order system is completely observable if there exits a finite time K such that the composite observability matrix,* $\mathrm{O_K}\left(\theta\right) \in \mathbb{R}^{Km\times n}$

$$\mathbf{O}_K\left(\theta\right) = \left[\mathbf{C}\left(\theta\right)\mathbf{G}_0\left(\theta\right) \quad \mathbf{C}\left(\theta\right)\mathbf{G}_1\left(\theta\right) \quad \cdots \quad \mathbf{C}\left(\theta\right)\mathbf{G}_{K-1}\left(\theta\right)\right]^T$$

is of rank n. $[*]^T$ *denotes the transpose of a matrix.*

Proofs of theorems can be found in [16] and [17]. Theorems 1 and 2 were applied to the fractional order respiratory system models and controllability and observability matrix ranks were compared with the number of states. Since constant parameter values (θ) given in the literature were used in the calculations of the matrices, controllability and observability matrices are time-invariant matrices (see Table 1 for the parameter values, explanations and related references).

2.4.1. The effect of the maximum time delay (K)

First we should investigate the effect of the maximum time delay on the rank of controllability and observability of matrices. Model equations play a very important role to ensure that the rank of $\mathrm{P_K}\left(\theta\right)$ and $\mathrm{O_K}\left(\theta\right)$ are n. First we observe that even though $\mathbf{A}\left(\theta\right)$ is a low rank matrix (as in FOM1), $\mathbf{A}_0\left(\theta\right)$ is full rank, which results in a full rank time varying transition matrix $\mathbf{G}_k\left(\theta\right)$ in (7). However, it is not sufficient to have full rank $\mathbf{G}_k\left(\theta\right)$ to satisfy the Theorems 1 and 2. If both $\mathbf{G}_k\left(\theta\right)\mathbf{B}_d\left(\theta\right)$ and $\mathbf{C}\left(\theta\right)\mathbf{G}_k\left(\theta\right)$ result in zero row and column vectors for every k respectively, regardless of the maximum time delay, augmented matrices $\mathrm{P_K}\left(\theta\right)$ and $\mathrm{O_K}\left(\theta\right)$ will have a rank lower than n.

2.4.2. The effect of the fractional order vector (γ)

There is no direct effect of fractional orders to the rank of $\mathrm{P_K}\left(\theta\right)$ and $\mathrm{O_K}\left(\theta\right)$, but since the fractional orders in the model (α and β) related to the model structure, fractional order vector (γ) affects the rank indirectly.

2.4.3. The effect of the parameters (θ)

Parameter values also do not have a direct effect on the rank of $\mathrm{P_K}\left(\theta\right)$ and $\mathrm{O_K}\left(\theta\right)$. However, parameter sensitivities of the controllability and observability matrices with respect to numerical instabilities of the matrices should be investigated as a future study.

2.5. Stability Analysis

Estimated parameters in biological models may not lead to stable model solutions, because fitting models to the acquired

impedance data with a minimum fitting error does not guarantee the stable dynamic properties of the system. In this case any external and internal perturbations in the states (pressures in respiratory system) result in diverged output (airflow). In other words, dynamic properties of the models become unreliable to indicate physiological variations. Thus we propose to analyze the models with estimated parameters in terms of stability before any evaluation of the physiological meaning of states. Stability analysis of the discrete time-delay system in (3) and (5) can be done by considering two different type of the stability, namely, asymptotic stability and finite time stability. In this work, we focus only on asymptotic stability and leave the finite time stability for the future work.

Definition 3. Linear discrete time system in (3) and (5) is asymptotically stable with respect to $\{\mathbf{B}_x, \mathbf{B}_0, \mathbf{B}_u, K\}$, $\mathbf{B}_x, \mathbf{B}_0, \mathbf{B}_u \in \mathbb{R}^+$, $K \in \mathbb{Z}$, for each $k \geq 1$, any initial condition $\|\mathbf{x}(0)\| < \mathbf{B}_0$ and any input signal $\|\mathbf{u}(k)\| < \mathbf{B}_u$ if

$$\|\mathbf{x}(k)\| < \mathbf{B}_x$$

where $\|\mathbf{x}(k)\| = \sqrt{\sum_{i=1}^{n} |x_i(k)|^2}$ is Euclidean norm of the state vector.

Basically, the requirement for the asymptotically stable system is that [18]:

$$\sum_{j=0}^{K} \|\mathbf{A}_j(\theta)\| < 1 \tag{8}$$

where discrete state transition matrix is defined as in (5) and $\|\mathbf{A}_j(\theta)\| = \sqrt{\lambda_{\max}\left(\mathbf{A}_j^T(\theta)\mathbf{A}_j(\theta)\right)}$ and $\lambda_{\max}(\bullet)$ are the Euclidean norm and maximum eigenvalue of the matrix respectively. Condition in (8) can be obtained by considering the solution in (6) and definition of time varying transition matrix in (7). If above requirement is evaluated by discrete state transition matrix in (5), one can find restrictive stability condition of discrete time fractional order system. In [19] theorem given below was proved for the asymptotic stability of commensurate FOM given in (3) and (5). However, for the non-commensurate FOM, the condition is slightly modified.

Theorem 4. *A system in (3)–(5) is asymptotically stable for all states at time instant k if the following condition is satisfied for all fractional orders:*

$$\|\mathbf{A}_0(\theta)\| < \max_{\gamma_i}(r(K,\gamma_i))$$

where $r(K,\gamma_i) = \begin{cases} 1 & \gamma_i = 0 \\ \gamma_i + \dfrac{\Gamma(K+2-\gamma_i)}{\Gamma(K+2)\Gamma(1-\gamma_i)} & \gamma_i > 0 \end{cases}$ *is called a spectral radius of the matrix* $\mathbf{A}_0(\theta)$.

Proof of Theorem 3: By using the fact that $\|\mathbf{A}+\mathbf{B}\| \leq \|\mathbf{A}\| + \|\mathbf{B}\|$, (8) can be written as

$$\|\mathbf{A}_0(\theta)\| < 1 - \left\|\sum_{j=1}^{K}(-1)^j \Upsilon_{j+1}\right\|$$

If the closed form for the above sum is existed, by using partial sums of general binomial coefficients as $\sum_{j=0}^{k}(-1)^j \binom{\gamma_i}{j} = \binom{k-\gamma_i}{k}$ ($\gamma_i \in \mathbb{R}$ and $k \geq \gamma_i, k \in \mathbb{Z}^+ \cup \{0\}$) and by replacing the definition of Υ_{j+1} in (4), the upper bond for the matrix norm of $\mathbf{A}_0(\theta)$ can be written as:

$$\|\mathbf{A}_0(\theta)\| < 1 - \left\|\mathbf{I}_n + diag\left\{-\gamma_1 - \binom{k+1-\gamma_1}{k+1}, \cdots, -\gamma_n - \binom{k+1-\gamma_n}{k+1}\right\}\right\| \tag{9}$$

Finally, when Gamma function is replaced instead of the non-integer binomial coefficients, $\binom{K+1-\gamma_i}{K+1} = \dfrac{\Gamma(K+2-\gamma_i)}{\Gamma(K+2)\Gamma(1-\gamma_i)}$ spectral radius of the matrix is found as in Theorem 3

Theorem 3 is a special case of one of the matrix metrics defined in [18] (Theorems 3, 4 and 5) for the non-commensurate FOM. However, the advantage of Theorem 3 should be also noted that Theorem 3 is less restrictive than the stability requirement in (8).

2.5.1. *The effect of the maximum time delay* (K)

Spectral radius ($\max_{\gamma_i}(r(K,\gamma_i))$) of the matrix $\mathbf{A}_0(\theta)$ only depends on the fractional order γ_i and maximum time delay K. In Fig. 2 $r(K,\gamma_i)$ is plotted for $1 \leq K \leq 200$ with a fixed γ_i in FOM4. Similar figures were obtained in FOM1, FOM2 and FOM3. We found that spectral radius inversely changes by K with a decreasing trend. In this study we assumed $K = 100$, because $\Gamma(.)$ function increases to the level causing the numerical instabilities.

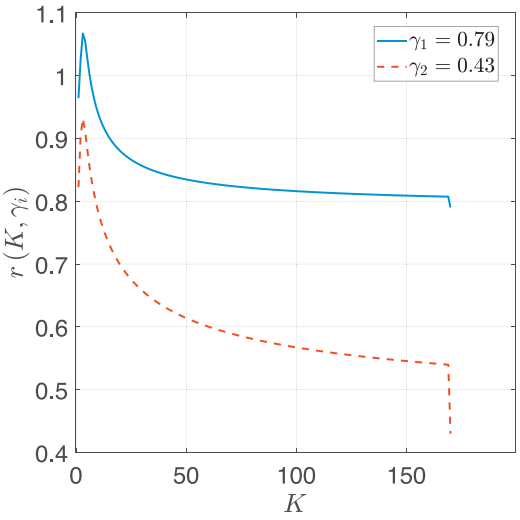

Fig. 2. $r(K,\gamma_i)$ in FOM4.

2.5.2. *The effect of the fractional order vector* (γ)

Fractional orders directly affect the spectral radius of the matrix $\mathbf{A}_0(\theta)$. To explore the effects, consider the Fig. 3. Fig. 3 shows the spectral radius versus fractional order for $K = 10$ and $K = 100$. From the figure, it is observed that spectral radius is minimum when $0.2 \leq \gamma_i \leq 0.4$ and decreases when maximum time delay increases.

2.5.3. *The effect of the parameters* (θ)

It should be stated that, parameter values have a direct effect on the norm of $\mathbf{A}_0(\theta)$, which is constructed by the state transition matrix. However, the bound on the stability, which is called as a spectral radius has no influence on the parameters. This further means that only model structure and fractional orders can change the upper bounds of the stability criterion.

3. Results

Before the results, it should be emphasized that, in this study the state-space analysis is done based on the estimated parameter values given in the literature. Therefore, this analysis only

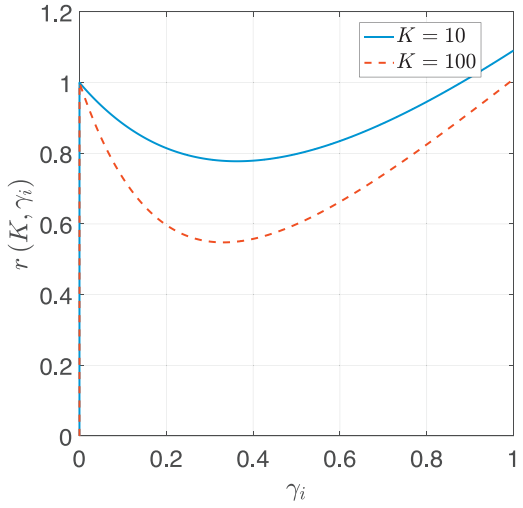

Fig. 3. $r(K, \gamma_i)$ for $0 \leq \gamma_i \leq 1$ and $K = 10$ $K = 100$.

Table 3
Controllability and Observability Results

Models		Controllability rank $(P_K(\theta))$	Observability rank $(O_K(\theta))$
FOM1	Healthy	2	1
	COPD	2	1
FOM2	Healthy	2	2
	COPD	2	2
FOM3	Healthy	2	2
	COPD	2	2
FOM4	Healthy	2	2
	COPD	2	2

Table 4
Stability Results

Models		Euclidean Norm $\|\mathbf{A}_0(\theta)\|$	Spectral Radius $\max_{\gamma_i}(r(K, \gamma_i))$	Stability
FOM1	Healthy	0.9795	1.0004	YES
	COPD	4.4519	0.6154	NO
FOM2	Healthy	2.0865	1.0004	NO
	COPD	1.2990	1	NO
FOM3	Healthy	0.7813	1	YES
	COPD	1.1228	1	NO
FOM4	Healthy	0.6474	0.8161	YES
	COPD	1.1856	0.6556	NO

requires parameter values (Table 1) and model structures given in (1). Controllability $(P_K(\theta))$ and observability $(O_K(\theta))$ matrices were constructed with the help of Theorems 1 and 2. The controllability and observability results are shown in Table 3. As can be seen from the table, results prove that all models, except FOM1 are both controllable and observable, because the ranks of $P_K(\theta)$ and $O_K(\theta)$ match to the number of the states in the models.

Asymptotic stability analysis were performed according to the Theorem 3. Table 4 shows spectral radius $(\max_{\gamma_i}(r(K, \gamma_i)))$ of the matrix $\mathbf{A}_0(\theta)$ for all models. Norm of the matrix $\mathbf{A}_0(\theta)$ and stability results are also given in the same table.

4. Discussion

In FOMs input (control) signal is the mouth pressure and output signal is the total airflow. However states of FOMs do not have direct physiological explanations. All elastic pressure related to the compliance parameter (C) and airflow related to the inertance parameter (L) are dynamic elements in the models. We can assume that $X_1(t)$ and $X_2(t)$ represent the pressure and the airflow related dynamics in FOMs respectively due to the definitions in the models.

Table 3 shows the results of the controllability and observability analysis. Results prove that all models, except FOM1 are both controllable and observable, because the ranks of $P_K(\theta)$ and $O_K(\theta)$ match to the number of the states in the models. First of all, in section 2.4.3, it is stated that controllability and observability do not depend on the parameter values, thus they are not linked to the healthy and diseased conditions. Physiological explanation for the existence of the controllability condition is that mouth pressure can manipulate time-varying dynamics in respiratory system. This further explains that as irrelevant to the FOM structure, pressure and flows in respiratory system can be estimated from mouth pressure. On the other hand, absence of the observability condition was observed in FOM1. Physiological explanation for this result is that measured airflow alone cannot affect the time-varying dynamics in the respiratory system, if it is modelled by FOM1. Also, it is observed that the loss of an inertance parameter (L) in FOM1 results in unobservable models. This further means that although structural static properties of FOM1 is known, it cannot be dynamically identified by the measured airflow signal. The only remedy for this modelling problem is to change the model structure by including or excluding the parameter s.

Discrete-time version of FOMs is the infinite memory time-delay systems. This is the one of the reasons that FOMs represent the stress relation of the lung tissue. Controllability and observability analysis also indicated that the effect of the mouth pressure and the airflow on the system dynamics is not a function of the memory of the system. Also, parameter values and fractional orders do not alter controllability and observability results. It seems that model structure plays an important role on determination of the mouth pressure and airflow effects in FOMs.

Table 4 shows the results of the stability analysis. Firstly, conservative and sufficient delay-independent stability criterion in (8) yields that the norm of the indefinite state transition matrix is responsible for the stability of FOMs. This result is expected and can be explained by the basic stability theorem in discrete-time systems. However stability bonds for the FOMs in Theorem 3 is established as an upper bounds for the stability restriction. This means that Theorem 3 also bounds the parameter ranges.

Fig. 2 reveals the interesting relationship between the system memory, which is the maximum time delay and stability bound of the system. In all FOMs stability bounds decrease more slowly after $K = 100$. This is because of the gamma function. $\Gamma(K)$ in the ratio increases rapidly and at the limit only $\Gamma(\gamma_i)$ determines the ratio. This can be seen from Fig. 3 which shows the stability bounds for different fractional orders. We observed that fractional orders are noticeably lower for COPD data. This may be the reason that COPD patients data provided non-stable models. On the contrary, all models except FOM2 are stable models for the parameter values of healthy subjects. Physiological explanations of the stability results can be done accordingly. The link between model parameter values and diseased conditions (airway obstruction, change in tissue elasticity and morphological changes due to the tissue heterogeneity) were already established in recent studies [6], [7] and [8]. Here, we proved mathematically that lower fractional orders have some consequences in the stability of FOMs. This result develops the association between the capabilities of FOMs in the representation of the respiratory system and the fractional orders. In this stage, we are very reluctant to assume a relationship between stability and pathology in the underlying system, since it needs further proof.

5. Conclusion

In this study, controllability, observability and stability analysis of FOMs were performed by using state-space representation of the models evaluated by reference values given in the literature. Results showed that there is an uncontrollable and unobservable mode in FOM1. Furthermore, stability analysis revealed that all COPD patients data provided unstable models. Clinical applicability of the proposed approach in this study is directly linked to the applicability of the fractional order models to the respiratory system. This study revealed that straight adoption of the estimated parameters in the clinical studies may be misleading or suboptimal due to the model behaviour revealed by the state-space analysis of the fractional order models. Thus, careful consideration must be given when interpreting the findings in FOMs during the respiratory tests. Results indicate that parameters have different effects on the models. However, this needs further study which may reveal how the imprecisions in the parameter values affect the accuracy of the system dynamics (states and the output). Finally, results and outcomes of this study provided some improvements in the understanding of the models in the literature.

Acknowledgements

This study was partially supported by the Research Fund of Istanbul Kultur University, Grand No: IKU-BAP1801. The Study has ethical approval from Ethical Committee of Istanbul Kultur University, (2018.01 and dated 1, April 2018).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A.

First transfer admittance in (1) can be written as

$$Y_{FOM}(s) = \frac{1}{Z_{FOM}(s)} = \frac{Q(s)}{P(s)} = \frac{Cs^{\beta}}{1 + RCs^{\beta} + LCs^{\alpha+\beta}} \tag{10}$$

where $P(s)$ and $Q(s)$ are the mouth pressure and the airflow through mouth respectively. If admittance is decomposed into two parts by using intermediate variable $W(s)$:

$$Y_{FOM}(s) = \frac{Q(s)}{W(s)}\frac{W(s)}{P(s)}$$

where parts are $\frac{Q(s)}{W(s)} = Cs^{\beta}$ and $\frac{W(s)}{P(s)} = \frac{1}{1+RCs^{\beta}+LCs^{\alpha+\beta}}$, second part is transformed into time domain as:

$$P(t) = W(t) + RC\Delta_t^{\beta}W(t) + LC\Delta_t^{\alpha+\beta}W(t) \tag{11}$$

Then two equations in time domain are built as:

$$\begin{aligned} X_1(t) &= W(t) \\ X_2(t) &= \Delta_t^{\beta}W(t) = \Delta_t^{\beta}X_1(t) \end{aligned} \tag{12}$$

where $X_1(t)$ and $X_2(t)$ are states in (2). αth order fractional derivative of $X_2(t)$ can be obtained from (11) and (12) as:

$$\Delta_t^{\alpha}X_2(t) = -\frac{1}{LC}X_1(t) - \frac{R}{C}X_2(t) + \frac{1}{LC}P(t) \tag{13}$$

Next, first part is transformed into time domain as:

$$Q(t) = C\Delta_t^{\beta}W(t) = CX_2(t) \tag{14}$$

Finally, from (12), (13) and (14) corresponding state-space representation is derived:

$$\begin{aligned} \begin{bmatrix} \Delta_t^{\beta}X_1(t) \\ \Delta_t^{\alpha}X_2(t) \end{bmatrix} &= \begin{bmatrix} 0 & 1 \\ -\frac{1}{LC} & -\frac{R}{C} \end{bmatrix}\begin{bmatrix} X_1(t) \\ X_2(t) \end{bmatrix} + \begin{bmatrix} 0 \\ \frac{1}{LC} \end{bmatrix}P(t) \\ Q(t) &= \begin{bmatrix} 0 & C \end{bmatrix}\begin{bmatrix} X_1(t) \\ X_2(t) \end{bmatrix} + [0]P(t) \end{aligned} \tag{15}$$

References

[1] B. Suki, A.L. Barabasi, K.R. Lutchen, Lung tissue viscoelasticity: a mathematical framework and its molecular basis, J. Appl. Physiol. 76 (1994) 2749–2759.
[2] J. Hildebrandt, Comparison of mathematical models for cat lung and viscoelastic baloon derived by Laplace transform methods from pressure-volume data, Bull. Math. Biophys. 31 (1969) 651–667.
[3] C. Ionescu, I. Muntean, J.A. Tenreiro-Machado, R. De Keyser, M. Abruden, A theoretical study on modeling the respiratory tract with ladder networks by means of intrinsic fractal geometry, IEEE T Bio-med Eng. 57 (2) (2010) 246–253.
[4] D.W. Kaczka, J.L. Smallwood, Constant-phase descriptions of canine lung, chest wall, and total respiratory system viscoelasticity: effects of distending pressure, Respir. Physiol. Neurobiol. 183 (2012) 75–84.
[5] I. Assadi, A. Charef, D. Copot, R. De Keyser, T. Bensouici, C. Ionescu, Evaluation of respiratory properties by means of fractional order models, Biomed. Signal Process. 34 (2017).
[6] C. Ionescu, Fractional Order Models of the Human Respiratory System, Ghent University, Faculty of Engineering, Ghent, Belgium, 2009.
[7] C. Ionescu, P. Segers, R. De Keyser, Mechanical properties of the respiratory system derived from morphologic insight, IEEE T Bio-med Eng. 56 (4) (2009) 949–959.
[8] C. Ionescu, E. Derom, R. De Keyser, Assessment of respiratory mechanical properties with constant-phase models in healthy and COPD lungs, Comput. Meth. Prog. Bio. 97 (1) (2010) 78–85.
[9] D. Copot, R. De Keyser, E. Derom, M. Ortigueira, C. Ionescu, Reducing bias in fractional order impedance estimation for lung function evaluation, Biomed. Signal Process. 39 (2018) 74–80.
[10] C. Ionescu, J. Kelly, Fractional calculus for respiratory mechanics: Power law impedance, viscoelasticity, and tissue heterogeneity, Chaos Solitons Fract. 102 (2017) 433–440.
[11] C. Ionescu, A. Lopes, D. Copot, J.A.T. Machado, J.H.T. Bates, The role of fractional calculus in modeling biological phenomena: a review, Commun. Nonlinear Sci. 51 (2017) 141–159.
[12] H. Yuan, K.R. Lutchen, Sensitivity analysis for evaluating nonlinear models of lung mechanics, Ann. Biomed. Eng. 26 (1998) 230–241.
[13] K. Ogata, State-Space Analysis of Control Systems, Prentice Hall, 1997.
[14] C. Ionescu, R. De Keyser, K. Desager, E. Derom, Fractional-Order Models for the Input Impedance of the Respiratory System, 2009, www.intechopen.com.
[15] D. Baleanu, A.N. Ranjbar, S.J.R. Sadati, H. Delavari, T. Abdeljawad, V. Gejji, Lyapunov-Krasovskii stability theorem for fractional systems with delay, Rom. J. Phys. 56 (5-6) (2011) 636–643.
[16] S. Guermah, S. Djennoune, M. Bettayeb, Discrete-time Fractional-order Systems: Modeling and Stability Issues, 2012, www.intechopen.com.
[17] S. Guermah, S. Djennoune, M. Bettayeb, Controllability and observability of linear discrete-time fractional order systems, Int. J. Appl. Math. Comput. 18 (2) (2008) 213–222.
[18] D. Debeljkovic, M. Aleksendric, N. Yi-Yong, Q.L. Zhang, Lyapunov and non-Lyapunov stability of linear discrete time delay systems, Facta Universitatis 1 (9) (2002) 1147–1160.
[19] A. Dzielinski, D. Sierociuk, Stability of discrete fractional order state-space systems, in: Proceed 2nd IFAC Workshop on Fractional Differentiation and its App, Portugal, 2006.