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A Comparison of Linear Respiratory System Models Based on Parameter Estimates from PRN Forced Oscillation Data

B. Diong[1], J. Grainger[1], M. Goldman[2] and H. Nazeran[2]

[1] Department of Engineering, Texas Christian University, Fort Worth, TX 76129, USA
[2] Department of Electrical and Computer Engineering, The University of Texas at El Paso, El Paso, TX 79968, USA

Abstract—The forced oscillation technique offers some advantages over spirometry for assessing pulmonary function. It requires only passive patient cooperation; it also provides data in a form, frequency-dependent impedance, which is very amenable to engineering analysis. In particular, the data can be used to obtain parameter estimates for electric circuit-based models of the respiratory system, which can in turn aid the detection and diagnosis of various diseases/pathologies. In this study, we compare the least-squares error performance of the RIC, extended RIC, augmented RIC, augmented RIC+I_p, DuBois, Nagels and Mead models in fitting 3 sets of impedance data. These data were obtained by pseudorandom noise forced oscillation of healthy subjects, mild asthmatics and more severe asthmatics. We found that the aRIC+Ip and DuBois models yielded the lowest fitting errors (for the healthy subjects group and the 2 asthmatic patient groups, respectively) without also producing unphysiologically large component estimates.

Keywords—Forced oscillation, pseudorandom noise, respiratory impedance, respiratory system models, asthma

I. Introduction

At present, respiratory function is most commonly assessed by spirometric tests, while increasingly the method of forced oscillation is being utilized. The main concerns with spirometry are: a) it requires considerable cooperation and coordinated maximal respiratory muscle efforts from patients that make it difficult and uncomfortable for patients and time-consuming to perform, and b) may not be particularly sensitive to mechanical dysfunction in smaller airways, where much of the pathological changes occur in asthma and COPD. In contrast, pulmonary function testing by the forced oscillation technique (FOT) [1] requires only passive patient cooperation during normal breathing to measure the air pressure and rate of air flow at the entrance to the respiratory system, which defines that system's mechanical impedance.

The two main implementations of FOT are known as impulse oscillometry (IOS) and pseudorandom noise (PRN) forced oscillation (FO) [2]. Differences between them are in the nature of the pressure oscillations delivered at the mouth. However, both methods derive an impedance spectrum (frequency response) using the Fast Fourier Transform (FFT) and both methods are limited in defining that spectrum below 5 Hz because of interference from the harmonics of normal respiratory airflow.

In PRN FO, the pressure oscillations are a mixture of sinusoidal waves of varying frequency and amplitude, most commonly lasting 16 seconds in duration. Relatively greater power is delivered to the oscillations at lower frequencies (less than 8 Hz) to enhance the signal-to-noise ratio (SNR) of the resulting impedance spectrum at lower frequencies. In contrast, IOS delivers a 70-80 ms nearly triangular pulse of pressure every 200 ms (5 times/s). The method of Fourier analysis differs between the two techniques: because IOS is inherently a discontinuous input signal, it is analyzed by a Fourier integral, yielding a continuous output in the frequency domain. In contrast, PRN FO delivers a continuous waveform which is analyzed by a Fourier series, resulting in a frequency resolution of 1/(pressure waveform duration). When 16 s blocks of PRN FO data are analyzed, the frequency resolution is more than adequate (1/16 Hz). However, the time resolution limits the discrimination between inspiratory and expiratory phases of respiration, since 16 s will include 3 or more complete breaths. IOS provides continuous frequency resolution, allowing analysis of impedance at frequencies below the fundamental 5 Hz pressure oscillations; and increasingly, data at 3 Hz are being analyzed. In addition, each pulse is input into the FFT individually, such that the time resolution is 200 ms and respiratory phase-differences are easily detected.

Since FOT measurements involve frequencies and impedances, it is possible to correlate the measurements to respiratory system models consisting of analogous electrical components. In particular, parameter estimates for such lung models can serve as reference values for the detection and diagnosis of various respiratory diseases. This paper describes work to try and identify the most appropriate linear electric circuit-based respiratory system model(s) to use for such a purpose given PRN FO data.

II. Description Of The Models

Of the seven linear electric circuit-based respiratory system models considered in this study, considerable work has previously been done on the RIC model and the DuBois model [1, 3, 4], as well as the Mead model [5, 6, 7]; the Nagels' [8, 9] model is a slight simplification of the Mead model. Three of these models (extended RIC, augmented RIC and augmented RIC +I_p) have been recently proposed by our research group [10, 11, 12]. They have been studied fairly extensively over the past few years with respect to IOS data but not for PRN FO data. And a comparison of the IOS with PRN FOT found that these measurement methods yield similar but not identical respiratory system impedance values [13].

A. *RIC model*

The resistance of the airways R, lung inertance I, and the compliance of the alveoli C, are modeled as a simple three-element circuit (see Fig. 1), with R typically in $cmH_2O/l/s$ or $kPa/l/s$, I in $cmH_2O/l/s^2$ or $kPa/l/s^2$, and C in l/cmH_2O or l/kPa).

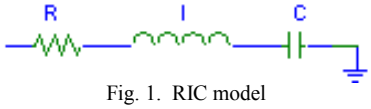

Fig. 1. RIC model

B. *Extended RIC model* [10]

This model was proposed as an improvement to the RIC model. Specifically, the additional peripheral resistance associated with the compliance (see Fig. 2) allows for the frequency dependence observed of typical real impedance data, which is beyond the RIC model's capability.

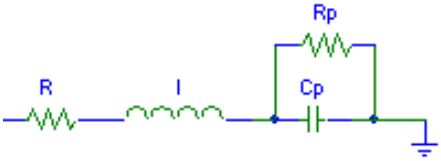

Fig. 2. Extended RIC model

C. *Augmented RIC model* [11]

This model is an improvement of the extended RIC model. The additional element C_e (see Fig. 3) models extra-thoracic (upper airway) compliance, which is thought to increase the real part of the respiratory system's impedance at the higher frequencies due to upper airways shunt effects, as observed in a significant proportion of the IOS data under analysis. Such an upturn at the higher frequencies cannot occur with the extended RIC model [10].

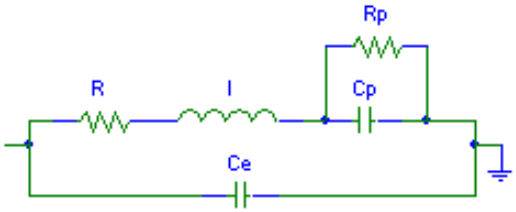

Fig. 3. Augmented RIC model

D. *Augmented RIC+I_p model* [12]

The aRIC+I_p model subsumes the RIC, eRIC and aRIC models. Its six components represent central and peripheral resistances (R, R_p), large airway inertance (I), small airway and extrathoracic compliances (C_p, C_e), as for the aRIC model, as well as an additional small airway inertance (I_p): see Fig. 4.

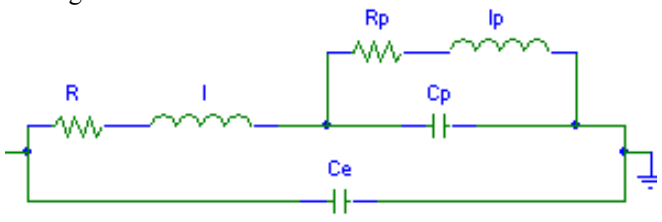

Fig. 4. Augmented RIC+Ip model

E. *Mead's model* [5, 6, 7]

Mead's model simulates different mechanics in the lung and chest wall. Its seven parameters are central and peripheral resistances (R_c and R_p), inertance (I), and lung, chest wall, bronchial tube, and extrathoraic compliances (C_l, C_w, C_b, C_e) as shown in Fig. 5.

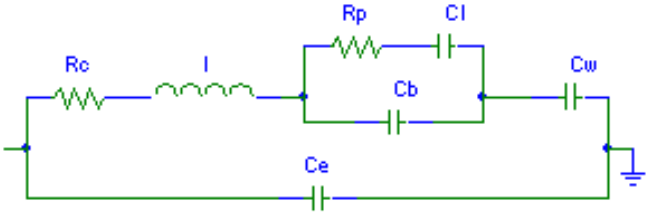

Fig. 5. Mead's model

F. *Nagels' model* [8, 9]

The Nagels' model shown in Fig. 6 is essentially the Mead model without the extrathoraic compliance component. Since an input impedance measurement is unable to distinguish the separate contributions of resistances R_c and R_w that are in series, one can lump them into a single resistance R.

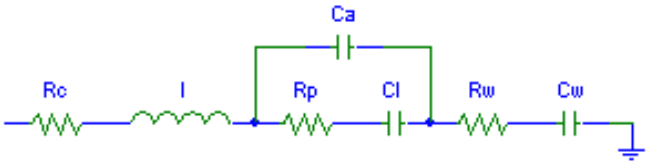

Fig. 6. Nagels' model

G. *DuBois' model* [1, 3, 4]

This model was proposed by DuBois *et al* [1]. It divides the airway, tissue, and alveolar properties into different compartments. The parameters are airway and tissue resistance (R_{aw}, R_t), airway and tissue inertance (I_{aw}, I_t), and tissue and alveolar compliance (C_t, C_g).

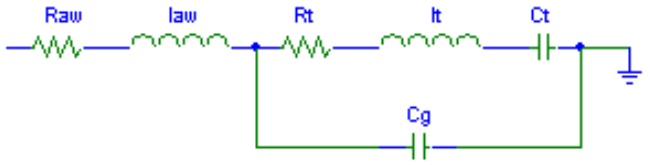

Fig. 7. DuBois' model

Clearly, these 7 models are related to each other in structure, which has considerable implications in terms of their modeling error performance relative to each other. Fig. 8 shows their places in this family tree.

III. Data and Methods

The FOT data used to derive the various models' parameters were obtained from data described in [9]. Briefly, the data were obtained from 15 healthy subjects (group 1), and 30 patients with bronchial hyperreactivity – 15 of whom did not use inhaled corticosteroids (group 2) while the remaining 15 did (group 3, more severe asthma than group 2). The FOT-acquired resistive impedance (R_{rs} or Z_R), and

reactive impedance (X_{rs} or Z_X) data included oscillatory frequencies between 4 and 52 Hz, reported at 4 Hz intervals at FRC, FRC – 1 L and FRC + 1 L lung volumes. For our study, we elected to use the mean R_{rs} and X_{rs} values for each group from 4 to 24 Hz only (at the FRC level and at 4 Hz intervals) in performing the model estimations, consistent with the range and number of frequencies used in our previous modeling studies with IOS data [10, 11, 12].

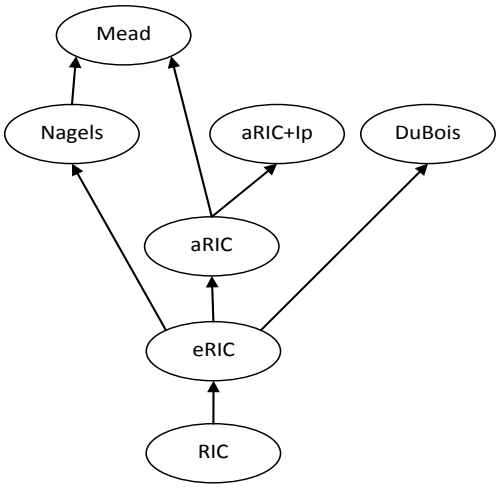

Fig. 8. Family tree of models.

Parameter estimation is similar in concept to curve-fitting. Therefore, it is necessary to first select a suitable error criterion E that is to be minimized, where

$$E = g\{f_1(\mathbf{x}), f_2(\mathbf{x}),..., f_m(\mathbf{x})\} \quad (1)$$

in which $f_1(\mathbf{x}), f_2(\mathbf{x}),..., f_m(\mathbf{x})$ are functions involving the n-vector $\mathbf{x}$ of parameters $x_1, x_2,..., x_n$ and the independent variables, *e.g.*, frequency, of the m data samples [12]. Error criteria that are commonly used in parameter estimation problems include least absolute value (LAV), least squares (LS), minimax, and maximum likelihood. But the LS criterion is by far the most commonly used one for curve fitting and parameter estimation. In its generalized form, the LS criterion

$$\min\left[E = \sum_{i=1}^{m} \{w_i f_i(\mathbf{x})\}^2\right] \quad (2)$$

minimizes the weighted (by w_i) sum of the squared errors (differences from the m data samples). It was chosen for this work due to its commonplace use, its relation with other system identification algorithms [13, 14], and its availability in different software packages.

A linear LS algorithm and a nonlinear LS algorithm were used to estimate the parameters of the various models. The former can be applied to relatively simple functions and was used for the RIC model. The latter was necessary for the other models because of the nonlinear dependence of their impedance functions on the parameters. Unlike the linear LS algorithm, the nonlinear LS algorithm may produce parameter estimates that correspond to a local error minimum rather than a global minimum. In order to circumvent this problem, a procedure was used whereby each estimation run began with an initially guessed parameter estimate vector produced by a random number generator, with a uniform distribution over a range of positive values bounded below by 0. A total of at least 15 guesses were used per model in the attempt to find the globally optimal (least-squares error) solution for fitting each set of data.

IV. Results And Discussion

A. Model estimation errors

Tables 1, 2 and 3 show the estimation errors obtained for each model in fitting the FOT data acquired from the group 1, 2 and 3 subjects, respectively. The "Z_R LS error" and "Z_X LS error" refer to the least-squares error in fitting the Z_R (R_{rs}) and Z_X (X_{rs}) data, respectively, while the "Z LS error" equals the sum of these two errors.

Table 1. Comparison of parameter estimate errors for each model using the nonlinear least squares algorithm on the healthy subjects' data.

Group 1	Z_R LS error	Z_X LS error	Z LS error
RIC model	0.02132	0.01743	0.03875
Ext. RIC model	0.02132	0.01743	0.03875
Augm. RIC model	0.00062	0.01857	0.01918
DuBois' model	0.00743	0.01419	0.02162
aRIC+Ip model	0.00054	0.01592	0.01646
Nagels' model	0.02132	0.01743	0.03875
Mead's model	0.00062	0.01857	0.01918

Table 2. Comparison of parameter estimate errors for each model using the nonlinear least squares algorithm on the Group 2 patients' data.

Group 2	Z_R LS error	Z_X LS error	Z LS error
RIC model	0.38973	0.08050	0.47023
Ext. RIC model	0.04777	0.04897	0.09674
Augm. RIC model	0.04777	0.04897	0.09674
DuBois' model	0.01420	0.02046	0.03466
aRIC+Ip model	0.04777	0.04897	0.09674
Nagels' model	0.01419	0.02046	0.03466
Mead's model	0.01420	0.02046	0.03466

Table 3. Comparison of parameter estimate errors for each model using the nonlinear least squares algorithm on the Group 3 patients' data.

Group 3	Z_R LS error	Z_X LS error	Z LS error
RIC model	1.10780	0.28323	1.39103
Ext. RIC model	0.08846	0.07384	0.16230
Augm. RIC model	0.08846	0.07384	0.16230
DuBois' model	0.00802	0.01069	0.01870
aRIC+Ip model	0.08843	0.07387	0.16230
Nagels' model	0.01069	0.01124	0.02193
Mead's model	0.00597	0.00718	0.01315

For all 3 groups, it is seen that Mead's model provides a better fit than the aRIC model, which in turn provides an equally good or better fit than the eRIC model. This is expected since the eRIC model is a simplification of the aRIC model, which is in turn a simplification of Mead's model. Also as expected, the Nagels' model provides a worse fit than the Mead model, while the aRIC+I_p model fits better than the aRIC model.

It is significant that the aRIC+I_p model provides the best

fit for the healthy subjects, while Mead's model provides the best fit for both groups of asthmatic patients. This finding is similar to what we found for modeling IOS data from normal and COPD adults [12]. Also note that the RIC model's fitting error increases in progression from healthy subjects to mild asthmatics to severe asthmatics.

B. *Model component values*

Considering the various model component values for minimal fitting error, we found unphysiologically large estimates (mostly of C_l but occasionally of C_w) in the Mead models of all 3 groups' impedances. We also found a mix of mostly unphysiologically large (mostly C_l but occasionally C_w and C_a) and occasionally physiologically reasonable estimates in the Nagels models of all 3 groups' impedances. Moreover, we found that our estimation results for the Mead and Nagels models produced least-squares-optimized estimates (mostly of C_l but occasionally of C_w) in the Mead and (mostly C_l but occasionally C_w and C_a) in the Nagels models that could vary by 2 to 3 orders of magnitude, i.e., multiple near-optimal solutions. On the other hand, the estimation results for the aRIC, aRIC+I_p and DuBois models produced precise, reliable optimal estimates. We believe this phenomenon indicates that the Mead and Nagels models are overparameterized. See Table 4 for an illustrative example of these estimated model parameter values.

We also noted that the eRIC model has an unphysiologically small estimate of peripheral airway compliance for the group of healthy subjects (resulting in a fitting error equal to that of the RIC); this must be due to its lack of ability to model positive frequency dependence of Z_R, which is exhibited by the group 1 data. A lack of inherent capability probably explains why the aRIC model yielded an unphysiologically large peripheral airway resistance estimate for group 1 data. Finally, the C_e estimates were negligible for the group 2 and group 3 data, most likely due to the fact that their Z_R measurements decrease to a minimum at 28 Hz before increasing, so only negative frequency dependence of Z_R is being modeled.

V. Conclusions and Future Work

In this study, we compared the least-squares error performance of the RIC, eRIC, aRIC, aRIC+I_p, DuBois, Nagels and Mead models in fitting PRN FO-acquired respiratory impedance data from healthy subjects, mild asthmatics and severe asthmatics. We found that the aRIC+I_p and DuBois models yielded the lowest fitting errors (for the healthy subjects group and the 2 asthmatic patients groups, respectively) without also producing unphysiologically large component estimates. Hence, these models appear to be the most useful ones (at present) for further studies on PRN FO-based computer-aided detection and treatment of asthma, such as investigating which of these models' parameters can discriminate between normal and abnormal airway function.

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Table 4. Estimated model parameter values for Group 2 (mild asthmatics) data

Model	**Estimated parameter values** (with units of $cmH_2O/l/s$, $cmH_2O/l/s^2$ and l/cmH_2O for resistances, inertances and compliances)
RIC model	R = 4.0867, I = 0.0068211, C = 0.022331
Ext. RIC model	R = 3.8895, R_p = 4.7694, I = 0.0073491, C = 0.019236
Augm. RIC model	R = 3.8895, R_p = 4.7692, I = 0.0073491, C_p = 0.019236, C_e = 2.22E-14
Mead's model	R_c = 3.646, R_p = 0.98159, I = 0.009738, C_b = 0.01492, C_l = 204.02, C_w = 0.027941, C_e = 2.41E-14
Nagels' model	R = 3.6461, R_p = 1.232, I = 0.0097379, C_a = 0.013319, C_l = 0.11062, C_w = 0.036067
aRIC+I_p	R = 3.8896, R_p = 4.7692, I = 0.007349, C_p = 0.019306, I_p = 0.001602, C_e = 2.44E-14
DuBois' model	R_{aw} = 3.6535, I_{aw} = 0.0097301, C_g = 0.010323, R_t = 2.4501, I_t = 0.0029401, C_t = 0.017614