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Ireneusz Jabłoński, Janusz Mroczka

Wroclaw University of Technology
Chair of Electronic and Photonic Metrology
Poland, e-mail: ireneusz.jablonski@pwr.wroc.pl

FREQUENCY INDEXES OF RESPIRATION DURING INTERRUPTER EXPERIMENT

A new issue of the respiratory mechanics evaluation by the frequency mode of the interrupter technique is undertaken in the paper. The aim of the computer-aided research is to show the abilities to separate airways and tissue properties of the respiratory system. The proposed evaluation procedure of the identification quality in the modified DuBois model proves the possibility to conduct repeatable measurements of the important diagnostic indexes. The obtained precision of the parametric description of the investigated physiological system suggests the need to continue the work in the outlined direction. Their final effect can be a portable device with applicability to clinically difficult subjects – infants and pre-school children.

Keywords: respiratory mechanics; interrupter technique; frequency-domain identification

1. INTRODUCTION

Interest in the evaluation of respiratory mechanics results from its direct correlation with the state of one of the most important systems in the human organism. The complexity of the system and the pathological changes which accompany various diseases give the possibility to propose more and more effective diagnostic and useful measurement tools.

In the latest works [1, 2, 3], the authors have concentrated on improvement of the interrupter technique algorithm (IT) in its classical time-domain mode. In the meantime, it is possible to find in literature reports [4, 5, 6] pointed at an important potential of the method in the area of frequency analysis of the data. This regime is proper for many popular commercial and laboratory methods, e.g. negative expiratory pressure (NEP) [7, 8], forced oscillation technique (FOT) [9, 10] or impulse oscillometry [11]. They allow the separation of tissue and airways properties, which is important for medical insight. According to a suggestion in [4, 6], it is expected that metrological conditions for the frequency domain interrupter technique (FDIT) are more favourable than for FOT. Together with the classical IT, it gives the possibility to design an attractive measurement algorithm cumulating the diagnostical penetration of the other

techniques. Investigation of the above-mentioned issues is additionally supported by the fact that IT is characterized by the most profitable utilitarian characteristic among them, i.e.:
– small invasiveness,
– short time of measurement,
– low hardware requirements,
– minimal requirements regarding patient co-operation.
Application to infant and pre-school children – particularly diagnostically difficult subjects – is especially interesting in this context.

Up-to-date research of the IT in the frequency domain leads to the elementary analysis which evaluates frequency characteristics and their quantitative indexes [4, 5]. However, there is lack of regular physical-mathematical description of the relationships for the acquired data. For these reasons, the authors decided to study the potential of the technique in this domain of the experimental data analysis during the next stage of works on evolutionary IT solutions.

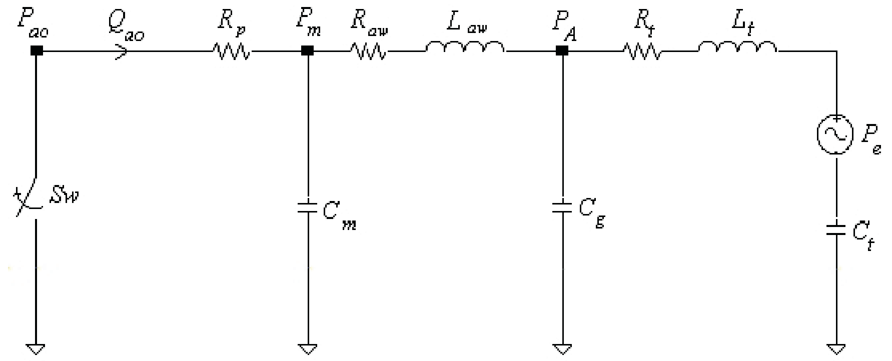

Fig. 1. Electrical replacement model of the respiratory system during airflow interruption: Sw – switch which represents the shutter with R_{sr} resistance [Pa · s/dm^3], R_p – pressure transducer resistance [Pa · s/dm^3], C_m – upper airways compliance [dm^3/Pa], R_{aw} and L_{aw}– resistance [Pa · s/dm^3] and inertance [Pa ·s^2/dm^3] of airways, C_g – alveolar gas compliance [dm^3/Pa], R_t, L_t and C_t – resistance [Pa · s/dm^3], inertance [Pa ·s^2/dm^3] and compliance [dm^3/Pa] of lung tissue and chest wall, P_e – source adequate to respiratory muscle activity [Pa], P_A – alveolar pressure [Pa], P_m – mouth pressure [Pa], P_{ao} – pressure at the airways opening [Pa].

The approach presented here is typical for the simulation-estimation computer experiment. It uses a modified DuBois‘ model (Fig. 1) for the solution of the inverse problem, according to the rules of indirect measurement. The analog usefulness to generation pressure (P_{ao}) and flow (Q_{ao}) characteristics at the mouth was confirmed in [3, 12]. The analysis, which the authors have conducted hitherto in the outlined area [1, 2, 3, 12] served as a methodological determinant for the computer interrupter experiment.

2. METHODS

2.1. Model of the respiratory system during airflow interruption

The model of the respiratory system during airflow interruption, shown in Fig. 1, was used in our research both as a forward model – to generate standard data and an inverse model (or in other words: a metrological model), applied to the estimation procedure of the "real" system properties (here: of the forward model, which imitated the physiological object). This idea is convergent to the research protocol realized in [13].

The structure from Fig. 1 is the modified equivalent of the DuBois *et al.* [14] analogue, used for the time domain IT algorithm verification [3]. It was also a fundamental equivalent of the physiological system during FOT investigations [15]. Values of the parameters were fixed accordingly to the circuit in [3].

2.2. Model identification in the frequency domain

Identification in the frequency domain can consist in fitting of the model impedance to the respiratory impedance Z_{rs}, estimated on the basis of pressure and flow signals, acquired at the mouth. Therefore, the discrete Fourier transform (DFT) is used to calculate the power spectrum of pressure G_{PP} and flow G_{QQ} signal and cross-power spectrum of these signals G_{QP}. To increase the impedance estimation accuracy, the measured data are often divided into N_g groups and the power spectra are calculated for each of them. In case of the frequency analysis of the results of the airflow test proposed in the paper, the groups can be the data which are connected with the subsequent interruptions [16]. The spectra are then averaged to the values $\bar{G}_{PP}$, and $\bar{G}_{QQ}$ and $\bar{G}_{QP}$, and the respiratory impedance is finally determined as:

$$\hat{Z}_{rs}(j\omega) = \frac{\bar{G}_{PP}(j\omega)}{\bar{G}_{QP}(j\omega)}. \tag{1}$$

Considering the averaged power spectra, we can also calculate a coherence function γ which is a measure of the estimation quality of impedance Z_{rs}:

$$\gamma^2(f) = \frac{\left|\bar{G}_{QP}\right|^2}{\bar{G}_{PP}\bar{G}_{QQ}}, 0 \le \gamma^2 \le 1 \tag{2}$$

and then we can assess the variance S^2 of the impedance estimator for each frequency:

$$S^2(f) = \left|\hat{Z}_{rs}(j2\pi f)\right|^2 \frac{\left[\gamma^2(f)\right]^{-1} - 1}{N_g - 2}. \tag{3}$$

Since airflow interruption takes place during passive expiration, we realize that in the analysis of the impedance of the respiratory system model we can ignore the source of the excitation signal (P_e), as it is inactive then. In this way, the input impedance Z_{in} of the model equals:

$$Z_{in}(j\omega) = R_p + \frac{Z_m Z_g Z_t + Z_m Z_{aw} Z_g + Z_m Z_{aw} Z_t}{Z_g Z_m + Z_t Z_m + Z_g Z_t + Z_{aw} Z_g + Z_{aw} Z_t}, \tag{4}$$

where: $Z_m(j\omega)$ – impedance of the compliance C_m, $Z_{aw}(j\omega)$ – impedance of the series connection of R_{aw} and L_{aw}, $Z_g(j\omega)$ – impedance of the compliance C_g and $Z_t(j\omega)$ – impedance of series connection of R_t, L_t and C_t. Additionally, $Z_{in}(0) = \mathrm{R_p} + \mathrm{R_{aw}} + \mathrm{R_t}$, because the flow is forced by discharging the compliance C_t during passive expiration. While constructing the model identification procedures, it is worth to use the premises imposed by the discussion on the forced oscillation technique and to apply an iterative algorithm of parameters estimation of the nonlinear model. It results in minimizing the criterion function the value of which depends on adjustment of the model impedance to the impedance measured in a real object:

$$\hat{\theta} = \arg\min_{\theta} (\mathbf{z}_{rs} - \mathbf{z}_{in}(\theta))^{\mathrm{T}} \mathbf{R}^{-1} (\mathbf{z}_{rs} - \mathbf{z}_{in}(\theta)), \tag{5}$$

where $\mathbf{z}_{\mathrm{rs}}$ and $\mathbf{z}_{\mathrm{in}}$ are vectors of impedance estimated and calculated in the model, respectively, θ is a vector of unknown parameters (C_m, R_{aw}, L_{aw}, C_g, R_t, L_t, C_t), and R is a weight matrix: $\mathbf{R} = diag\left(S^2\right)$.

2.3. Variance analysis of the estimators

Frequency-domain identification of the proposed model of the respiratory system during airflow interruption needs applying the iterative algorithms. The result of their application is the vector of parameter estimators $\hat{\boldsymbol{\theta}}$ and the estimator of their variances $\boldsymbol{\Sigma}$:

$$\Sigma\left(\hat{\theta}\right) = \left[\eta^{\mathrm{T}}\left(\hat{\theta}\right)\mathbf{R}^{-1}\eta\left(\hat{\theta}\right)\right]^{-1}, \tag{6}$$

where $\boldsymbol{\eta}$ is a sensitivity matrix of the output $\mathbf{y}$ of the model in relation to the parameters:

$$\eta = \frac{\partial \mathbf{y}}{\partial \theta}. \tag{7}$$

According to [1], the approach proposed in the paper of forward-inverse modeling has the advantage that we know both the structure of the model and the chosen vector of parameters θ_0 of the forward model representing the real system. In this situation $\hat{\theta} \approx \theta_0$ is the expected effect of work of the identification procedure. So, it is possible to assess the variance of the obtained estimators as $\Sigma(\theta_0)$, and calculate the vector of relative uncertainties of estimation $\mathbf{d}$, defined as follows:

$$\begin{aligned}\mathbf{d} &= \theta_0^{-1} \operatorname{diag}(\Sigma(\theta_0))^{1/2}\,, \\ \theta_0 &= \operatorname{diag}(\theta_0)\,.\end{aligned} \tag{8}$$

3. RESULTS

The basis for the determination of properties of identification of the respiratory system model in the frequency domain is an evaluation of the variance of Z_{rs} impedance estimator for the given frequencies and calculation of the sensitivity matrix of the model for the true vector of parameters θ_0.

In simulations of pressure and flow changes at the airways opening, implementation of the model which is described above was used. The four interruptions during passive expiration were imitated. Each of them lasted 50 ms and was separated by the same intervals of normal, not occluded breathing. Data were sampled at 1 kHz. Then, Gaussian noise with a standard deviation of 1 Pa and 0.01 $\mathrm{dm}^3 \cdot \mathrm{s}^{-1}$ was added to the pressure and flow signals, respectively. In this way, four groups of measurement data (each consisted of one interruption manoeuvre) were prepared and the impedance Z_{rs}, the coherence function and the variance of estimators were calculated. For an estimation of the power spectrum density the Hanning window was used. The sampling frequency and the time of collecting one data group (100 ms) give resolution in the frequency domain equal to 10 Hz. To increase the accuracy of evaluation of the variance s^2 of the estimated impedance, it was calculated 200 times for each frequency and then averaged.

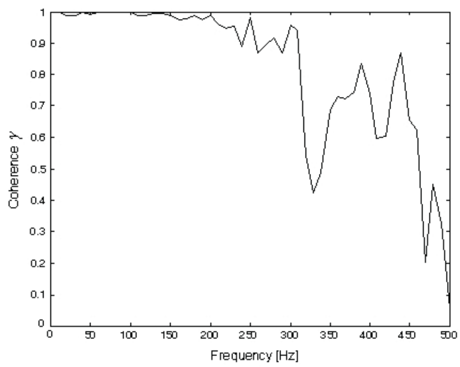

Fig. 2. Coherence function calculated during occlusion for the system represented by modified DuBois' analog.

In the frequency analysis of the respiratory mechanics, we can conclude about the system usually on the basis of the course of its magnitude and phase characteristics, which point at resistive property domination in case of the first of them and reactant (capacities, inertances) in the other, suitably. Thus, from the measurement point of view, we can ask a question about contribution of the determined real and imaginary parts or modulus and phase of impedance to the completeness of inference about the status of the system [17, 18, 19]. An exemplary plot of the calculated coherence function is presented in Fig. 2.

Evaluation of identification quality for the respiratory system can be based on the sensitivity analysis. For real and imaginary parts of impedance ReZ_{in} and ImZ_{in}, the elements of sensitivity matrix can be determined analytically:

$$\begin{aligned} \eta_{\mathrm{Re}_k}(f) &= \frac{\partial \mathrm{Re}\,(Z_{in})}{\partial \theta_k}, \\ \eta_{\mathrm{Im}_k}(f) &= \frac{\partial \mathrm{Im}\,(Z_{in})}{\partial \theta_k}. \end{aligned} \tag{9}$$

It is useful to normalize the vectors of sensitivity and then compare them graphically:

$$\eta_N = \mathbf{R}^{1/2}\eta \operatorname{diag}\left(\operatorname{diag}\left(\mathbf{E}_t^{1/2}\right)\right). \tag{10}$$

The dependence of the real and imaginary parts of the respiratory input impedance on frequency is depicted respectively in Fig. 3a and Fig. 3c, and the frequency distribution of the normalized vectors of the model sensitivity is shown in turn in Fig. 3b, Fig. 3d.

All the following figures suggest what important information is obtained from the data up to about 120 Hz. It should be also noticed that the signals η_{Re_k} i η_{Im_k} reach a comparable level, differing in the frequency trend of the parameters. The results of the analysis according to the Eq. (8) for such data configuration (see Table 1) show that estimation in the frequency domain, in case of most parameters is burdened with an important random error. Among other things, it is also connected with significant collinearity of influence of the capacity C_g and resistances R_t and R_{aw} on the impedance. Additionally, this phenomenon causes that the matrix $\eta^{\mathrm{T}}\mathbf{R}^{-1}\eta$ inversion is ill-conditioned numerically, which can be the reason of further unpredictable errors during estimation. Similar difficulties were observed earlier, during the analysis of precision of estimation of the DuBois‘ model parameters by the forced oscillation technique [15]. In this situation, C_g calculation on the basis of the functional residual capacity (FRC) and elimination of the parameter from the identification procedure, are proposed.

For the model analyzed in the paper, the operation consisting in the elimination of parameter C_g from the identification process significantly improves the credibility of estimators (vector $\mathbf{d}_{C_g}$ in Table 1) and, at the same time, improves numerical conditions of the applied algorithm. Due to that, first of all, the decrease of estimation uncertainty of airways resistance and resistance of chest wall and lung tissue is observed. As

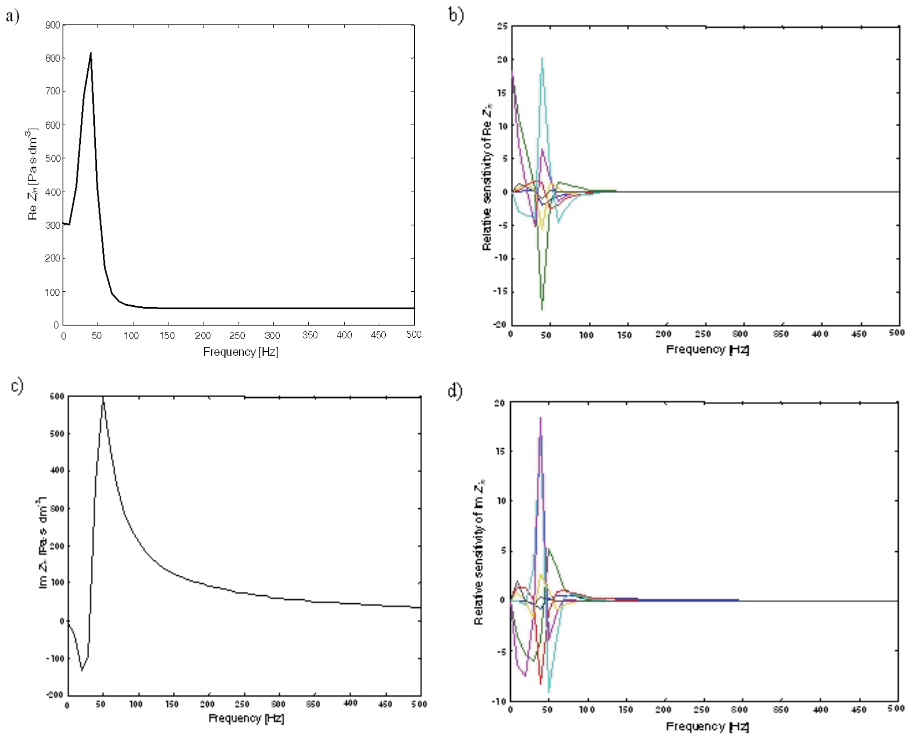

Fig. 3. Frequency changes of the real (a) and imaginary (c) part of Z_{in} impedance of the modified DuBois‘ analog and their normalized sensitivity functions, respectively (b) and (d).

important diagnostically, these parameters can be estimated with the error not exceeding respectively ~6.0 % and 12.5 % during Z_{in} signal fitting, which is a better result than the result typical for the classic monoparametric interrupter algorithm; the most general conclusion and advantage (in the light of measurement possibilities of the occlusional algorithm), at the same time, following from this part of investigations is the ability to distinguish the properties of the tissue and airways segment, which constitutes a desirable *novum* of designed enhanced interrupter technique (EIT) in relation to IT. Besides, we can expect greater repeatability of the estimates for a greater number of the estimated parameters than so far.

Table 1. Results of the parameters uncertainty evaluation of the model for the respiratory system in the frequency domain; *CN* – condition number.

Relative uncertainty	C_m	R_{aw}	L_{aw}	C_g	R_t	L_t	C_t	CN
d	1.32	46.4	6.52	113	93.0	45.4	42.7	$2.15 \cdot 10^{18}$
$\mathbf{d_{Cg}}$	1.16	5.70	3.72	–	12.1	33.6	37.8	$2.92 \cdot 10^{16}$

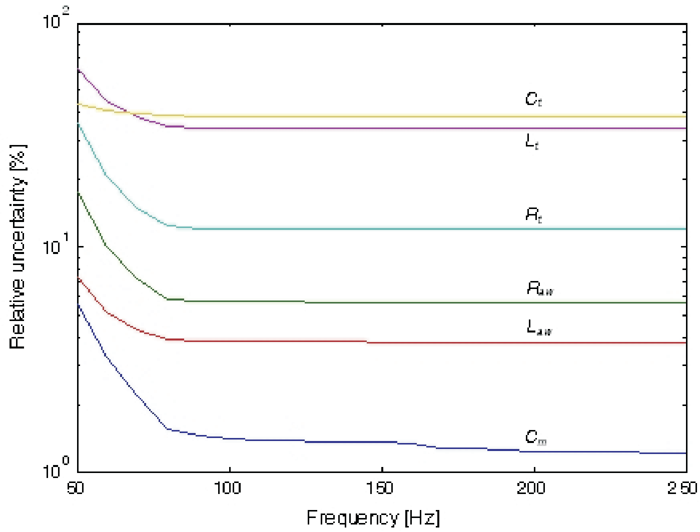

Fig. 4. Dependence of estimation accuracy $\mathbf{d}_{Cg}$ of the six parameters on the frequency range of measurement data for the signal $Z_{in} = X_{in} + jY_{in}$.

The courses of the sensitivity functions (Fig. 2, Fig. 3) show that the values of the parameter estimators of the proposed model are obtained on the basis of the measurement data, mainly with frequencies up to about 70 Hz, which is consistent with the results of research devoted to the forced oscillation technique. The foregoing observations are valid also for Fig. 4, where the dependence of estimation accuracy of the six parameters of the model on the frequency range is presented.

4. CONCLUSIONS

The issue of reliable and careful insight into the properties and the processes taking place in the respiratory system is a lively research area, e.g. [20–24]. The interrupter technique, which is the key subject of the paper, is distinguished by an essential utilitarian virtue. Effective tools dedicated to quantitative concluding about the respiratory system on the basis of occlusional data have not been developed until now. Traditional approaches assume [25, 26, 27] an analysis in the time domain, consisting in the extrapolation of pressure changes at the mouth and the evaluation of the diagnostical parameter – the interrupter resistance R_{int} – erroneously interpreted as a measure of the respiratory airways resistance. Sparse and elementary attempts at a frequency analysis of the interrupter data can be also found in the literature [4, 5], but optimistic observations against the background of the other techniques of system stimulation (e.g. FOT) have not been brought to final algorithmic solutions.

In the present paper, the authors try to revise and improve the above-mentioned idea of Frey *et al*. [4, 16]. Showing abilities to separate tissue (R_t, L_t, C_t) and airways (R_{aw}, L_{aw}) properties during such experiment is the most important result of the simulation analysis. The obtained precision of the evaluation (Table 1) depends on the way of acquiring and pre-processing (configuration) of the collected data. In this sense, the paper postulates the multi-occlusional manoeuvre and using the complementary information contained in the complex input respiratory impedance: $Z_{in} = X_{in} + jY_{in}$. As results from the computer simulation, the elimination of shunting of the alveolar gas compliance C_g (which separates airways and tissue segments) is important for the results of modified interrupter tests (see Table 1). This fact is analogous to the observations of measurement abilities of the forced oscillation technique [15]; C_g can be calculated independently by the other methods. As a matter of fact, the conditions of measurement imitated during the experiment reduced the useful diagnostical range of the obtained frequency characteristics (Fig. 3, Fig. 4). Nevertheless, it made possible to note the satisfying precision of the parameter estimation. Matching up hardware characteristics and increasing the resolution of the frequency spectrum [16] gives the possibility to improve the accuracy of the frequency interrupter method, especially within the limits of tissue section as results from the analogous reports on FOT, such features manifestation occurs mainly in the low frequency range (up to 8, maximally 32 Hz).

The prospective area of analysis for FDIT and the potential source of its diagnostical penetration increasing, is also the issue of mathematical modeling of the respiratory system in adequate conditions. An expression of this task, poorly realized so far, can be found in [4]. From this point of view, in our computer experiment it was possible to obtain the evidence of identifiability of the future useful information on the undertaken system during the real measurements, even for the adapted DuBois‘ structure.

The attempt of the cause-effect modeling makes it possible to evaluate the systematic factor of uncertainty during the frequency interrupter experiment (without a regular analysis of random noise influence). The subject of such estimation is the indirect algorithm of parametric identification. The issues of structural adequacy (thus, the next systematic error component) of the model (here: very simple, linear) to the real object aren‘t a matter of presented investigations. This important question is the other independent part of the author‘s research and will be a subject of the future reports.

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