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A NOVEL PARAMETRIC MODEL FOR THE HUMAN RESPIRATORY SYSTEM

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ABSTRACT

The purpose of this work is to present some recent results in an ongoing research project between Ghent University and Chess Medical Technology Company Belgium.

The overall aim of the project is to provide a fast method for identification of the human respiratory system in order to allow for an instantaneously diagnosis of the patient by the medical staff.

A novel parametric model of the human respiratory system as well as the obtained experimental results are presented in this paper. A prototype apparatus developed by the company, based on the forced oscillation technique is used to record experimental data from 4 patients in this paper. Signal processing is based on spectral analysis and is followed by the parametric identification of a non-linear mechanistic model.
The parametric model is equivalent to the structure of a simple electrical RLC-circuit, containing a non-linear capacitor. These parameters have a useful and easy-to-interprete physical meaning for the medical staff members.

Keywords: respiratory system, respiratory mechanics, biomedical modelling, optimisation, non-linear model, forced oscillation technique

1. Introduction

During the last decennium the field of biomedical engineering has been characterized by important progress thanks to the new technologies of information processing and new methods of analysis, diagnosis and simulation of the human body.
Previous work has applied intelligent control systems, artificial neural networks, recursive methods for on-line estimation of respiratory parameters of lung mechanics [1], as well as mathematical analysis and computer simulation. An on-line investigation of inspiratory pressure-volume curves is mentioned in [2] and also the sensitivity analysis and an optimal experiment design has been performed for estimating mechanical parameters [3]. Some basic knowledge about respiratory system is presented in detail in [4], and medical applications of computer modelling of the respiratory system are presented in [5]. Clinical applications and modelling of the respiratory system by use of oscillation mechanics can be studied in [6].

Since the very first description of the forced oscillation technique in [7], its applicability has been developed over decades. The forced oscillation technique has its advantages and disadvantages [4], but it is mainly used in characterization of the respiratory function, assessment of bronchial challenge, mechanical ventilation and sleep studies [4,8]. It has proven to be of great use in investigating the respiratory oscillation mechanics in infants and preschool children [9]. An improved forced oscillatory estimation of respiratory impedance is mentioned in [10], pointing out a solution to avoid the systematic error due to interference between normal respiratory signal components and the forced oscillatory signals.

The paper is organized as follows: in the second section the apparatus used and the forced oscillation technique are described, the third section presents the signal processing based on spectral analysis. The identification of the non-linear parametric model is presented in section 4. As an illustration of the developed method in the fifth section the experimental data for 4 subjects are processed and the results are presented. Finally a conclusion section summarizes the main outcome of this investigation and formulates some ideas concerning the future work.

2. Apparatus and Test

The mechanical properties of the respiratory system may be obtained by applying the forced oscillation technique (FOT), measuring thus the air-flow and trans-respiratory

pressure. As the application of this non-invasive technique does not require the patient's cooperation, it is suitable for routine evaluation of respiratory function, described in detail in [6,7,8]. However, it should be pointed out that with FOT respiratory mechanics is assessed at a frequency-range (4:48 Hz), which is higher than the spontaneous breathing frequency.

The conventional FOT set-up is based on superimposing a low-amplitude pressure oscillation at the mouth while the patient is breathing spontaneously as illustrated in Fig.1:

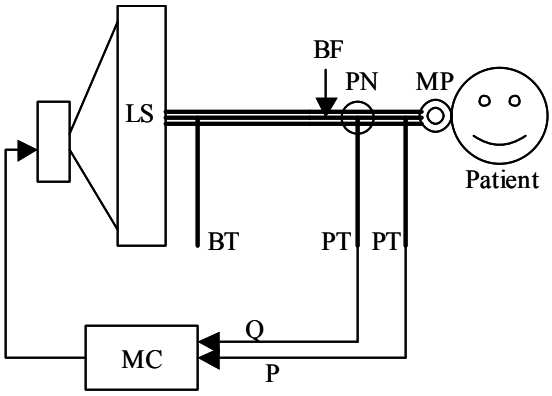

Figure 1: Conventional FOT set-up

with the corresponding notations: MC - microcomputer; LS - loudspeaker; BT – bias-tube; BF – bias-flow; PN - pneumotachograph; MP - mouth-piece; PT - pressure transducer; Q – flow and P - pressure.

The oscillation pressure is generated by a loudspeaker connected to a chamber, driven by a power amplifier fed with the oscillating signal generated by a computer. The movement of the loudspeaker cone generates a pressure oscillation inside the chamber, which is applied to the patient's respiratory system by means of a tube connecting the loudspeaker chamber and the mouthpiece. As the patient breathes spontaneously through a bias tube - ideally presenting low impedance to the breathing frequency and high impedance to the forced oscillation frequency - a constant bias flow avoids re-breathing. It is advisory that during the measurements, the patient should wear a noseclip and keep the cheeks firmly supported.

Pressure and flow are measured at the mouthpiece by means of 1) a pressure transducer and 2) a pneumotachograph plus a differential pressure transducer, respectively. These signals are then analogically low-pass filtered, sampled and stored in a microcomputer. Before starting the measurements, in order to get accurate data, the frequency response of the transducers and of the pneumotachograph should be calibrated. Anyway, some technical requirements specified in [11] should be provided before using the apparatus.

Oscillatory mechanics may be obtained by using different types of forcing signals. The simplest signal is sinusoidal oscillation since it provides a direct interpretation of the mechanical load of the respiratory system. Moreover, this signal has the advantage of providing the highest signal-to-noise ratio (SNR). Nevertheless, a drawback of sinusoidal oscillation is that the assessment of the frequency dependence of respiratory impedance over a wide frequency band requires several measurements at different frequencies. That is only one of the reasons why in collecting the experimental data to analyse it was used a pseudorandom (multi-sine) signal, also the most commonly used test signal. More advantages are detailed in [8].

Both the oscillatory pressure P(t) and flow Q(t) are periodic with the same period T. The modulus of oscillatory impedance ($|Z_r|$) is defined as the quotient between the amplitude of oscillatory pressure and the amplitude of oscillatory flow. The higher the $|Z_r|$, the greater the pressure amplitude required to induce a given flow. Thus, $|Z_r|$ is a measure of the total mechanical load of the respiratory system at the oscillation frequency. The phase of respiratory impedance (Φ_r) is defined as the phase lag between P(t) and Q(t) and it is computed as the ratio between the time lag and the oscillation period (Φ_r = 360° x Δt/T). The frequency where $\Phi_r = 0$ is called the «resonance frequency» and it depends on the balance between the different kind of mechanical properties (resistive, elastic, inertial) determining thus the mechanics of the respiratory system.

3. Signal Processing (Spectral Analysis)

The global experimental set-up can be modelled by the electrical analogy of Fig. 2, where:

U_g = generator test signal (known)

U_r = effect of spontaneous breathing (respiratory system / unknown)

Z_r = impedance of interest (to be estimated): the impedance of the total respiratory system (including the airways, lung tissues and chest wall)

Z_1 = impedance (unknown) describing the transformation of driving voltage (U_g) to chamber pressure

Z_2 = impedance (unknown) of both bias tubes and loud-speaker chamber

Z_3 = impedance (unknown) of tube segment between bias tube and mouth piece (effect of pneumotachograph essentially)

P = (measured) pressure

Q = (measured) flow

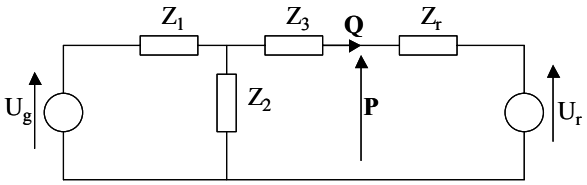

Figure 2: Electrical Scheme Analogy

Using the basic laws for analysing electrical networks, the following relationships can be derived:

$$P = \frac{(Z_m - Z_3)Z_r}{(Z_m + Z_r)Z_1} U_g + \frac{Z_m}{Z_m + Z_r} U_r \qquad (1)$$

$$Q = \frac{Z_m - Z_3}{(Z_m + Z_r)Z_1} U_g - \frac{1}{Z_m + Z_r} U_r \qquad (2)$$

$$\text{with} \quad Z_m = Z_3 + \frac{Z_1 Z_2}{Z_1 + Z_2} \qquad (3)$$

This is a system

$$\begin{bmatrix} P(s) \\ Q(s) \end{bmatrix} = \underline{H}(s) \begin{bmatrix} U_g(s) \\ U_r(s) \end{bmatrix} \qquad (4)$$

with 2 'inputs' U_g and U_r, 2 'outputs' P and Q and transfer matrix:

$$\underline{H} = \begin{bmatrix} \frac{(Z_m - Z_3)Z_r}{(Z_m + Z_r)Z_1} & \frac{Z_m}{Z_m + Z_r} \\ \frac{Z_m - Z_3}{(Z_m + Z_r)Z_1} & \frac{-1}{Z_m + Z_r} \end{bmatrix} \qquad (5)$$

(all impedances Z_* being also a function of 's'; the symbol 's' denotes Laplace-operator).

Define now the vectors:

$$\underline{S}_{YU} = \begin{bmatrix} S_{PU_g} \\ S_{QU_g} \end{bmatrix} \quad \text{and} \quad \underline{S}_{UU} = \begin{bmatrix} S_{U_g U_g} \\ S_{U_r U_g} \end{bmatrix} \qquad (6)$$

containing cross-power-spectra $S_{yu}(j\omega)$ between 2 signals y(t) and u(t) and auto-power-spectra $S_{uu}(\omega)$ of a signal u(t).

From well-known [12] identification and signal-processing theory it then follows that:

$$\underline{S}_{YU}(j\omega) = \underline{H}(j\omega)\underline{S}_{UU}(j\omega) \qquad (7)$$

In case of 'absence of breathing' ($U_r = 0$) the expression (7) reduces to:

$$\begin{bmatrix} S_{PU_g} \\ S_{QU_g} \end{bmatrix} = \begin{bmatrix} \frac{(Z_m - Z_3)Z_r}{(Z_m + Z_r)Z_1} \\ \frac{(Z_m - Z_3)}{(Z_m + Z_r)Z_1} \end{bmatrix} \bullet S_{U_g U_g} \qquad (8)$$

and it would be 'exact' to estimate the 'impedance of interest' $Z_r(j\omega)$ from:

$$\hat{Z}_r(j\omega) = \frac{S_{PU_g}(j\omega)}{S_{QU_g}(j\omega)} \qquad (9)$$

However, it is supposed that the test is done in 'normal breathing conditions', which may result in an interference between the (unknown) breathing signal U_r and the test signal U_g, making the identification exercise more difficult. From the point of view of the forced oscillatory experiment, the signal components of respiratory origin, (U_r) have to be regarded as pure noise for the identification task!

Nevertheless, if the test signal U_g is designed to be uncorrelated with the normal respiratory breathing signal U_r, then $S_{U_r U_g} \equiv 0$, and the approach (9) is still valid, based on (7) with $S_{U_r U_g} \equiv 0$, (ref. also [10]).

4. Identification of a Non-Linear Mechanistic Model

The main topic of this paper can be described briefly as following: derive a parametric model for the impedance $Z_r(s)$ of the human respiratory system, starting from given frequency response data of this impedance, as obtained in section 3.

The impedance is defined as the transfer function "air pressure/air flow" in the lungs of a patient, as mentioned in section 2. The parametric model should have the structure of a simple electrical RLC-circuit (resistor, inductor, capacitor), but the most important "detail" of this particular model is that the capacitor is non-linear (because a linear RLC cannot explain the "observed" frequency response).

Having a linear RLC circuit, the impedance is given by

$$Z(s) = R + Ls + \frac{1}{Cs} \qquad (10),$$

where *s* is the Laplace operator.
Here, the structure should be (based on input from Chess mT Company):

$$Z(s) = R + Ls + \frac{1}{Cs^{\alpha}} = R + Ls + \frac{D}{s^{\alpha}}, \text{ with } 0<\alpha \le 1 \qquad (11).$$

The frequency response can then be written as:

$$Z(j\omega) = R + Lj\omega + \frac{D}{(j\omega)^{\alpha}} = (R + aD) + j(\omega L - bD)$$
$$\text{with } a = \frac{\cos(\alpha\frac{\pi}{2})}{\omega^{\alpha}} \text{ and } b = \frac{\sin(\alpha\frac{\pi}{2})}{\omega^{\alpha}} \quad (12).$$

Given the 2 vectors $\{\mathbf{R}(n) \text{ and } \mathbf{I}(n) \text{ for } n = 1\cdots N\}$, containing the data of the frequency response $Z_r(j\omega)$ (**R**=real part and **I**=imaginary part), measured in N frequency points ω_n, the solution is thus obtained by minimizing the error function $\mathrm{V}(R, L, D, \alpha)$ by choosing the best values for the parameters $\{R, L, D, \alpha\}$:

$$\mathrm{V} = \left\{ \sum_{n=1}^{N} \left[\mathbf{R}(n) - (R + a_n D)\right]^2 + \sum_{n=1}^{N} \left[\mathbf{I}(n) - (\omega_n L - b_n D)\right]^2 \right\}$$
$$\text{with } a_n = \frac{\cos(\alpha\frac{\pi}{2})}{\omega_n^{\alpha}} \text{ and } b_n = \frac{\sin(\alpha\frac{\pi}{2})}{\omega_n^{\alpha}} \quad (13)$$

To be of any practical diagnostic value, it has been also specified that the results should be obtained very fast (a FOT measurement of the frequency response of a patient takes 8 seconds and the parameters $\{R, L, C, \alpha\}$ should be available to the medical doctor 'immediately afterwards').

If above problem is solved 'blindly', it leads to a non-linear minimization task, with special difficulty because of the presence of constraints for the parameter α ($0<\alpha\leq 1$). It has to be solved then with "a constrained non-linear programming" software, which is complex, time-consuming and does not necessarily converge to the global minimum.

For that reason, the following simpler - but correct - procedure is suggested. It is based on the observation that the impedance is linear in the parameters R, L, D but non-linear only in the parameter α. For a given value of α, being a priory specified, the variables a_n and b_n become constants (different for each n) and the values of R, L, D can then be obtained in a straightforward and very fast manner. A more elegant solution can thus be obtained by 'pre-specifying' the parameter α instead of 'estimating' it. Thus reducing the problem to a simple Least Squares Parameter Estimation problem [12].

Starting from equation (12), the real and respectively imaginary part, measured in N frequency points (n=1..N), can be described as following in matrix notation:

$$\begin{bmatrix} R(1) \\ R(2) \\ \vdots \\ R(N) \end{bmatrix} = \begin{bmatrix} 1 & a_1 \\ 1 & a_2 \\ \vdots & \vdots \\ 1 & a_N \end{bmatrix} \begin{bmatrix} R \\ D \end{bmatrix} + \begin{bmatrix} \delta_1 \\ \delta_2 \\ \vdots \\ \delta_N \end{bmatrix}$$
$$\begin{bmatrix} I(1) \\ I(2) \\ \vdots \\ I(N) \end{bmatrix} = \begin{bmatrix} \omega_1 & -b_1 \\ \omega_2 & -b_2 \\ \vdots & \vdots \\ \omega_N & -b_N \end{bmatrix} \begin{bmatrix} L \\ D \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \vdots \\ \varepsilon_N \end{bmatrix} \quad (14)$$

where $\{\delta_i, \varepsilon_i\}$ are the "closing terms" (residual errors).

The description in a compact form (LS-method) results in:

$$\mathbf{R} = \mathbf{\Phi}_1\boldsymbol{\theta}_1 + \boldsymbol{\delta} \quad \text{and} \quad \mathbf{I} = \mathbf{\Phi}_2\boldsymbol{\theta}_2 + \boldsymbol{\varepsilon} \quad (15).$$

The error function to be minimized can be written as (16):

$$V(\theta_1, \theta_2) = \boldsymbol{\delta}^T\boldsymbol{\delta} + \boldsymbol{\varepsilon}^T\boldsymbol{\varepsilon} =$$
$$= \left[\mathbf{R} - \mathbf{\Phi}_1\boldsymbol{\theta}_1\right]^T \left[\mathbf{R} - \mathbf{\Phi}_1\boldsymbol{\theta}_1\right] + \left[\mathbf{I} - \mathbf{\Phi}_2\boldsymbol{\theta}_2\right]^T \left[\mathbf{I} - \mathbf{\Phi}_2\boldsymbol{\theta}_2\right]$$

resulting in:

$$V = \left(\mathbf{R}^T\mathbf{R} - 2\mathbf{R}^T\mathbf{\Phi}_1\boldsymbol{\theta}_1 + \boldsymbol{\theta}_1{}^T\mathbf{\Phi}_1{}^T\mathbf{\Phi}_1\boldsymbol{\theta}_1\right) +$$
$$+ \left(\mathbf{I}^T\mathbf{I} - 2\mathbf{I}^T\mathbf{\Phi}_2\boldsymbol{\theta}_2 + \boldsymbol{\theta}_2{}^T\mathbf{\Phi}_2{}^T\mathbf{\Phi}_2\boldsymbol{\theta}_2\right) \quad (17).$$

Define the following notations:

$$a_1 = \mathbf{R}^T\mathbf{R};\ \begin{bmatrix} b_1 & c_1 \end{bmatrix} = \mathbf{R}^T\mathbf{\Phi}_1;\ \begin{bmatrix} d_1 & e_1 \\ e_1 & f_1 \end{bmatrix} = \mathbf{\Phi}_1{}^T\mathbf{\Phi}_1$$
$$a_2 = \mathbf{I}^T\mathbf{I};\quad \begin{bmatrix} b_2 & c_2 \end{bmatrix} = \mathbf{I}^T\mathbf{\Phi}_2;\ \begin{bmatrix} d_2 & e_2 \\ e_2 & f_2 \end{bmatrix} = \mathbf{\Phi}_2{}^T\mathbf{\Phi}_2 \quad (18),$$

and thus the error function to be minimized becomes (19):

$$V = a_1 - 2\begin{bmatrix} b_1 & c_1 \end{bmatrix}\begin{bmatrix} R \\ D \end{bmatrix} + \begin{bmatrix} d_1R + e_1D & e_1R + f_1D \end{bmatrix}\begin{bmatrix} R \\ D \end{bmatrix} +$$
$$a_2 - 2\begin{bmatrix} b_2 & c_2 \end{bmatrix}\begin{bmatrix} L \\ D \end{bmatrix} + \begin{bmatrix} d_2L + e_2D & e_2L + f_2D \end{bmatrix}\begin{bmatrix} L \\ D \end{bmatrix}$$

From equation (19), if it is expanded, follows:

$$V = a_1 - 2b_1R - 2c_1D + d_1R^2 + 2e_1RD + f_1D^2 +$$
$$+ a_2 - 2b_2L - 2c_2D + d_2L^2 + 2e_2LD + f_2D^2 \quad (20).$$

Minimizing $V(R, L, D)$ with respect to the 3 variables, leads to:

$$\begin{cases} \frac{dV}{dR} = 0 \quad \Rightarrow \quad -2b_1 + 2d_1R + 2e_1D = 0 \\ \frac{dV}{dL} = 0 \quad \Rightarrow \quad -2b_2 + 2d_2L + 2e_2D = 0 \\ \frac{dV}{dD} = 0 \quad \Rightarrow \quad -2c_1 + 2e_1R + 2f_1D - 2c_2 + 2e_2L + 2f_2D = 0 \end{cases}$$

Now it is straightforward to obtain the simplified matrix form:

$$\begin{bmatrix} d_1 & 0 & e_1 \\ 0 & d_2 & e_2 \\ e_1 & e_2 & f_1+f_2 \end{bmatrix} \begin{bmatrix} R \\ L \\ D \end{bmatrix} = \begin{bmatrix} b_1 \\ b_2 \\ c_1+c_2 \end{bmatrix} \quad (21)$$

or $\mathbf{A\theta} = \mathbf{b}$ or $\boldsymbol{\theta} = \mathbf{A}^{-1}\mathbf{b}$

If this simple linear regression is done for several pre-specified values of α - equally distributed in the range 0→1 - and if the resulting minimum cost V for each α is calculated, it is then sufficient to select that α-value which leads to the overall smallest cost V. Thus resulting in the global optimal parameter values for $\{R, L, C(=1/D), \alpha\}$.

5. Experimental Results

As described in sections 2 and 3, the FOT was used to obtain data from 4 patients, and then the model described in section 4 calculates the required values for R, L, D and α. The frequency points where the frequency response has been calculated are between 4Hz and 48Hz, in steps of 2Hz. Thus there are N=23 frequency points.

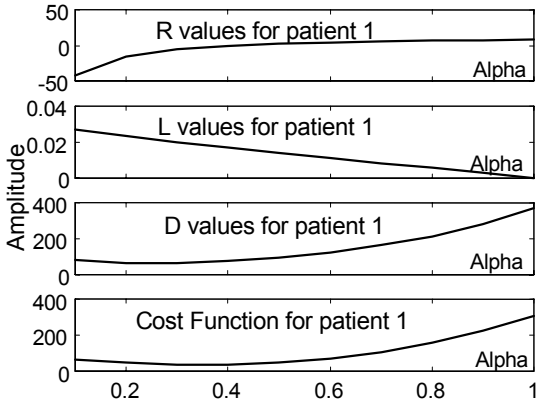

Figure 3: R, L, D values and Cost Function for patient 1

It is easy to observe that the α-value leading to the overall smallest cost is assumed to be 0.3<α<0.4.

In Fig. 3 are presented the values of R, L and D computed from different values of α respectively, using experimental data from patient 1 (as a typical example). Also, in the last plot can be observed the cost function and its evolution with respect to different α-values.

In Fig. 4 are presented the experimental (bold) vs. estimated (dotted) real and imaginary part of the frequency response of impedance of the first patient for an α-value corresponding to the linear RLC circuit, respectively α= 1 (see section 4, equation 11).
In the following figures (Figs. 4-7), 1 Volt corresponds to approximately 0.5 cm $H_2O*L^{-1}*s$.

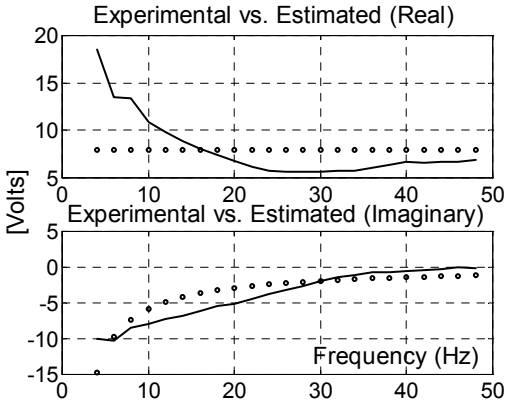

Figure 4: Estimation for α=1

In Figs. 5, 6 and 7 are presented the estimation (dotted) of real and imaginary part with respect to α-values (α → 0.8 / 0.6 / 0.4).
It can be seen that the approximations are strongly depending on the α-values and thus the main reason of using such a non-linear RLC-circuit as a good approximation for the respiratory model.

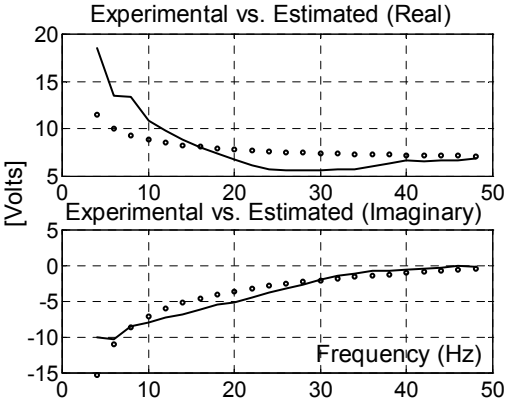

Figure 5: Estimation for α=0.8

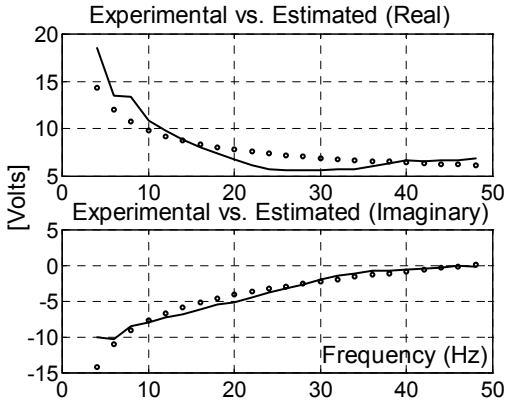

Figure 6: Estimation for α=0.6

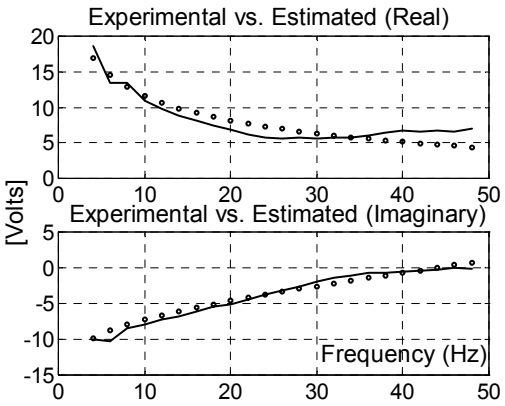

Figure 7: Estimation for α=0.4

Taking into account the "flat-surface" of the cost function between $0.1<\alpha<0.6$ (Fig. 3), and taking into account that only R>0 has a physical meaning, this exercise for patient #1 would result in $R\approx 0$; L=0.015; C=0.0118 (C=1/D) and α=0.45. Thus, from a realistic standpoint, Fig.7 depicts the estimation of the respiratory impedance (real & imaginary part) leading to the overall smallest cost for patient 1.
The pictures for the other 3 patients are more or less the same as the one presented for the first patient, and only the final results for all patients will be mentioned in the table below.

Patient	R	L	C	α
1	0.31	0.015	0.0118	0.45
2	0.78	0.010	0.0366	0.22
3	1.27	0.172	0.0115	0.45
4	0.39	0.012	0.0887	0.30

6. Conclusions

This paper deals with the modelling of the human respiratory impedance as a function of air flow and pressure, measured with the pseudo-random noise forced oscillation technique between 4 and 48Hz.

The forced oscillation technique is, despite its simplicity, a promising method to investigate respiratory mechanics as a function of frequency and suited for use in clinical medicine. Its application in assessing and interpreting abnormalities in disease is still in a developmental stage, but nevertheless step-by-step more accepted.

The main contribution in this paper was a new (non-linear) parametric representation of the FOT frequency response data (equivalent to an electrical RLC-circuit, with a non-linear capacitor). The parameters in this model have – according to the involved company specialized in this field – a useful meaning to the medical staff.
A next step will be to try collecting experimental data consisting of flow and pressure at lower frequencies; more specifically, between 0.5 and 10Hz. This is rather complicated due to interference with the frequency of 'normal' breathing of the patient.

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