Estimation of respiratory impedance at low frequencies during spontaneous breathing using the forced oscillation technique

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***Abstract*— The forced oscillation technique (FOT) is a non-invasive method to measure the respiratory impedance Z, defined as the complex ratio of transrespiratory pressure P to the airflow at the airway opening Q as a function of frequency. FOT determines Z by superimposing small amplitude pressure oscillations on the normal breathing and measuring the resulting air flow. In this work a new approach for the analysis of the respiratory impedance Z at low frequencies (0.1-5 Hz) during spontaneous breathing is presented. When the respiratory impedance is measured in frequency ranges that overlap with the frequency of spontaneous breathing (0.1-1 Hz), the measured air flow will contain both the breathing of the patient and the response of the respiratory impedance to the pressure oscillations.**

A nonlinear estimator is developed which is able to separate the breathing signal from the respiratory response in order to obtain the respiratory impedance. The estimated results are used to obtain accurate estimates of airway and tissue components of a constant phase model.

I. INTRODUCTION

Measurement and estimation of the respiratory impedance Z by means of the forced oscillation technique (FOT) has been a widely investigated topic for several years [1]–[3]. The most commonly used application of FOT is the measurement of the input impedance of the respiratory system. This is defined as the complex ratio of transrespiratory pressure P to the airflow at the airway opening Q as a function of frequency

$$Z(\omega) = \frac{P(\omega)}{Q(\omega)} \tag{1}$$

with $\omega = 2\pi f$ the angular frequency. The respiratory impedance gives powerful insight into the mechanical phenomena of the lungs [4]. Compared to more widely used lung function tests, it has been shown that FOT can provide unparalleled information on the respiratory mechanics [1].
Most FOT applications determine the respiratory impedance outside the frequency range of spontaneous breathing [5], [6]. Mostly pistons or loudspeakers based measurement systems are used to determine the respiratory impedance at frequencies between 4 and 50 Hz [7], [8]. However, it has been shown that lower frequency ranges (below 10 Hz) are most sensitive to normal physical processes and pathologic structural alterations [1].

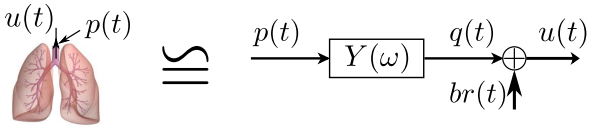

Fig. 1. Schematic representation of the measurement of the respiratory system. The respiratory system is approximated by a linear time invariant admittance Y. A pressure signal $p(t)$ is used to excite the respiratory admittance. The total measured air flow $u(t)$ contains both the response of the respiratory system $q(t)$ and the breathing signal $br(t)$.

The proposed method was designed to be used together with the fan-based FOT device described in [9]. This device superimposes small amplitude pressure oscillations (in the order of 0.1 kPa) on the tidal breathing and measures the resulting air flow. The imposed pressure is a broadband signal exciting a range of frequencies between 0.1 and 5 Hz. The main benefit of using small pressure oscillations as excitation signal is the clinical applicability of the measurement procedure. The patient can continue tidal breathing and will not be impeded by the measurement which eliminates the need for patient training before a measurement can be performed.

The resulting air flow will not only contain the response of the respiratory impedance but will also be strongly disturbed by the breathing of the patient. The breathing signal has large amplitude contributions at low frequencies (0.1-1 Hz). This frequency overlap with the frequency range of interest jeopardizes the analysis of the respiratory impedance. Therefore, a novel technique was developed to eliminate the breathing signal without losing the information about the respiratory response.

The paper is organized as follows: In section II, the approach and the models used to estimate FOT measurements are presented. In section III, the estimation algorithm and optimization techniques are discussed. In section IV, a simulation developed to mimic real measurements using measured breathing patterns and using a constant phase impedance model is presented. Finally, in section V, the results of the optimization techniques on these simulations are discussed. Conclusions are drawn in section VI.

II. MODELING OF BREATHING AND LUNG RESPONSE

Fig. 1 shows a schematic representation of the measurement of the respiratory system. A pressure oscillation $p(t)$ is used as the excitation signal and the resulting air flow $q(t)$ is considered as the response to this excitation. Therefore the respiratory admittance $Y = Z^{-1}$ is considered instead of the respiratory impedance. The respiratory system is considered

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as a linear time invariant (LTI) system and its response $q(t)$ is therefore assumed to be independent from the breathing pattern. This assumption is made to ease the interpretation of the measured signals.

Using this approximation, the resulting air flow $u(t)$ can be considered as the sum of the respiratory response $q(t)$, and the breathing signal $br(t)$.

$$u(t) = q(t) + br(t) \tag{2}$$

Since $q(t)$ and $br(t)$ contain energy in the same frequency range, common filtering techniques can not be used to separate both signals. Therefore, a nonlinear model for the breathing signal is proposed additionaly to a linear model of the respiratory response.

A. Model for breathing

The breathing signal is modeled as a sum of H harmonically related sine waves with a nonlinearly varying phase [10]. This leads to the model

$$br(t,\theta_{br}) = \sum_{h=0}^{H} A_h(t)\cos(h\phi(t)) + A_{H+h}(t)\sin(h\phi(t)) \tag{3}$$

A varying phase

$$\phi(t) = 2\pi f_{br}\left(t + \sum_{l=1}^{L} B_l \cos(\frac{2\pi lt}{T}) + B_{L+l}\sin(\frac{2\pi lt}{T})\right) \tag{4}$$

is introduced because the frequency of the breathing f_{br} is not perfectly constant. The phase $\phi(t)$ is written as the sum of a fixed frequency contribution $2\pi f_{br}t$ and a sum of L harmonically related sinewaves with fundamental frequency $1/T$, with T the duration of the measurement. Furthermore, the amplitudes of the sine waves are modeled as polynomials of order M to cope with changing breathing amplitudes during the measurement:

$$A_h(t) = A_{h0} + A_{h1}t + A_{h2}t^2 \ldots + A_{hM}t^M \qquad h = 1 \ldots 2H \tag{5}$$

All model parameters are collected in the vector

$$\theta_{br} = [A_{00}, \ldots A_{0P}, \ldots A_{2H0}, \ldots A_{2HP}, B_1, \ldots B_{2L}, f_{br}] \tag{6}$$

B. Model for response of Y

The pressure excitation signal $p(t)$ is a random phase multisine described by

$$p(t) = \frac{1}{\sqrt{N_{exc}}} \sum_{k=1}^{N_{exc}} P_k \sin(2\pi k f_0 t + \varphi_k) \tag{7}$$

with f_0 the frequency resolution of the signal, $N_{exc} \in \mathbb{N}$ the number of frequency components, and P_k the amplitude spectrum of the k-th frequency line. The phases φ_k are drawn from an independent uniformly distributed random process on $[0, 2\pi)$ [11].

The steady state response of the respiratory admittance excited by (7) is a sum of harmonically related sines and cosines on the excited frequencies:

$$q(t,\theta_q) = \sum_{k=1}^{N_{exc}} \alpha_k \sin(k\omega_0 t) + \beta_k \cos(k\omega_0 t) \tag{8}$$

with $\omega_0 = 2\pi f_0$ the angular frequency and where

$$\theta_q = [\alpha_1, \beta_1, \ldots \alpha_{N_{exc}}, \beta_{N_{exc}}] \tag{9}$$

represents the harmonic signal parameters of the response of the respiratory admittance. This leads to a model which is linear in the parameters (8) since the excitation frequencies kf_0 are known.

III. Estimation algorithm

The model of the measured air flow u can be represented as

$$u(t,\theta_u) = q(t,\theta_q) + br(t,\theta_{br}) \tag{10}$$

where θ_u represents the parameters of both the breathing signal and the respiratory response

$$\theta_u = [\theta_{br} \quad \theta_q] \tag{11}$$

The model (10) is used to minimize the least squares cost function

$$V(\theta_u) = \frac{1}{N}\sum_{n=1}^{N} \left(u(t_n) - u(t_n,\theta_u)\right)^2 \tag{12}$$

over θ_u with N the number of measured time samples of the measured air flow signal $u(t)$.

Since the model represented in (10) is nonlinear in θ_{br}, good starting values are mandatory for the nonlinear optimization. The fundamental breathing f_{br} is initially estimated by use of the Interpolated Fast Fourier Transform (IFFT) as described by Grandke [12]. Initial estimates for the remaining nonlinear parameters in θ_{br}, are obtained by the algorithm described in [10].

The parameter set θ_u is then estimated using a Levenberg-Marquardt algorithm (LMA) to determine the minimizer of the nonlinear least squares problem [13]. The convergence of this algorithm is strongly dependent on the condition number of the jacobian matrix J with

$$J_{[n,i]} = \frac{\partial y(t_n,\theta_u)}{\partial \theta_{u,i}} \tag{13}$$

for the n^{th} time sample and the i^{th} parameter of θ_u. To improve the condition number of J, the time axis is rescaled by use of Legendre polynomials. Another influence on the condition number is the order for the model of $br(t)$, determined by the parameters H, L and M in (3). High values for L and M strongly deteriorate the condition number which leads to bad estimates for $q(t)$.

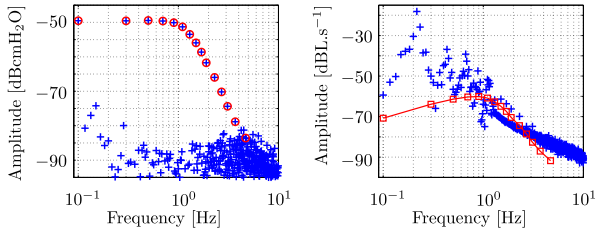

Fig. 2. The amplitude spectra show that the response of the respiratory impedance $Q(\omega)$ has a much lower amplitude than the total output $U(\omega)$. (left): $P(\omega)$ (+) with the excited frequency lines (○) and (right): $Q(\omega)$ (□) and $U(\omega)$ (+).

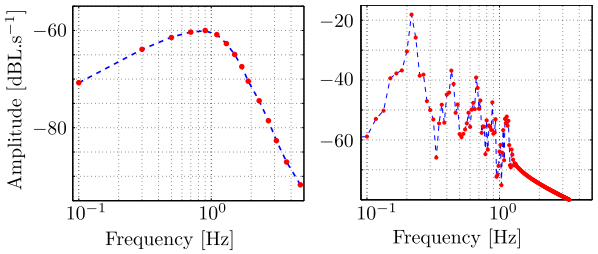

Fig. 3. By use of the LMA, an accurate estimate of $Q(\omega)$ on the excited frequency lines is obtained. The estimation results (•) correspond to the simulation data (– –) for $Q(\omega)$ (left) and $BR(\omega)$ (right).

IV. Verification on Simulations

A simulation approximating the real FOT measurements and using real breathing patterns is considered. Fig. 2 shows the amplitude spectra of $P(\omega)$, $Q(\omega)$ and $U(\omega)$, the frequency domain representations of respectively $p(t)$, $q(t)$ and $u(t)$, obtained by the discrete fourier transform [11].

The simulation is build up as follows: an excitation signal, as given in (7), is used as an input to a respiratory admittance model (Fig. 2 (left)). This excitation signal is realized by filtering a flat random phase multisine by a 3^{rd} order butterworth filter with a cutoff frequency at 1.2 Hz. This leads to a high magnitude in the frequency band of spontaneous breathing [9]. Since the filtered multisine is used as input to the respiratory admittance, the phase contribution of the butterworth filter will not influence the estimation results.

The respiratory admittance $Y = Z^{-1}$ is modeled by a frequency-domain variant of Hildebrandt's stress-relaxation model (14)

$$Z(\omega) = R_{aw} + j\omega I_{aw} + \frac{G - jH}{\omega^{\alpha}} \tag{14}$$

with

$$\alpha = \frac{2}{\pi} tan^{-1}(\frac{H}{G}) \tag{15}$$

The model consists of a homogeneous airway compartment containing an airway resistance (R_{aw}) and inertance (I_{aw}) elements leading to a viscoelastic, constant-phase tissue compartment [1]–[4], [14], [15]. This tissue compartment is modeled by tissue damping (G) and tissue elastance (H). The model is compatible with the structural-damping hypothesis which assumes that the ratio of dissipative and elastic processes is constant with angular frequency ω. Studies by Hantos and co-workers [3] showed that this model describes low-frequent respiratory impedance data better than other viscoelastic models. The values used for R_{aw}, I_{aw}, G and H are taken from [2].

The response $q(t)$ is then obtained as the inverse discrete fourier transform [11] of

$$Q(\omega) = Y(\omega)P(\omega) \tag{16}$$

The output of the respiratory admittance is strongly disturbed by a breathing signal $br(t)$. This breathing signal is obtained by measurements performed with the device described in [9]. By measuring the air flow without imposing an excitation signal $p(t)$, no contribution of the respiratory admittance is present and hence the resulting air flow equals $br(t)$. This leads to 60 seconds measurements of $br(t)$ gathered at a sample frequency of 183 Hz [9].

To illustrate the proposed method, 2 cases are considered:

1) To demonstrate the method in the absence of model errors, the measured breathing is approximated by a model as described in (3). In this example, $H = 5$ breathing harmonics, $L = 4$ phase harmonics and an amplitude order of $M = 2$ is used. To illustrate the conditions under which the LMA can operate, the measured input signal $P(\omega)$ is attenuated with 26 dB.
2) The method is verified on the measured breathing without approximation. An optimal model order needs to be selected during the estimation. The measured input signal is used without attenuation.

Emphasis is placed on the first case, for which the amplitude spectra of the input $P(\omega)$, the total output $U(\omega)$ and the respiratory response $Q(\omega)$ are shown in Fig. 2. Due to the large amplitude contributions of the breathing, the respiratory response $Q(\omega)$ is deeply hidden in the total output. In order to obtain an estimate of the respiratory impedance, the respiratory response $Q(\omega)$ needs to be extracted from the total output spectrum.

V. Results

The estimated $BR(\omega)$ and $Q(\omega)$ are shown in Fig. 3. Even though an analysis of $Q(\omega)$ was initally jeopardized due to the breathing influence (Fig. 2), an accurate nonparametric estimate has now been obtained (Fig. 3).

By use of the ratio between the estimated air flow $Q(\omega)$ and the measured pressure excitation $P(\omega)$ at the excited frequency lines, a nonparametric estimate for $Y(\omega)$ and thus $Z(\omega)$ can be acquired. To express the frequency dependence of Z, resistive R and reactive components X are most commonly used [1]:

$$Z(\omega) = R(\omega) + jX(\omega) \tag{17}$$

This allows for separation of energy dissipation and energy storage respectively. The accuracy of the estimate of the frequency dependent behavior of both R and X over the whole frequency range of interest can be seen in Fig. 4.

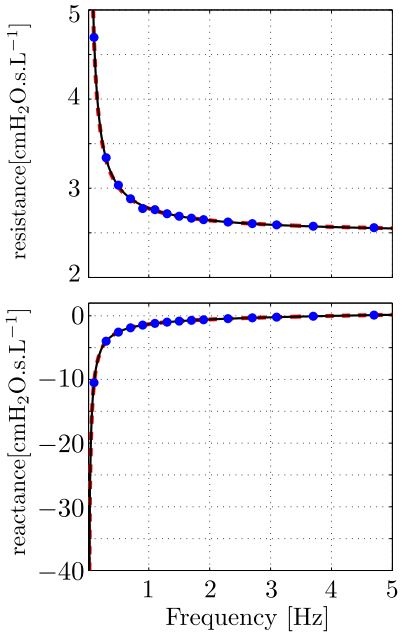

Fig. 4. Resistance and reactance of simulated (– –), nonparametrically estimated (•) and parametrically estimated (—) respiratory impedance model.

	R_{aw} $cmH_2O.s/L$	I_{aw} $cmH_2O.s^2/L$	G cmH_2O/L	H cmH_2O/L
true	2.480	0.016	1.450	7.050
estimate approx breathing	2.475	0.016	1.483	7.024
estimate real breathing	2.680	0.036	1.058	9.015

TABLE I

TRUE AND ESTIMATED DATA OF RESPIRATORY IMPEDANCE MODEL FOR R_{aw}, I_{aw}, G AND H. RESULTS FOR BOTH APPROXIMATED BREATHING (NO MODEL ERRORS) AND REAL BREATHING ARE GIVEN.

Starting from this nonparametric estimate of $Z(\omega)$, a parametric estimate can be obtained using the model presented in (14). Using the MATLAB function *fminunc*, a unconstrained nonlinear optimization is performed in order to obtain estimates for R_{aw}, I_{aw}, G and H. The mean of the values measured from 9 patients in [1] are used as starting values.The results are depicted in Table I. The method is first applied on the simulation using an approximation of the measured breathing signal. In this case, no model errors are present which leads to accurate estimates of R_{aw}, I_{aw}, G and H. To conclude, parametric estimates are obtained for a simulation using a real breathing signal. This will introduce modeling errors since the order of the real breathing is unknown. For the same breathing signal as previously used, an optimal order is found with $H = 5$ breathing harmonics, $L = 10$ phase harmonics and an amplitude order of $M = 5$. Due to the presence of model errors, the accuracy of the parameter estimates decreases. However, sensible results are obtained for R_{aw}, I_{aw}, G and H which illustrates the use of the method for real breathing signals.

VI. CONCLUSIONS

A new method is presented to measure the respiratory impedance in the frequency range of spontaneous breathing in a clinically practical way. The performance of the method is illustrated with simulations using measured breathing patterns and pressure oscillations performed with a previously developed device. It is shown that at low frequencies, the respiratory response is jeopardized by the breathing contribution. A nonlinear least square estimator based on a breathing model with varying amplitude and phase has been developed. Nonparametric estimates of the respiratory impedance are obtained after separation of respiratory response and breathing. These nonparametric estimates lead to accurate values of airway and tissue compartment elements. The experimental verification on measurements performed on a number of patients is currently ongoing. In future work, it will be verified if it's worthwhile to take nonlinear behavior or time-variation of the respiratory impedance into account.

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