Vrije Universiteit Brussel

Adaptive excitation signals for low frequency FOT

Cedric Busschots*, Andy Keymolen*, Hannes Maes, Dries Peumans, Johan Pattyn, Gerd Vandersteen, John Lataire

ELEC

Vrije Universiteit Brussel

Brussels, Belgium

cedric.busschots@vub.ac.be, andy.keymolen@vub.ac.be

Abstract—The low frequency Forced Oscillation Technique (FOT) has a high diagnostic potential for the detection of respiratory diseases. However, it is not yet widely accepted in clinical practice. The presence of the patient's breathing generally results in patient-unfriendly measurement protocols. These are needed to extract the important low frequency information about the patients' respiratory system.

This work presents a novel technique to apply the low frequency FOT during spontaneous breathing. This is accomplished by adding an external visual stimulus to encourage the patient to approximately synchronize his/her breathing in combination with an excitation signal that is adapted to the patient's natural breathing frequency. The breathing and FOT contributions can therefore be separated. This paper contains a proof of concept of this method and proposes measurements on healthy subjects.

Index Terms—Medical measurement, system identification, forced oscillation technique.

I. Introduction

In 2007, the World Health Organization (WHO) predicted that Chronic Obstructive Pulmonary Disease (COPD) will become the world's fourth cause of mortality by 2030. Asthma nowadays affects the lives of 300 million people worldwide. As an early diagnose is a key to patient relief, the framework for action of the WHO calls for an improved diagnosis of these types of diseases [1].

In the current state of the art, spirometric measurements are the leading diagnostic tool for these diseases. This is mainly due to the availability of a massive amount of representative measurements of both healthy and unhealthy patients to aid the diagnostic.

A lesser known, but very promising technique is the Forced Oscillation Technique (FOT). This non-invasive measurement technique for the pulmonary function has the advantage that it allows to measure the lung impedance of a broader range of patients, even if they suffer from severe breathing issues, while still providing insight into the mechanical status of the patient's respiratory system [2].

In contrast to spirometry measurements, the FOT does not measure the lung capacity and speed of exhalation. It rather measures the air pressure $p(t)$ and airflow $q(t)$ at the airway opening. These quantities are measured as a function
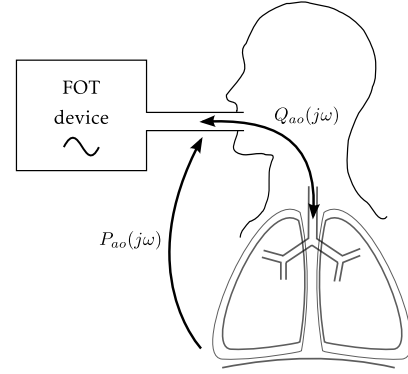
Fig. 1. A FOT device applies pressure oscillations $P_{ao}(j\omega)$ and measures the resulting flow $Q_{ao}(j\omega)$ at the airway opening to measure the respiratory impedance $Z(j\omega)$.

of time. Next, they are converted to the frequency domain using the (Discrete) Fourier Transform. The air pressure $p(t)$ is interpreted as an excitation signal for the respiratory system. The ratio of the resulting complex valued flow spectrum and the spectrum of the excitation pressure yields the input impedance of the total respiratory system $Z(j\omega)$. It is defined as

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

with P the pressure drop over the total respiratory system and Q the flow measured at the airway opening. $Z(j\omega)$ is evaluated at all the frequencies where an excitation signal is applied. For visualisation purposes, this complex valued impedance is plotted as its real and imaginary parts as functions of the frequency. The real and imaginary parts represent, respectively, the resistive and reactive components of the impedance [3]. This frequency dependent impedance can be used to distinguish the behavior of upper airways, smaller airways and lung tissue. Figure 1 shows a schematic representation of the measurement setup.

While this technique has been applied in a wide range of frequencies [2], low frequency FOT has been shown to have the highest diagnostic potential [3]. This is due to the possibility to separate airway and tissue contributions. It empowers the early diagnosis of asthma and COPD [3], [4].
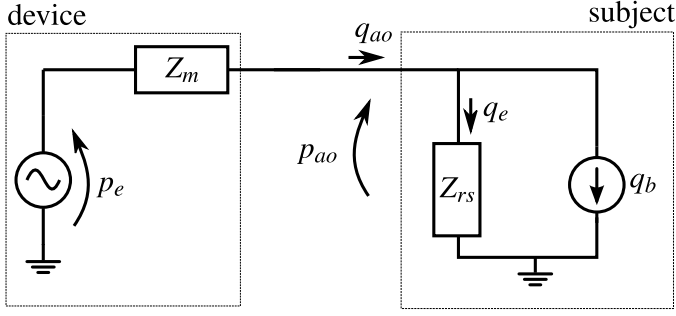
Fig. 2. Electrical equivalent of measuring Z_{rs} by using a pressure controlled FOT apparatus. The device is considered as a pressure source $p_e(t)$ with a non-zero output impedance Z_m. The subject is represented as its impedance Z_{rs} in parallel with a breathing flow $q_b(t)$. The measured air flow at the airway opening $q_{ao}(t)$ is the sum of the response of the respiratory system, $q_e(t)$, and of $q_b(t)$ [6].
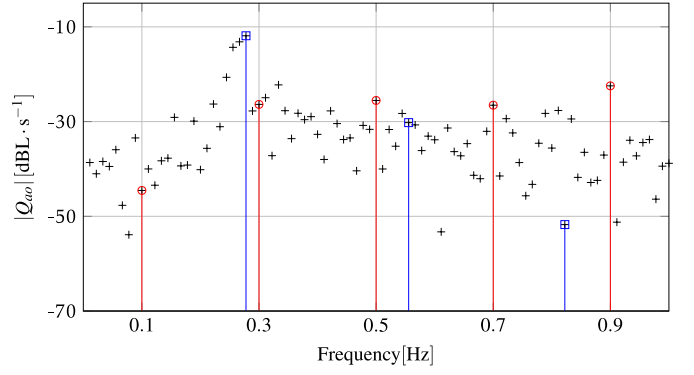

Fig. 3. When patient breathing is present during the measurement of $Q_{oa}(j\omega)$ (black pluses), the excitation signal (red circles) disappears in the noise and/or breathing harmonics. The blue lines are an indication of the breathing contributions.

However, the main difficulty is the presence of the patient's spontaneous breathing which typically inserts an important contribution to the measurement spectra between 0.1 and 1 Hz but is not useful to measure $Z(j\omega)$. The presence of the breathing and additional associated harmonics strongly disturb the measurements of pressure and flow. Therefore, state of the art solutions to successfully perform low frequency FOT requires either the absence or the control of the patient's breathing. This leads to highly impractical measurement conditions, requiring a high effort from the patient [3], [5], [6]. Post processing methods to separate the breathing from the excitation signal have been investigated as well. They do not offer a solution when there is a substantial spectral overlap between the excitation signal and the patient's breathing [6], [7].

In this paper, a novel technique is proposed that combines a visual stimulus to synchronize the patient's breathing with an excitation signal adapted to the patient's breathing frequency. In this way, we prevent the measurement from being jeopardized by the patient's breathing. In Section II, the measurement problem is defined and demonstrated. Section III discusses our proposed method and its implementation. The measurements obtained with this new measurement technique are discussed in Section IV. Finally, conclusions are drawn and future work is discussed in Section V.

II. Problem statement

In several reference works [6], [8], [9], an electric equivalent model is used to gain a better understanding of the interaction between the FOT measurement apparatus and the patient. Figure 2 shows the electric equivalent we use. Here, the FOT device is represented by a non-ideal voltage source. The patient is described by a non-ideal current source. Their non-idealities are expressed by their respective impedances, Z_m and Z_{rs}. The pressure $p_e(t)$ represents the pressure generated by the FOT measurement apparatus and $p_{ao}(t)$ the pressure at the airway opening. The total flow is described by $q_{ao}(t)$ and can be split in two parts: $q_e(t)$, the flow caused by the

apparatus, and $q_b(t)$, the flow resulting from the breathing of the patient. This can be expressed as

$$q_{ao}(t) = q_e(t) + q_b(t) \qquad (2)$$

For the calculation of Z_{rs}, only the contribution of $q_e(t)$ is of interest as the uncontrolled and unknown breathing flow will disturb the excitation signal. A multisine excitation signal will be used for p_{ao} to measure Z_{rs}. Using this type of signal prevents leakage [10] (in absence of q_b). In the frequency domain, the expression for the impedance becomes

$$Z_{rs}(j\omega) = \frac{P_{ao}(j\omega)}{Q_e(j\omega)}. \qquad (3)$$

As can be understood from Figure 2, the FOT apparatus measures the total flow $q_{ao}(t)$ and the pressure $p_{ao}(t)$ at the airway opening. Figure 3 displays $Q_{ao}(j\omega)$ when the patient's breathing is present during the measurement. The figure shows that it is difficult or even impossible to separate the excitation signal from the breathing. More specifically, the measurement suffers from the following problems:

- **leakage**: the breathing period and the measurement time window are not related,
- **frequency variation**: the breathing frequency typically varies during the measurement, which introduces a widening of the spectral lines,
- **spectral overlap**: the spectral content of the breathing flow signal overlaps with the frequencies present in the excitation signal.

Some options are currently available to remove the breathing contribution from Q_{ao}. Making the patients hold their breath is a first solution. However, for patients with severe breathing issues this poses problems. Using excitation signals without spectral content in the frequency range that corresponds to the breathing spectrum miss out on the diagnostically interesting breathing frequency band [3].

The main contribution of this paper is an improved measurement technique that remains patient friendly, but improves the measurement quality drastically. This technique has been
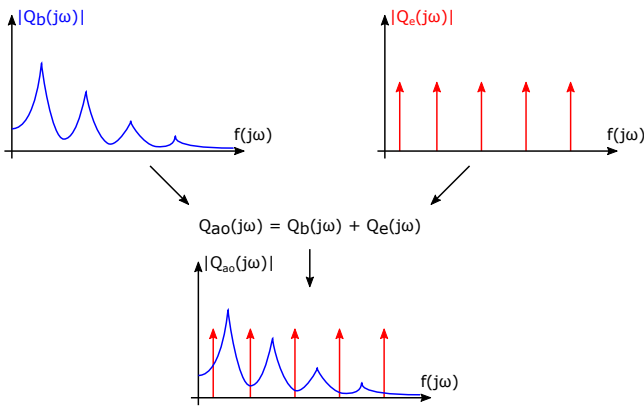
Fig. 4. Selecting excitation signal frequency lines where the spontaneous breathing signal is low in magnitude improves the measurement's Signal-to-Noise Ratio. In addition, the patient is encouraged to maintain a constant breathing frequency by using an external visual stimulus. This reduces leakage and frequency variation, sharpening the spectral contributions of $Q_b(j\omega)$.
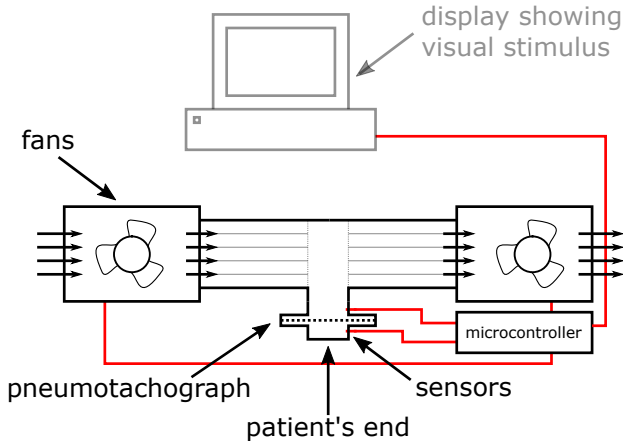

Fig. 5. Schematic representation of the improved test setup. The mechanical improvements over the device described in [12] are highlighted in light gray, the electrical parts are highlighted in red.

proposed in the PhD thesis [11] (a co-author of the present article). The technique we propose starts with measuring the breathing frequency before the measurement starts. The spectral content of this breathing signal is analyzed. The spectral information is then used to adapt the multisine excitation signal so that the excited frequency lines do not interfere with the spectral content of the breathing. In addition, a visual stimulus is displayed so that the patient's breathing frequency remains constant throughout the measurement. Figure 4 clarifies this idea. The implementation details will be discussed in the next section.

III. METHOD

In [12], a setup with two fans is described. The fans operate in a push-pull configuration to allow a continuous flow of fresh air to the patient. For our measurements, a similar system is used. A schematic representation of this setup is shown in Figure 5.

This pressure controlling device measures Z_{rs} in a clinically practical manner and can be used to apply a pressure excitation signal at the airway opening while the subject continues to breathe spontaneously. This pressure signal should have an amplitude that is large enough to enable the detection and small enough not to disturb the patient. Here, peak values of $\pm 200\,\mathrm{Pa}$ are used. The frequency band of the excitation signal is $0.1 - 2\,\mathrm{Hz}$, such as to cover the diagnostic frequency range.

To measure impedances with a low uncertainty, the pressure excitation signal by itself should have a sufficiently high signal-to-noise ratio (SNR). More than $30\,\mathrm{dB}$ SNR is desired over the full excitation band [13]. This should be attained in the presence of the subjects' breathing disturbances.

To deal with the breathing disturbance on the flow signal, the following approach is suggested.

The aim is to proactively prevent that the breathing disturbances influence the measurement of Q_e by avoiding that Q_b and Q_e occur at the same frequencies. Consequently, the different causes of spectral overlap, that are mentioned in Section II, have to be taken into account.

It often occurs that combinations of perturbations happen when the patient is breathing spontaneously if the measurement frequencies are chosen without prior knowledge of the patient's breathing contribution. As a result, an adaptation of the measurement protocol is necessary. The simplest solution would be to keep the original excitation signal and force the patient to breathe at a fixed frequency. However, since it is our goal to apply these measurements to patients with a variety of respiratory complaints, it cannot be expected that each patient can undergo a measurement at a breathing frequency that differs from his/her natural breathing frequency. Therefore, we will significantly adapt the excited frequencies, noted as f_e, to the natural breathing frequency, noted as f_b, of the patient instead.

The proposed protocol relies on two elements. On the one hand, we have the FOT device whose excitation signal will be adapted to the patient's breathing. On the other hand, the patient will need to maintain a fixed breathing frequency during the measurement. The novel measurement protocol is listed below and is displayed in a schematic representation in Figure 6.

Step 1 To initialize the adaptation of the excitation signal, the patient's breathing frequency f_b is measured and estimated.

Step 2 The initial excitation signal is modified by shifting the base frequency f_e such that it is harmonically related to f_b. This results in a significant decrease of the spectral leakage as discussed in Section II, since an integer number of breathing cycles will be measured. Furthermore, spectral engineering of the excitation signal prevents the coincidence of the excited frequencies and the breathing frequencies and its harmonics. This results in a further enhancement of the measurement quality.

Step 3 To keep the breathing frequency relatively constant, an external (visual) stimulus is added to reduce the amplitude
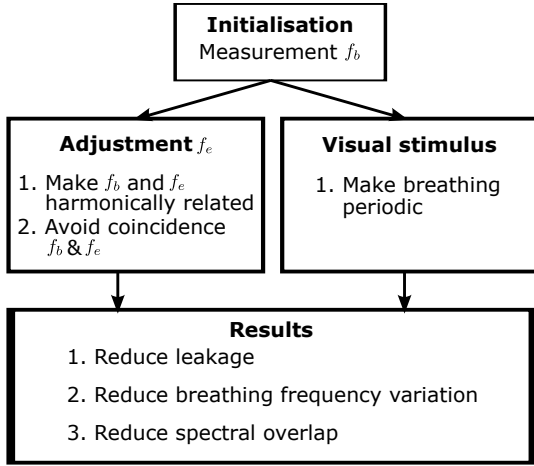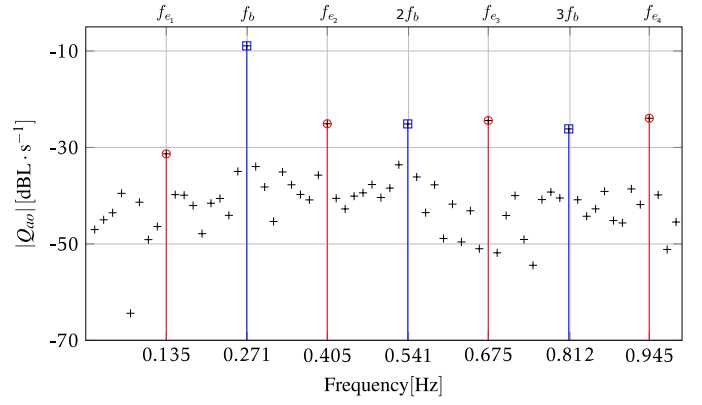
Fig. 6. Protocol of the adaptive measurement.

Fig. 7. Amplitude spectrum of Q_{ao} with use of the adaptive method (black plus). Red circles indicates the excited frequencies and the blue squares indicates the breathing harmonics. When comparing the excited frequency lines, an amplitude difference is noticable. This is due to the acoustical properties of the lungs.
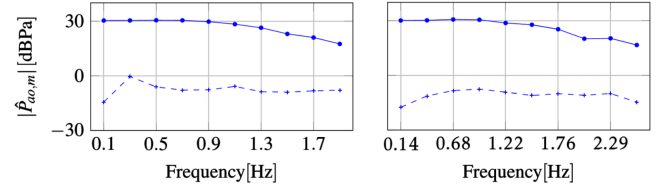

Fig. 8. Amplitude spectrum of $P_{ao,m}$ (full line) and $\hat{\sigma}_{\hat{P}_{ao,m}}$ (dashed line) with (right) and without (left) the use of the adaptive method. The adaptive method shifts the excitation frequencies but does not increase $\hat{\sigma}_{\hat{P}_{ao,m}}$ such that the SNR of 30dB at the input signal is maintained.

and frequency variation of the patient's breathing. During the measurement, the patient is supposed to synchronize his/her breathing with the external stimulus which is oscillating at f_b. The effort demanded from the patient during the measurement is minimized by using the patient's own natural breathing frequency for the external stimulus [14]. As can be seen on Figure 8, this proposed method obtains an SNR of more than 30 dB on the input signal.

The selected frequency lines are arbitrarily chosen relative to the adapted sampling frequency. They have been placed in between the different breathing harmonics such that the interference between the measurement and the breathing is as low as possible. Exciting other (or more) frequency lines is possible, but a trade off between measurement time, frequency resolution, excitation signal energy and breathing interference had to be made.

IV. EXPERIMENTAL RESULTS AND DISCUSSION

Measurements on healthy subjects are performed with and without the use of the adaptive excitation signals. One patient measurement is used as an example. First, the patient breathes spontaneously, without the guidance of an external (visual) stimulus. An excitation signal with a base frequency of 0.1 Hz is applied. No synchronization of the breathing is used. In this way the state of the art patient friendly measurement of Q_{ao} is performed with a FOT device. This measurement is displayed in Figure 3.

Secondly, the adaptive measurement protocol is applied. Starting with the determination of the breathing frequency.
Step 1 the patient breathes spontaneously when the FOT device measures Q_b. A frequency of $f_b = 0.271$ Hz is estimated.
Step 2 the excitation signal is adjusted based on the prior knowledge of f_b. This yields a frequency adjustment of f_e towards 0.135 Hz as a fundamental frequency.

Step 3 the pressure excitation signal is applied to the patient's mouth while f_b is kept as constant as possible by displaying a visual stimulus.

The result is shown in Figure 7. The impact of the adaptive measurement protocol can be seen by comparing Figures 3 and 7. Without the protocol, spectral leakage, frequency variation and spectral overlap are present. The creation of an harmonic relation between f_b and f_e and the visual stimulus reduce this significantly, as promised in Section III.

V. CONCLUSION AND FUTURE WORK

The low frequency Forced Oscillation Technique has been shown to have diagnostic potential, but up until now, no patient friendly implementation existed. Adapting the excitation frequencies to the patient's breathing and synchronizing the patient's breathing to the measurement using an external visual stimulus improves the measurement quality significantly. Since the patient's breathing is the starting point for the adaptive excitation signal, the patient's comfort increases drastically. Measurements on multiple healthy subjects show that the method works as expected and has diagnostic potential.

However, measurements on healthy subjects as presented in this paper are not sufficient to guarantee usability in practical disease detection. A clinical trial with a larger and more diverse group of subjects is ongoing. It is intended to validate

the results obtained on a small scale with healthy patients on a larger group of patients that are affected by COPD or asthma.

REFERENCES

[1] A. Haden and P. Desloovere, Eds., *Global surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach*. World Health Organization, 2007.

[2] J. H. Bates, C. G. Irvin, R. Farré, and Z. Hantos, *Oscillation Mechanics of the Respiratory System*. American Cancer Society, 2011, pp. 1233–1272. [Online]. Available: https://onlinelibrary.wiley.com/doi/abs/10.1002/cphy.c100058

[3] D. W. Kaczka and R. L. Dellacá, "Oscillation mechanics of the respiratory system: application to lung disease," *Critical Reviews in Biomedical Engineering*, vol. 39, no. 4, pp. 337–359, 2011.

[4] D. W. Kaczka, E. P. Ingenito, B. Suki, and K. R. Lutchen, "Partitioning airway and lung tissue resistances in humans: effects of bronchoconstriction," *Journal of Applied Physiology*, vol. 82, no. 5, pp. 1531–1541, 1997.

[5] Z. Hantos, B. Daroczy, B. Suki, G. Galgoczy, and T. Csendes, "Forced oscillatory impedance of the respiratory system at low frequencies," *Journal of Applied Physiology*, vol. 60, no. 1, pp. 123–132, jan 1986.

[6] H. Maes, M. Zivanovic, J. Schoukens, and G. Vandersteen, "Estimating respiratory impedance at breathing frequencies using regularized least squares on forced oscillation technique measurements," *IEEE Transactions on Instrumentation and Measurement*, vol. 66, no. 3, pp. 479–491, mar 2017.

[7] H. Maes, G. Vandersteen, and C. Ionescu, "Estimation of respiratory impedance at low frequencies during spontaneous breathing using the forced oscillation technique," in *2014 36th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, Aug 2014, pp. 3410–3413.

[8] H. Franken, J. Clement, and K. Van de Woestijne, "Systematic and random errors in the determination of respiratory impedance by means of the forced oscillation technique: A theoretical study," *Biomedical Engineering, IEEE Transactions on*, vol. BME-30, no. 10, pp. 642–651, Oct 1983.

[9] R. Farre, M. Rotger, and D. Navajas, "Time-domain digital filter to improve signal-to-noise ratio in respiratory impedance measurements," *Medical and Biological Engineering and Computing*, vol. 29, no. 1, pp. 18–24, 1991. [Online]. Available: http://dx.doi.org/10.1007/BF02446291

[10] R. Pintelon and J. Schoukens, *System identification: a frequency domain approach*. John Wiley & Sons, Inc., 2012.

[11] H. Maes, "Low frequency forced oscillation technique in clinical practice," Ph.D. dissertation, Vrije Universiteit Brussel, October 2017.

[12] H. Maes, G. Vandersteen, M. Muehlebach, and C. Ionescu, "A fan-based, low-frequent, forced oscillation technique apparatus," *IEEE Transactions on Instrumentation and Measurement*, vol. 63, no. 3, pp. 603–611, March 2014.

[13] R. Pintelon, Y. Rolain, and W. V. Moer, "Probability density function for frequency response function measurements using periodic signals," *IEEE Transactions on Instrumentation and Measurement*, vol. 52, no. 1, pp. 61–68, Feb 2003.

[14] A. Pikovsky, M. Rosenblum, and J. Kurths, *Synchronization*. Cambridge University Press, 2001, cambridge Books Online. [Online]. Available: http://dx.doi.org/10.1017/CBO9780511755743