

# A non-invasive method for estimating lung function

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## Abstract

Conventional methods for monitoring lung function usually require complex gas analysers and the co-operation of the patient. Therefore, they are not compatible with the crowded environment of the Intensive Care Unit (ICU) or operating theatre, where the patient co-operation is usually impossible. However, it is precisely these patients that would benefit the most from accurate monitoring of lung function.

This paper develops a compact and non-invasive system for the measurement and monitoring of lung function in a clinical setting, such as lung volume, airway dead space volume, and pulmonary blood flow. In contrast with conventional methods, the compact apparatus and non-invasive nature of the proposed method allow it to be used in the ICU, as well as in general clinical settings.

The system implements a breath-by-breath computer ventilation model using a non-invasive technique, in which a tracer gas is injected into the patient's inspired breath. Experimental results are shown for both an artificial lung and a healthy volunteer. Our findings show that the proposed technique has several advantages over the conventional method for the estimation of lung function.

## 1 Motivation

Patients are often admitted into the Intensive Care Unit (ICU) due to the need for mechanical ventilatory support using a ventilator [1]. Lung function tests could benefit ICU patients significantly, because they could help to determine the most suitable ventilator settings, and help to avoid the common problem of Ventilator Induced Injury (VILI).

Three lung function measurements of particular use in avoiding adverse events are

1.  $V_D$ , airway dead space volume; i.e, the volume of the conducting airways. The airway is the path that the air follows to enter and exist the lung.

2.  $V_A$ , lung volume at the end of an expiration.
3.  $\dot{Q}_P$ , pulmonary blood flow through the lung.

Measurement of  $V_A$  typically requires the co-operation of the patient. However, ICU patients depend on complex life support and monitoring equipment, and so are unable to co-operate with clinicians. Hence, ICU patients are the most difficult to assess using conventional lung function tests, but their critical condition makes them the most important patients to monitor.

Zwart et al. pioneered the non-invasive oscillating gas-forcing technique [2, 3], in which a sinusoidally oscillating tracer gas is added to the patient's inspired gas. They used halothane as the tracer gas at low concentrations. Hahn et al. initially improved this method by using biologically non-toxic gases such as nitrous oxide ( $N_2O$ ) and argon, instead of halothane, to measure  $V_D$ ,  $V_A$ , and  $\dot{Q}_P$  non-invasively [4, 5]. However, their technique requires a respiratory mass spectrometer that is difficult to use in the ICU due to its size, noise, complexity, high maintenance requirements, and lack of portability [6]. Moreover, their prototype gas mixer, which is used to supply the appropriate gases, is not compatible with modern ICU ventilators. A new method needs to be designed to deliver tracer gases according to the patient's breathing flow rates in real time.

In this paper, we propose an on-line non-invasive gas-forcing technique that assesses the above three parameters,  $V_D$ ,  $V_A$ , and  $\dot{Q}_P$ . The apparatus is compact in size and is portable, consisting of a flow sensor, a gas concentration sensor, and a mass flow controller (MFC). Tracer gas  $N_2O$  is injected into the patient's airflow during inspiration.

## 2 A Breath-by-Breath Ventilation Model

### 2.1 On-line Tracer Gas Delivery

Modern ICU ventilators deliver inspired air at variable and unpredictable flow rates. In order to deliver a pre-determined concentration of the tracer gas throughout a single inspiratory breath, the tracer gas must be injected in real time at a rate proportional to the inspired flow. In our proposed method, tracer gas  $N_2O$  is injected into the patient's inspiratory breathing flow and mixed immediately prior to entering the mouth. An MFC is used to deliver the tracer gas at flow  $\dot{V}_{tg}(t)$  that are proportional to the patient's airway flow  $\dot{V}(t)$ ,

$$\dot{V}_{tg}(t) = [M + A \sin(2\pi ft)] \dot{V}(t), \quad (1)$$

where  $M$  and  $A$  are the mean and amplitude of the forcing sinusoid, respectively, and  $f$  is the frequency of the forcing sinusoid ( $f = 1/T$  where  $T$  is the forcing sinusoidal period). The concentration of the tracer gas oscillates sinusoidally, shown in Figure 1.

A gas flow sensor was used to measure the inspired and expired gas flows and volumes. The tracer gas concentration was measured by a concentration sensor. Sensor calibration data can be found in [6, 7]. Both the flow sensor and the concentration

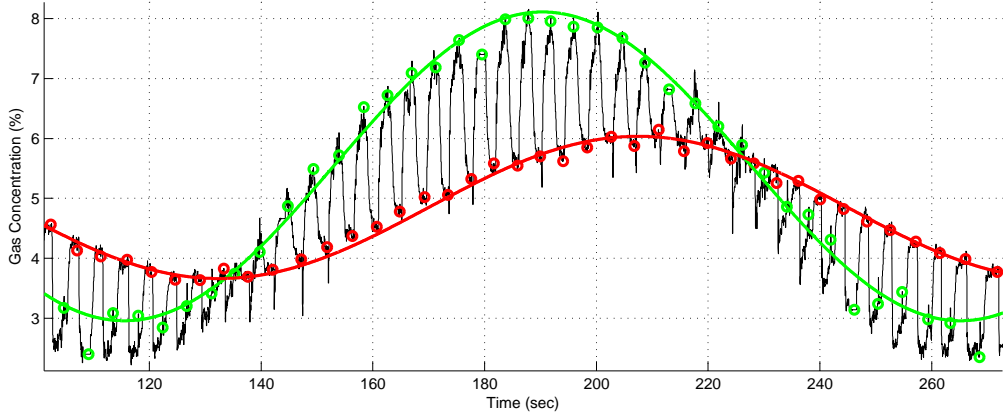


Figure 1: Concentration of the tracer gas in the airway flow of a healthy male volunteer. The forcing sinusoidal period  $T = 2.5$  mins. The green and red circles are placed at where the flow signal changes its direction, indicating the end of inspiration and expiration, respectively. The green and red sinusoids are fitted to the green and red circles, respectively. The sinusoids show that the concentration of the tracer gas varies sinusoidally, at the chosen value of  $T$ .

sensor are mounted in the breathing tube connected to the patient. Compared with the apparatus for previous continuous [4, 5] and tidal models [8], the proposed setup is portable, simple to use, and is suitable for the ICU because of its non-invasive approach.

## 2.2 Theory

In a traditional continuous ventilation lung model [2, 4, 5, 9], the lung is treated as a rigid volume with a constant and continuous flow passing through it. A tidal ventilation model for Zwart technique was first introduced by Gavaghan et al. [10], and later modified by Williams et al. [8, 11, 12]. Compared with the rigid volume of the continuous model, a tidal model reflects the reality of breathing, where the lung expands during inspiration, and contracts during expiration. Here, we propose a breath-by-breath tidal ventilation model as follows.

The tracer gas is inhaled into the lung, and some is absorbed by the pulmonary capillary blood in the lung. It eventually returns to the lung via the venous blood. This process is known as “venous recirculation”. Let  $F_{A,n}$  be the tracer gas concentration in the lung during breath  $n$ , and  $V_{T,n}$  be the tidal volume, the volume of air inhaled and exhaled during breath  $n$ . The volume of tracer gas in the lung is  $V_A F_{A,n-1}$  at the end of breath  $n - 1$ , and is  $V_A F_{A,n}$  at the end of breath  $n$ . Let  $\mathcal{V}_I$  be the volume of tracer gas delivered into the lung during breath  $n$ ,

$$\mathcal{V}_I = V_D F_{A,n-1} + (V_{T,n} - V_D) \bar{F}_{I,n}, \quad (2)$$

where  $\bar{F}_{I,n}$  is the average tracer gas concentration during inspiration of breath  $n$ .

Let  $\mathcal{V}_E$  be the expired volume of the tracer gas during breath  $n$ ,

$$\mathcal{V}_E = V_{T,n} F_{A,n}. \quad (3)$$

Let  $\mathcal{V}_Q$  be the uptake of the tracer gas (i.e., the amount of tracer gas absorbed by the pulmonary capillary blood in the lung) during breath  $n$ ,

$$\mathcal{V}_Q = \dot{Q}_P \lambda_b (F_{A,n} - F_{\bar{V},n}) T_n, \quad (4)$$

where  $\lambda_b$  is blood solubility coefficient of the gas, and  $T_n$  is the duration of breath  $n$ .  $F_{\bar{V},n}$  is the average tracer gas concentration returned to the lung through venous recirculation in breath  $n$ .

The conservation of mass equation implies that

$$V_A F_{A,n} - V_A F_{A,n-1} = \mathcal{V}_I - \mathcal{V}_E - \mathcal{V}_Q, \quad (5)$$

where this is the volume change of tracer gas in the lung at the end of breath  $n$ .

Substituting (2), (3), and (4) into (5), we have

$$\begin{aligned} V_A (F_{A,n-1} - F_{A,n}) + \dot{Q}_P \lambda_b (F_{\bar{V},n} - F_{A,n}) T_n = \\ V_{T,n} F_{A,n} - [V_D F_{A,n-1} + (V_{T,n} - V_D) F_{\bar{I},n}]. \end{aligned} \quad (6)$$

We assume that  $F_{A,n}$  is constant during breath  $n$ , and is equal to  $F_{E',n}$ , which is the tracer gas concentration at the end of expiration in breath  $n$ ,

$$F_{A,n} = F_{E',n}. \quad (7)$$

Substituting (7) into (6) gives

$$\begin{aligned} V_A (F_{E',n-1} - F_{E',n}) + \dot{Q}_P \lambda_b (F_{\bar{V},n} - F_{E',n}) T_n = \\ V_{T,n} F_{E',n} - [V_D F_{E',n-1} + (V_{T,n} - V_D) F_{\bar{I},n}]. \end{aligned} \quad (8)$$

It has been previously shown that there exists a forcing sinusoidal frequency range of the tracer gas where venous recirculation effects are negligible [4, 13]. At a carefully chosen forcing frequency where the recirculation effects can be ignored, the oscillatory component of  $F_{\bar{V},n}$  diminishes,

$$F_{\bar{V},n} = M_A, \quad (9)$$

where  $M_A$  is the mean of alveolar sinusoid  $F_{A,n}$ .

Substituting (9) into (8) gives

$$\begin{aligned} V_A (F_{E',n-1} - F_{E',n}) + \dot{Q}_P \lambda_b (M_A - F_{E',n}) T_n = \\ V_{T,n} F_{E',n} - [V_D F_{E',n-1} + (V_{T,n} - V_D) F_{\bar{I},n}]. \end{aligned} \quad (10)$$

This is the mass balance equations for the lung function that we aim to estimate, expressed in terms of breath-by-breath changes in gas volumes. Our goal is to determine the values of  $V_A$  and  $\dot{Q}_P$  in (10). The measured variables are  $F_{E',n-1}$ ,  $F_{E',n}$ ,  $F_{\bar{I},n}$ , and  $V_{T,n}$ .  $M_A$  and  $V_D$  can be calculated (see Section 3.2 below), and  $\lambda_b$  is a constant for the chosen tracer gas. Every two successive breaths produces an equation using (10); therefore a total number of  $N$  breaths produces  $N - 1$  equations of two unknown values  $V_A$  and  $\dot{Q}_P$ . For this set of  $N - 1$  linear equations, the least-squares technique is employed to determine  $V_A$  and  $\dot{Q}_P$ .

## 3 Calculations

### 3.1 Response Time Enhancement

“Response time” is typically defined to be the time required for a sensor output to rise from 10% to 90% of its maximum [14]. The signal from the concentration sensor has a much longer response time than that from the flow sensor; therefore, response time enhancement of the concentration signal is required. Response time enhancement is a method to of reducing the response time of a sensor, and various methods have been proposed [14]. Here, we apply the first-order exponential model [15]. Let  $c(t)$  be the original signal, the response time enhanced signal  $c'(t)$  is given by

$$c'(t) = c(t) + \alpha \frac{d}{dt}c(t), \quad (11)$$

where  $\alpha$  is a parameter decided by the response time of the sensor. For the concentration sensor,  $\alpha = 0.1$  has been experimentally demonstrated to be a suitable value for the response time enhancement of the measured concentration signal  $c(t)$  without introducing large oscillations in  $c'(t)$ .

### 3.2 Dead Space Calculation

Various methods for calculating  $V_D$  are discussed in [6], among which two standard methods are Fowler’s method [16, 17] and the Bohr equation [18]. The latter states that

$$V_D = V_T \frac{F_A - F_{\bar{E}}}{F_A - F_{I'}}, \quad (12)$$

where  $F_{\bar{E}}$  is the average tracer gas concentration during expiration, and  $F_{I'}$  is the tracer gas concentration at the end of inspiration.

If we make the same assumption as in (7) (i.e.,  $F_A = F_{E'}$ ), then (12) becomes

$$V_D = V_T \frac{F_{E'} - F_{\bar{E}}}{F_{E'} - F_{I'}}. \quad (13)$$

We have used (13) for the calculation of  $V_D$  in the proposed method.

## 4 Results and Comparisons

### 4.1 Choosing Appropriate Sinusoidal Periods

The proposed breath-by-breath model assumes that venous recirculation of the oscillatory component in the concentration signal is negligible; therefore care has to be taken when choosing the forcing sinusoidal periods  $T$ . Gavaghan et al. found that the venous recirculation effects are negligible in the range of  $0.5 \leq T \leq 4$  mins for soluble gases halothane, acetylene, and  $N_2O$  [13], and become more pronounced at long forcing periods [4]. Williams et al. recommended using  $2 \leq T \leq 3$  mins [5, 8].

Here, we present the results obtained in the range of  $2 \leq T \leq 4$  mins using tracer gas  $\text{N}_2\text{O}$ , in order to determine the appropriate sinusoidal periods of the tracer gas.

## 4.2 Comparison of Results from Artificial Lung and Human Lung

The benefit of using an artificial lung is that it has known values for  $V_D$ ,  $V_A$ , and  $\dot{Q}_P$  is always zero; therefore, it can be used to verify a ventilation model. The apparatus of the artificial lung in our experiments and its detailed description can be found in [6, 19]. Compared with the artificial lung, there is no comparable “gold standard” for the estimation of lung function in humans. Healthy human volunteers were studied, and results obtained from one volunteer are presented in this paper, for illustration of the prototype system. Results obtained from the remaining volunteers are similar to those presented in this paper, and are not shown here.

Figure 2 compares the results obtained using the artificial lung and from the healthy volunteer. The detailed values from the artificial and human subjects are shown in Tables 1 and 2, respectively. The parameters of the artificial lung were set to be  $\dot{Q}_P = 0 \text{ L min}^{-1}$ ,  $V_A = 2.5 \text{ L}$ , and  $V_D = 0.2 \text{ L}$ . In (1), we have chosen tracer gas parameters  $M = 0.05$ ,  $A = 0.03$ , which is a non-toxic concentration level for  $\text{N}_2\text{O}$ .

Tables 1 and 2 show that  $V_D$  estimation is consistently close to the actual value; i.e., in Table 1, the estimated values of  $V_D$  are close to the actual value  $V_D = 0.2 \text{ L}$ . These estimates have small standard deviations, indicating that the Bohr equation that we have used is an appropriate method for estimation of  $V_D$ .

The proposed method underestimates  $V_A$  in the case of the artificial lung, at all five forcing sinusoidal periods  $T = 2, 2.5, 3, 3.5$ , and  $4$  mins. The difference between the estimates and the actual value is approximately  $0.25 \text{ L}$ , and thus the error is approximately  $0.25/2.5 = 10\%$ .

Estimates of  $\dot{Q}_P$  at  $T = 2$ , and  $2.5$  mins are further from the actual values, for both the artificial lung and the human lung. For the human lung, the shortest sine period of  $T = 2$  mins produces the most inaccurate estimate  $\dot{Q}_P = 10.71 \text{ L min}^{-1}$ . For the same human lung, the second shortest sine period of  $T = 2.5$  minutes produces an estimation of  $\dot{Q}_P = 4.73 \text{ L min}^{-1}$  that is closer to the expected value. The same can be seen in the results obtained from the artificial lung. One possible reason for this inaccuracy is that the measurement of concentration is more prone to errors for small  $T$ . This is because the concentration sensor provides better measurements when the rate of change in the concentration is gradual.

At  $T = 3, 3.5$ , and  $4$  mins, both the artificial lung and the human measurements produce consistent estimates of  $V_A$  and  $\dot{Q}_P$  that are close to the actual values for the artificial lung, and to predicted values for a human male volunteer, respectively. This indicates that these periods corresponds to negligible “venous recirculation” effects, and thus are suitable values for the estimation of lung function.

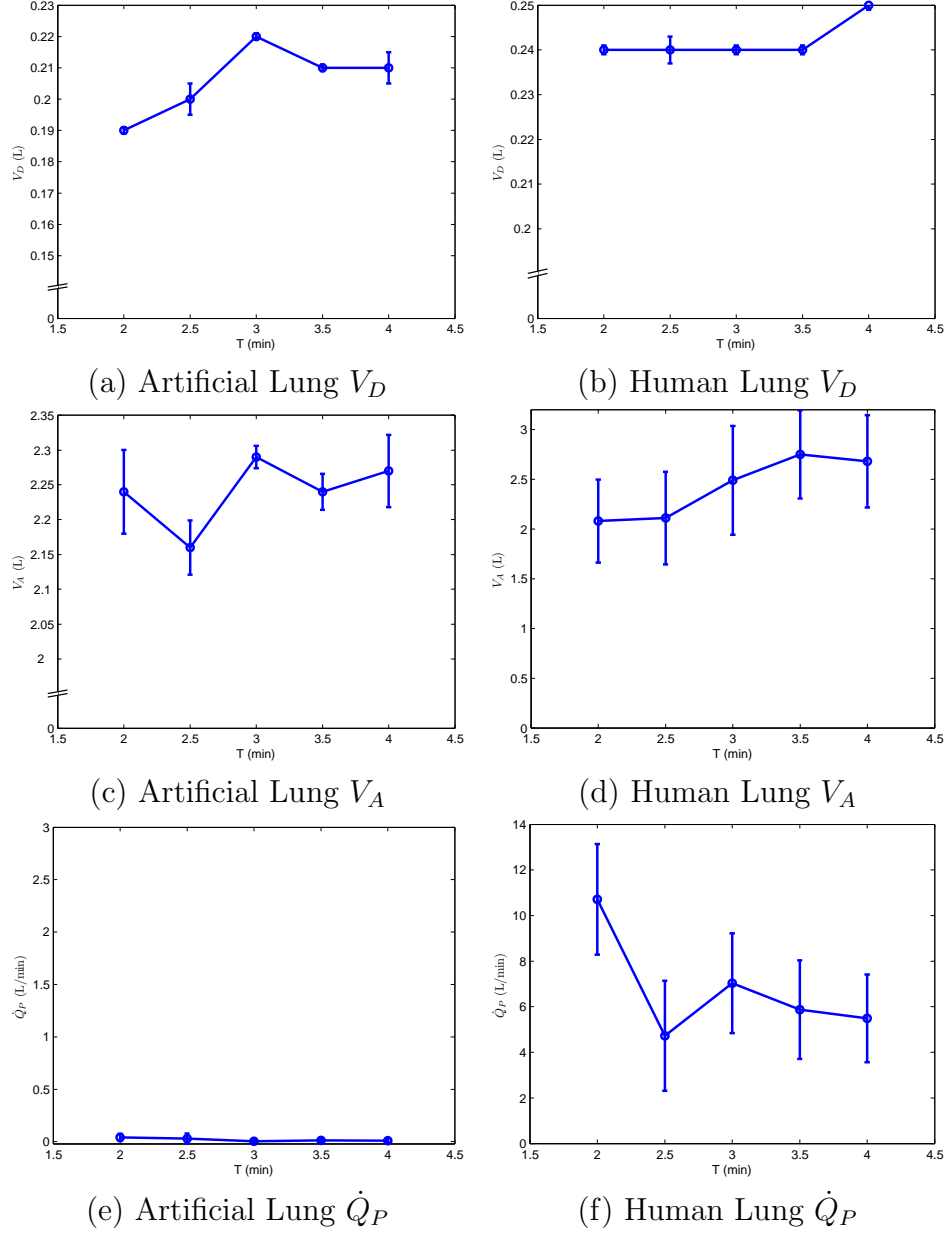


Figure 2: Estimates of  $V_D$ ,  $V_A$ , and  $\dot{Q}_P$  at five sinusoidal periods  $T = 2, 2.5, 3, 3.5$ , and 4 mins, obtained from an artificial lung and a healthy volunteer, respectively. For both the artificial lung and the human lung, six data sets were used to obtain the results at each forcing period  $T$ . Each of these data sets was used to obtain estimates of  $V_D$ ,  $V_A$ , and  $\dot{Q}$ , for each value of  $T$  (i.e.,  $5 \times 6 = 30$  data sets in total). At each value of  $T$ , the average values are plotted, with standard deviations shown as the error bar.

Table 1: Results obtained using an artificial lung. The actual parameter values of which the data in the table are estimates are  $V_D = 0.2$  L,  $V_A = 2.5$  L, and  $\dot{Q}_P = 0$  L min<sup>-1</sup>.  $T$  is the forcing sinusoidal period of tracer gas N<sub>2</sub>O in minutes.

$T$ (min)	$V_D$ (L)	$V_A$ (L)	$\dot{Q}_P$ (L min <sup>-1</sup> )
2	$0.19 \pm 0.001$	$2.24 \pm 0.060$	$0.04 \pm 0.034$
2.5	$0.20 \pm 0.005$	$2.16 \pm 0.039$	$0.03 \pm 0.049$
3	$0.22 \pm 0.001$	$2.29 \pm 0.016$	$0.01 \pm 0.010$
3.5	$0.21 \pm 0.001$	$2.24 \pm 0.026$	$0.01 \pm 0.020$
4	$0.21 \pm 0.005$	$2.27 \pm 0.052$	$0.01 \pm 0.017$

Table 2: Results obtained from a health male, age 63 years, weight 72 kg. The approximate parameter ranges are  $0.2 \leq V_D \leq 0.3$  L,  $2 \leq V_A \leq 3.5$  L, and  $5 \leq \dot{Q}_P \leq 7$  L min<sup>-1</sup>.  $T$  is the forcing sinusoidal period of tracer gas N<sub>2</sub>O in minutes.

$T$ (min)	$V_D$ (L)	$V_A$ (L)	$\dot{Q}_P$ (L min <sup>-1</sup> )
2	$0.24 \pm 0.001$	$2.08 \pm 0.418$	$10.71 \pm 2.429$
2.5	$0.24 \pm 0.003$	$2.11 \pm 0.467$	$4.73 \pm 2.410$
3	$0.24 \pm 0.001$	$2.49 \pm 0.547$	$7.03 \pm 2.191$
3.5	$0.24 \pm 0.001$	$2.75 \pm 0.444$	$5.87 \pm 2.160$
4	$0.25 \pm 0.001$	$2.68 \pm 0.464$	$5.49 \pm 1.923$



## 5 Conclusion

The proposed model is able to estimate lung function using two successive breaths. In practice, it is desirable to use more than two breaths for robust estimation. This is much faster than using the traditional continuous model, which requires a relatively long time to collect the patient data.

We have shown that a suitable range of the forcing sinusoidal periods is  $3 \leq T \leq 4$  mins, in order to avoid both large measurement errors and “venous recirculation” effects. Estimates of  $V_D$ ,  $V_A$ , and  $\dot{Q}_P$  obtained from using the proposed method are consistent and stable, using both the artificial lung and the human lung. The next stage of this research will include the validation of the model using data from patients in ICUs and operating theatres.

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