RESPIRATORY SYSTEM MODELLING BY USING NUMERICAL INTEGRATION TECHNIQUE VIA NONLINEAR DIFFERENTIAL EQUATION MODELS

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Abstract: Pulmonary elastance provides an important basis for deciding air pressure parameters of mechanical ventilators, and airway resistance is an important parameter in the diagnosis of respiratory diseases. The authors have proposed two types of second order nonlinear differential equation model of respiratory system. In the first type of model, elastic coefficient is expressed as polynomial function of air-volume, while in the second type of model, elastic coefficient is expressed by RBF network. In this paper, the polynomial expression based model and the RBF network expression based model are compared firstly. Secondly, a unified estimation algorithm is derived based on numerical integration technique. According to the proposed algorithm, the pulmonary elastance and the airway resistance can be directly estimated from sampled measurement data of airway pressure, air-flow and air-volume. Then, the proposed algorithm is validated by some examples of application to practical clinical data.

Keywords: Respiratory System, Nonlinear Differential Equation Model, Continuous-Time Model, Identification, Estimation, Numerical Integration

1. INTRODUCTION

Mechanical ventilation is generally used when spontaneous breathing is absent or insufficient. Characteristic of lung is very different in each patient. For setting appropriate ventilation conditions fitting to each patient, it is important to establish a mathematical model describing the mechanism of human respiratory system, and to know he pulmonary characteristic of each patient via identification of the model.

For this purpose, two types of respiratory system models have been proposed by the authors. These models are expressed as second order nonlinear differential equations with air-volume variant elastic coefficient and air-volume variant resistive coefficient. In the first type of model, elastic coefficient is expressed as polynomial function of air-volume (Kanae *et al.,* 2004*a*), while in the second type of model, elastic coefficient is expressed by RBF network (Kanae *et al.,* 2004*b*). The proposal of these models makes it possible to estimate pulmonary elastance and airway resistance from the measurements of air pressure, flow and volume at ventilator side, no need for any sensor inserted into body inside.

The above two types of models are continuous-time model. Therefore, the continuous-time estimation approach is adopted for identifying the models. In this paper, the polynomial expression based model and the RBF network expression based model are compared firstly. Secondly, a unified estimation algorithm is derived based on numerical integration technique. Then, the proposed algorithm is validated by some examples of application to practical clinical data. Final section concludes this paper.

2. TWO TYPES OF RESPIRATORY SYSTEM MODELS

In this paper, non-spontaneous-breathing cases of mechanical ventilation are considered. In the inspiration phase of mechanical ventilation, the air pressure of ventilator side is higher than the lung inside, so the fresh air is sent to lung by the different of air pressure, and the lung is expanded. In the expiration phase, the exhaust after gas exchange is excreted naturally by the shrinking force of lung.

The expansion and the shrinkage depending on variation of air pressure are characterized by pulmonary elastance. The pulmonary elastance is an important factor in decision of respiratory dynamics. Usually the elastance is expressed by a pressure-volume curve (*P-V* curve) of air volume versus air pressure. This curve is not linear, and it becomes flat in the range of high pressure. The elastance can be described by equation of

$$P_\ell(t) = f_E(V)V(t). \quad (1)$$

where, $P_\ell(t)$ is inside pressure of lung, $V(t)$ is air volume of lung, both of $P_\ell(t)$ and $V(t)$ are time-variant. $f_E(V)$ is the pulmonary elastance. It is not constant, but it is changed by volume of $V(t)$).

On the other hand, the lung and the ventilator are connected by the air tube and a long rubber tube, therefore there is loss of pressure. Denoting the pressure loss as P_r, then it can be written as:

$$P_r(t) = g_R(F)F(t). \quad (2)$$

where, $F(t)$ is air flow (mL/min). From the relation between flow $F(t)$ and volume $V(t)$:

$$\frac{d}{dt}V(t) = V(t) = F(t), \quad (3)$$

we have

$$P_r(t) = g_R(V)V(t). \quad (4)$$

g_R is so-called airway resistance, and it is not constant too. Usually it varies by flow ($F(t)$, namely $V(t)$). Considering the effect of flow up to second order, the pressure loss can be described by the Rohrer equation as follows:

$$P_r(t) = (r_1 + r_2|V|)V(t). \quad (5)$$

Next, a human has two, right and left, parts of lung. Even if each part is modeled by a simple first order differential equation, the synthesized overall respiratory system model becomes to a second order differential equation (Similowski and Baters, 1991).

Considering the above each factor, it is adequate to model the respiratory system as the following expression:

$$P_{ao}(t) + a_1\dot{P}_{ao}(t) = f_E(V)V(t) + g_R(\dot{V})\dot{V}(t) + b_2\ddot{V}(t) + P_{eea} + \epsilon(t), \quad (6)$$

where, $P_{ao}(t)$ is the airway opening pressure, P_{eea} is the end-expiratory alveolar pressure. $\epsilon(t)$ contains the modeling error and the measurement noise.

As mentioned above, pulmonary elastance $f_E(V)$ and airway resistance $f_R(V)$ are not constant, they are some nonlinear function of volume $V(t)$. The authors have proposed two types of respiratory system model in the previous works. In the first type of model, pulmonary elastance $f_E(V)$ is expressed by polynomial function of air-volume $V(t)$ (Kanae *et al.,* 2004*a*), and in the second type of model, pulmonary elastance $f_E(V)$ is expressed by RBF network with input of air-volume $V(t)$ (Kanae *et al.,* 2004*b*).

2.1 Polynomial expression based model

Here, he elastance $f_E(V)$ is described as a polynomial of volume $V(t)$:

$$f_E(V) = k_1 + k_2V + \dots + k_nV^{n-1}. \quad (7)$$

Substituting this equation (7) for equation (1), inside pressure of lung $P_\ell(t)$ is written as

$$P_\ell(t) = k_1V + k_2V^2 + \dots + k_nV^n. \quad (8)$$

It is an *n-th* degree polynomial. Consequently, overall model is obtained by substituting Equation (7) for Equation (6).

$$\begin{aligned} P_{ao}(t) + a_1\dot{P}_{ao}(t) &= k_1V(t) + k_2V^2(t) + \dots + k_nV^n(t) \\ &\quad + r_1\dot{V}(t) + r_2|\dot{V}(t)|\dot{V}(t) \\ &\quad + b_2\ddot{V}(t) + P_{eea} + \epsilon(t) \end{aligned} \quad (9)$$

In the case of polynomial expression, the structure is simple, and the degree of the polynomial can be relatively easily decided by priori knowledge such as shape of *P-V* curve. The static *P-V* curve is almost linear in the middle range, and it becomes flat in the range of low and high pressure. For expression of this shape of static *P-V* curve, it is necessary that the degree *n* is at least 3. On the other hand, the higher degree term is easily influenced by the measurement noise, and it may be numerically unstable in parameter estimation. Therefore, it is not preferable that the degree is excessively high.

By definition of data vector $\varphi_p(t)$ and parameter vector θ_p,

$$\varphi_p(t) = \begin{bmatrix} -\dot{P}_{ao}(t) \\ --- \\ V(t) \\ \vdots \\ V^n(t) \\ --- \\ \dot{V}(t) \\ |F(t)|F(t) \\ \dot{F}(t) \\ 1.0 \end{bmatrix}, \quad \theta_p = \begin{bmatrix} a_1 \\ --- \\ k_1 \\ \vdots \\ k_n \\ --- \\ r_1 \\ r_2 \\ b_2 \\ P_{eea} \end{bmatrix}, \tag{10}$$

the model equation can be written in short form as follows:

$$P_{ao}(t) = \varphi_p^T(t)\theta_p + \epsilon(t). \tag{11}$$

where the term of $|\dot{V}(t)|\dot{V}(t)$ and the term of $\ddot{V}(t)$ in the right of Equation (9) are replaced by $|F(t)|F(t)$ and $\dot{F}(t)$, because of the relation between volume and flow $\dot{V}(t) = F(t)$.

2.2 RBF network expression based model

Here, the elastance $f_E(V)$ is described by a RBF network with input of volume $V(t)$:

$$f_E(V) = \sum_{i=1}^{n_E} q_i \Psi_i(V), \tag{12}$$

where $\Psi_i(V)$ is Radial Basis Function with center V_{0i}, deviation σ_i:

$$\Psi_i(V) = \exp\left(-\frac{(V - V_{0i})^2}{2\pi\sigma_i^2}\right). \tag{13}$$

q_i is weight of *i-th* node, and n_E is the number of nodes of RBF network.

Substituting Equation (12) for Equation (6), overall respiratory model become to

$$\begin{aligned} &P_{ao}(t) + a_1\dot{P}_{ao}(t) \\ &= V(t)\sum_{i=1}^{n_E} q_i\Psi_i(V) + r_1\dot{V}(t) + r_2|\dot{V}(t)|\dot{V}(t) \\ &\quad + b_2\ddot{V}(t) + P_{eea} + \epsilon(t). \end{aligned} \tag{14}$$

Similarly as subsection 2.1, defining data vector $\varphi_r(t)$ and parameter vector θ_r as

$$\varphi_r(t) = \begin{bmatrix} -\dot{P}_{ao}(t) \\ --- \\ V(t)\Psi_1(V) \\ \vdots \\ V(t)\Psi_{nE}(V) \\ --- \\ \dot{V}(t) \\ |F(t)|F(t) \\ \dot{F}(t) \\ 1.0 \end{bmatrix}, \quad \theta_r = \begin{bmatrix} a_1 \\ --- \\ q_1 \\ \vdots \\ q_{nE} \\ --- \\ r_1 \\ r_2 \\ b_2 \\ P_{eea} \end{bmatrix}, \tag{15}$$

the model equation can also be written in short form as follows:

$$P_{ao}(t) = \varphi_r^T(t)\theta_r + \epsilon(t). \tag{16}$$

When use is made of RBF network expression, numerical stability can be expected, because the output of each node is in range of [0, 1], the balance between each node is good. However, the problems how to decide the number of nodes and how to decide center and deviation of each node are remained.

3 PARAMETER ESTIMATION

Irrespective of the polynomial expression based model (9) or the RBF network expression based model (14), both of them are described by second order nonlinear differential equation. Equation (9) and Equation (14) are all continuous-time model. But, air pressure$P_{ao}(t)$, flow$F(t)$, and volume $V(t)$ are usually sampled and measured in a fixed sampling period.

Here, one may want to take an approach, this approach directly transform the model (9) or the model (14) into discrete-time model, and to estimate the parameters, then inversely calculate original parameters of continuous-time model from estimated parameters of discrete-time model. However, one parameter of continuous-time model is usually appeared in many parameters of discrete-time model, and the transformation may be nuisance. Furthermore, the errors will be introduced by the transformation.

On the other hand, there is a simple way to approximate the derivatives of continuous-time model by the difference of sampled measurements, but this way may make the noise effect worse. Therefore, it is not desirable to calculate derivatives directly from the measurements.

In the next subsections, identification models are derived by applying the numerical integration technique which is known as an effective approach for continuous-time model identification, and then a unified estimation algorithm is given.

3.1 Identification model

In general, measurement data obtained from the mechanical ventilation system are sampled data of air pressure $P_{ao}(k)$, flow $F(k)$, and volume$V(k)$, where *k* denotes sampling instance *k = 1, 2,..., N, N* is the data size.

Denote the sampling period of data collection as *T*. At time instant *t = kT*, integrate both sides of Equation (16) over the interval $[(k-\ell)T, kT]$. Let *y(k)* be the left hand side of the resultant equation. Then *y(k)* can be calculated as:

$$y(k) = \int_{(k-\ell)T}^{kT} P_{ao}(\tau)d\tau = \sum_{j=0}^{\ell} g_j P_{ao}(k-j), \quad (17)$$

where, ℓ is a natural number that decides the window size of numerical integration. The coefficients $g_i (i = 0, 1, ..., \ell)$ are determined by formulae of numerical integration. For example, when the trapezoidal rule is taken, they are given as follows:

$$\begin{cases} g = g_\ell = T/2, \\ g_i = T, i = 1, 2, ..., \ell - 1 \end{cases} \quad (18)$$

For the polynomial expression based model the integral $\phi_p(k)$ of data vector $\varphi_p(t)$ can be calculated by

$$\phi_p(k) = \sum_{j=0}^{\ell} g_j \varphi_p(k-j) = \begin{bmatrix} -P_{ao}(k) + P_{ao}(k-\ell) \\ --- \\ \sum_{j=0}^{\ell} g_j V(k-j) \\ \vdots \\ \sum_{j=0}^{\ell} g_j V^n(k-j) \\ --- \\ V(k) - V(k-\ell) \\ \sum_{j=0}^{\ell} g_j |F(k-j)| F(k-j) \\ \frac{F(k) - F(k-\ell)}{\ell T} \end{bmatrix} \quad (19)$$

Here, analytical forms are taken for the terms where the integral can be calculated analytically. Get together the approximation error Δ_Σ caused by numerical integration and the integral of original error term $\epsilon(t)$ in $e(k)$. Namely, let $e(k)$ be

$$e(k) = \Delta_\Sigma + \int_{(k-\ell)T}^{kT} \epsilon(\tau)d\tau. \quad (20)$$

Consequently, an identification model corresponding to polynomial expression based respiratory system model is derived:

$$y(k) = \phi_p^T(k)\theta_p + e(k). \quad (21)$$

For the RBF network expression based model, similar form of Equation (21) can be derived. For convenience, use equation of

$$y(k) = \phi^T(k)\theta + e(k). \quad (22)$$

to indicate any case of polynomial expression or RBF network expression.

3.2 Parameter estimation

From the measurements of air pressure $P_{ao}(k)$, flow $F(k)$ and volume $V(k)$, it is easy to calculate $y(k)$ by Equation (17) and $\phi(k)$ by Equation (19) at each time instant $k = \ell + 1, ..., N$, then $N - \ell$ regression equations can be derived as:

$$y = \Phi\theta + e, \quad (23)$$

where, $y = [y(N)...y(\ell+1)]^T$, $\Phi = [\phi(N)...\phi(\ell+1)]$, and $e = [e(N)...e(\ell+1)]^T$, respectively.

The least squares estimate that minimizes the criterion function J defined as a sum of squared errors

$$J = ||y - \Phi\theta||^2 \quad (24)$$

is given by

$$\hat{\theta} = (\Phi^T\Phi)^{-1}\Phi^T y \quad (25)$$

provided the inverse exists. Then, the estimate of pulmonary elastance is obtained:

$$\hat{f}_E(V) = \sum_{i=1}^{n} \hat{k}_i V^{(i-1)}, \quad (26)$$

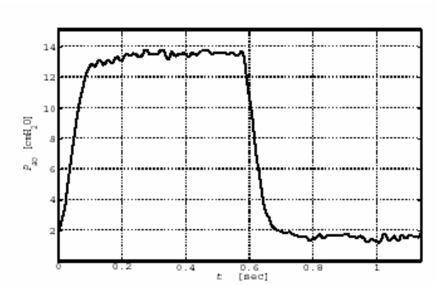
or

$$\hat{f}_E(V) = \sum_{i=1}^{n_f} \hat{b}_i \psi_i(V). \quad (27)$$

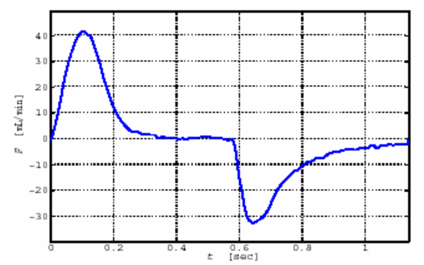
This approach is off-line in that the calculation is carried out after the data of length *N* are completely collected. But, in practical clinical cases, the data are recorded successively, and the state of lung may change, so on-line estimation algorithm is desired. The on-line algorithm for calculating the above LS estimate is as the follows (Ljung, 1987):

$$\begin{cases} \hat{\theta}(k) = \hat{\theta}(k-1) + L(k)(y(k) - \phi^T(k)\hat{\theta}(k-1)), \\ L(k) = \frac{S(k-1)\phi(k)}{\lambda + \phi^T(k)S(k-1)\phi(k)}, \\ S(k) = \frac{1}{\lambda}[S(k-1) - \frac{S(k-1)\phi(k)\phi^T(k)S(k-1)}{\lambda + \phi^T(k)S(k-1)\phi(k)}], \end{cases} \quad (28)$$

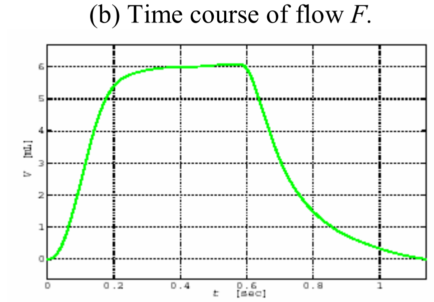
where, $\lambda (\lambda \leq 1)$ is the forgetting factor, and the initial values of $\hat{\theta}$ and *S* are taken as $\hat{\theta}(0) = 0, S(0) = s^2 I$ (*s* is a sufficiently large real number).



(a)Time course of airway opening pressure P_{ao}



(b) Time course of flow *F*.



(c) Time course of volume *V*.

Fig.1. A set of practical clinical data of artificial ventilation.

4. VALIDATION

In this section, the polynomial expression based model and the RBF network expression based model are compared through pulmonary elastance estimation results. The measurement data of mechanical ventilation are provided from a medical center. It is an example of a neonate who has 25 weeks of gestational age. The patient is diagnosed as respiratory distress syndrome (RDS), and is admitted to neonatal intensive care unit. The nature and aims of the investigation were explained to the nest of kin, and their informed consent was obtained.

Measurement data of airway opening pressure P_{ao} (Fig. 1(a)), flow *F* (Fig. 1(b)) and volume *V* (Fig. 1(c)) are shown in Fig.1. The sampling period T_{sp} is $T_{sp} = 0.005$ second, and the data size *N* is $N = 229$. These data corresponds to one cycle of breath. The dynamical *P* - *V* curve can be plotted from the data of airway opening pressure P_{ao} and volume V (Fig.2). For verification of estimated results of pulmonary elastance, experimental static elastic recoil *P* –*V* points during inspiration (□) and expiration (◯) are also plotted in the Fig. 2. The results of estimation are evaluated by degrees how the calculated static elastic *P* – *V* curve based on estimated parameters fit to the static recoil *P* – *V* points.

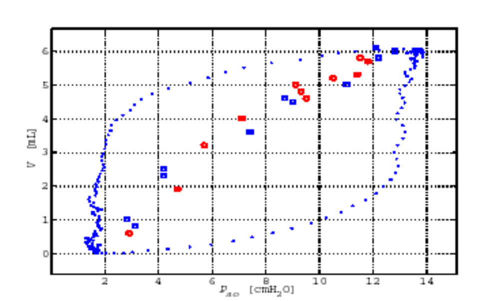


Fig. 2. Dynamical *P* – *V* curve (dotted line) and experimental static elastic recoil pressure volume points during inspiration(□) and expiration(◯).

The estimation results of static elastance by using polynomial expression model are shown in Table 1 and Fig. 3. In Table 1, *J* indicates the value of criterion function defined as Equation (24). E_{vl} is sum of squared errors between experimentally measured pressure values $P_\ell(i)$ at each static *P* – *V* points and the estimated pressure value $\hat{P}_\ell(i)$ corresponding to the points:

$$E_{el} = \sum_{i=1}^{N_v} (P_\ell(i) - \hat{P}_\ell(i))^2,$$

where N_v is the number of static *P* – *V* points used in validation. The values of *J* and E_{vl} when the elastic polynomial is taken as (1) $f_{E1}(V) = k_1 + k_2 V$;(2) $f_{E2}(V) = k_1 + k_2 V + k_3 V^2$; (3) $f_{E3}(V) = k_1 + k_2 V + k_3 V^2 + k_4 V^3$, are recorded, respectively. The value of *J* decreases as the degree *n* increases from 2 to 3 and 4. On the other hand, although the value of E_{vl} with $n = 3,4$ is smaller than that with $n = 2$, there is almost no variation in the case of $n = 3$ and $n = 4$. The data used in these test were performed pre-process such as correction of draft and integration previously. Without the pre-process, conspicuous bad influence of noise was appeared in the estimation results when the original measurement data is directly used.

The estimation results of static elastance by using the RBF network expression model are shown in Table 2 and Fig. 4. The node numbers of RBF networks used to express elastance are listed in the first column of Table 2. Corresponding values of J and E_{vl} are shown in second and third column.

Table 1. Evaluation of estimation results by using polynomial expression based model.

$f_E(V)$	J	E_{vl}
$k_1 + k_2V$	0.03588	13.7643
$k_1 + k_2V + k_3V^2$	0.02564	12.6802
$k_1 + k_2V + k_3V^2 + k_4V^3$	0.02505	12.7030

Table 2. Evaluation of estimation results by using RBF network expression based model.

n_E	J	E_{vl}
4	0.01509	13.1586
5	0.01416	12.6984
7	0.01024	14.8392

The value of E_{vl} is smallest at n_E = 5, though the value of J decreases as the number of nodes increases. It indicates that the number of nodes is insufficient for modeling in case of n_E = 4, an over fitting is occurred in case of n_E = 7. This phenomenon can also be observed in Fig. 4 phenomenon can also be observed in Fig. 4.

5. CONCLUSIONS

For setting the ventilation conditions of mechanical ventilator or diagnose many disease of respiratory system, pulmonary elastance and airway resistance provide decisive information. Therefore, it is very important to identify respiratory system model which includes pulmonary elastance and airway resistance terms. In this paper, the polynomial expression based model and the RNF network expression based model are compared. The polynomial expression based model has the advantage that the structure is simple, namely, third degree or 4-th degree is sufficient to describe the elastic property, while this model is sensitive to measurement noise. On the other hand, the RBF network expression based model has good numerical stability though the problems how to decide the number of nodes and how to decide center and deviation of each node are remained. Also, the unified estimation algorithm is derived based on numerical integration technique in this paper. The proposed algorithm is validated by some examples of application to practical clinical data.

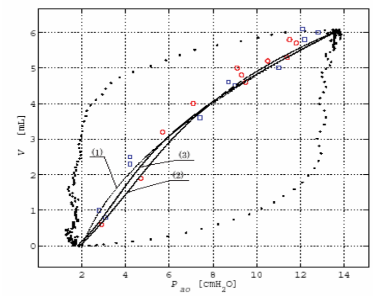


Fig. 3. Pulmonary elastance estimation results by using polynomialexpression based model, in case (1) $f_E(V) = k_1 + k_2V$; case (2) $f_E(V) = k_1 + k_2V + k_3V^2$; and case (3) $f_E(V) = k_1 + k_2V + k_3V^2 + k_4V^3$.

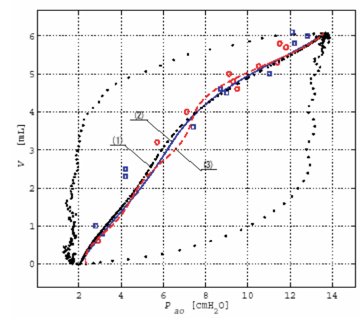


Fig. 4. Pulmonary elastance estimation results by using RBF network expression based model, in case (1) n_E = 4, in case (2) n_E = 5, and in case (3) n_E = 7.

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