Integral-Based Identification of an Inhomogeneity Model in Respiratory Mechanics

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***Abstract*—Individualized models of respiratory mechanics may help to reduce potential harmful effects of ventilation therapy by predicting the outcome of certain ventilator settings. The underlying models are commonly identified by iterative error-mapping methods, such as the Levenberg-Marquardt Algorithm, requiring initial estimates for the patient specific parameters. The quality of the initial estimates has a significant influence on identification efficiency and results. An iterative integral-based parameter identification method was applied to a linear 2nd order respiratory mechanics model. The method was compared to the Levenberg-Marquardt Algorithm using clinical data from 13 Acute Respiratory Distress Syndrome (ARDS) patients. The Iterative Integral-Based Method converged to the Levenberg-Marquardt solution two times faster and was independent of initial estimates. These investigations reveal that the Iterative Integral-Based Method is beneficial with respect to computing time, operator independence and robustness.**

Keywords-Respiratory Mechanics; Parameter Identification; Inhomogeneity Model;

I. INTRODUCTION

Non-adapted ventilator settings risk severe side effects in intensive care patients during ventilation therapy [1]. To find optimal, patient-specific ventilator settings, mathematical models of respiratory mechanics could be used to predict the outcome of specific ventilator configurations, and support the evaluation of protective lung ventilator settings [2-3]. To obtain optimal predications directly at the bedside requires robust and fast identification methods for the underlying model parameters. However, bedside data for parameter identification are generally restricted to measurements of airway pressure and flow rate. Hence, models must be as simple as possible, while capturing all necessary dynamics to be identifiable with the limited available measurement set.

Various parameter identification methods are available to minimize the least square error (LSE) between measured samples and model simulations. In higher order models, parameter identification is commonly performed by iterative error-mapping LSE methods [4-6]. These methods require initial estimation of variable model parameters and iterate towards LSE by approaching the minimum on the error surface. However, efficiency and quality of the solution can be highly sensitive to the initial guesses. Accurate initial parameter values can significantly reduce the incidence of spurious, non-optimal solutions [6].

This paper presents the Iterative Integral-Based Method (IIM) for parameter identification [7]. The IIM was originally developed for parameter identification of glucose-insulin models [8] and this paper adopts the method to a model of respiratory mechanics. The IIM creates a convex relaxation, and is thus comparatively simple to apply, requires comparatively minimal computing time, and does not require initial parameter values estimates [7-8].

II. MODEL & METHODOLOGY

A. Data

Measurement sets of thirteen mechanically ventilated patients were selected from a previous ARDS (Acute Respiratory Distress Syndrome) – Study [9], where SCASS-Maneuvers (Static Compliance Automated Single Step) were performed. The maneuver consists of airway occlusions within the inspiration phase of a breathing cycle. An occlusion of the airways is initiated when a randomized inspiration volume is reached and lasts for five seconds. The measurement set consisted of flow rate and airway opening pressure signals sampled at 125 Hz. For each patient, three breathing cycles were selected. The study was approved by local ethics committees. Informed consent was obtained from patients or their legally authorized representative.

B. Model

The Inhomogeneity Model (IHM) represents two different alveolar regions represented by two compliances (C_1 and C_2 in mL/mbar) with their own local airway (R_1 and R_2 in mbar·s/mL) connected to the airway opening.

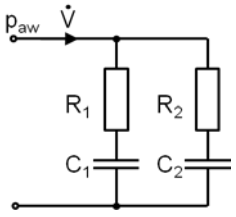

Figure 1. Electrical analog of the Inhomogeneity Model. p_{aw} corresponds to the airway opening pressure, $\dot{V}$ stands for the flow rate, R_1, C_1 and R_2, C_2 represent two different alveolar regions.

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This model assumes parallel ventilation inhomogeneity in the lung described by the two time constants $\tau_1 = R_1 \cdot C_1$ and $\tau_2 = R_2 \cdot C_2$. The presence of ventilation inhomogeneity could have a significant effect on the dynamic nature of lung mechanics since it enables redistribution processes between these two compartments (Pendelluft) [10-11]. The IHM is depicted as an electrical analog in Fig. 1 and the mathematical description is presented in state-space representation in (1). $\dot{V}$ is the *a-priori* known flow rate (mL/s) representing the model input and p_{aw} is the measured airway pressure (mbar) being the model output.

$$\begin{bmatrix}\dot{p}_{C1}\\ \dot{p}_{C2}\end{bmatrix} = \begin{bmatrix} -\frac{1}{C_1(R_1+R_2)} & \frac{1}{C_1(R_1+R_2)} \\ \frac{1}{C_2(R_1+R_2)} & -\frac{1}{C_2(R_1+R_2)}\end{bmatrix}\begin{bmatrix}p_{C1}\\ p_{C2}\end{bmatrix} + \begin{bmatrix}\frac{R_2}{C_1(R_1+R_2)}\\ \frac{R_1}{C_2(R_1+R_2)}\end{bmatrix}\dot{V} \quad (1a)$$

$$p_{aw} = \begin{bmatrix}1 - \frac{R_1}{R_1+R_2} & \frac{R_1}{R_1+R_2}\end{bmatrix}\begin{bmatrix}p_{C1}\\ p_{C2}\end{bmatrix} + \frac{R_1R_2}{R_1+R_2}\dot{V} \quad (1b)$$

where p_{C1} and p_{C2} (mbar) are state-signals and correspond to the pressure components generated by the volumes stored in the compartments with the compliance C_1 and C_2 (mL/mbar).

C. Parameter Identification

Structural Identifiability: As a fundamental prerequisite for successful parameter identification *a-priori* structural identifiability of the parameteric model is required [12]. This necessary criterion states that under ideal conditions of noise-free observations and error-free model structure, the unknown parameters of the postulated model can be uniquely recovered from known input-output signals. Therefore, the underlying model was tested for structural identifiability using DAISY [12]. Given the state-space equations, DAISY computes the input-output relation polynomial:

$$A = (C_1C_2R_1R_2)\dddot{V} + (C_1R_1 + C_2R_2)\ddot{V} + \dot{V} - (C_1C_2(R_1+R_2))\ddot{p}_{aw} - (C_1+C_2)\dot{p}_{aw} \quad (2)$$

By extracting the coefficients of the input-output polynomial the exhaustive summary was constructed. A range set was calculated by evaluating the coefficients at symbolic parameter values $P = [\alpha, \beta, \gamma, \delta]$. Solving the given system of nonlinear equations lead to the Gröbner basis of the IHM:

$$\begin{Bmatrix}\{R_1 = \alpha, C_1 = \beta, R_2 = \gamma, C_2 = \delta\},\\ \{R_1 = \gamma, C_1 = \delta, R_2 = \alpha, C_2 = \beta\}\end{Bmatrix} \quad (3)$$

Equation (3) shows the model has two global minima. According to DAISY, the model is not globally, but locally identifiable. Due to the symmetric model structure the two possible solutions have mirrored parameter values of the two branches. As there is no mathematical distinction between the two model branches, the two solutions are interchangeable and thus enable structural identifiability of the IHM.

Note that even if structural identifiablitiy is proven, the model might still be non-identifiable if the information content of the data is too low. Structural identifiability also does not prevent error-mapping methods from being caught in local minima. Hence, it is a necessary, but not sufficient, condition to guarantee successful parameter identification.

Iterative Integral Based Method: This parameter identification method is based on the input-output relation, derived in (2), which was rearranged and integrated twice to obtain an equation in terms of p_{aw}:

$$p_{aw} = \frac{R_1R_2}{R_1+R_2}\dot{V} + \frac{C_1R_1+C_2R_2}{C_1C_2(R_1+R_2)}V + \frac{1}{C_1C_2(R_1+R_2)}\int V dt - \frac{C_1+C_2}{C_1C_2(R_1+R_2)}\int p_{aw}dt \quad (4)$$

The coefficients in (4) were represented by new variables:

$$\begin{aligned} A &= \frac{R_1R_2}{R_1+R_2} & B &= \frac{C_1R_1+C_2R_2}{C_1C_2(R_1+R_2)} \\ C &= \frac{1}{C_1C_2(R_1+R_2)} & D &= -\frac{C_1+C_2}{C_1C_2(R_1+R_2)} \end{aligned} \quad (5)$$

yielding to:

$$p_{aw} = A\dot{V} + BV + C\int V dt + D\int p_{aw}dt \quad (6)$$

Equation (6) can be rewritten as an over-defined matrix system (7), where the lef-hand-side represents the measured pressure samples ($p_{aw,meas}$). The integrals of p_{aw} in the right-hand-side (RHS) refer to the simulated model output, which is currently unknown. The initial iteration represents p_{aw} using $p_{aw,meas}$, allowing the values of *A-D* in (5) to be calculated.

$$\begin{bmatrix}p_{aw,meas}(1)\\ p_{aw,meas}(2)\\ \vdots\\ p_{aw,meas}(N)\end{bmatrix} = \begin{bmatrix}\dot{V}(1) & V(1) & \int_0^1 V dt & \int_0^1 p_{aw}dt\\ \dot{V}(2) & V(2) & \int_0^2 V dt & \int_0^2 p_{aw}dt\\ \vdots & \vdots & \vdots & \vdots\\ \dot{V}(N) & V(N) & \int_0^N V dt & \int_0^N p_{aw}dt\end{bmatrix}\begin{bmatrix}A\\ B\\ C\\ D\end{bmatrix} \quad (7)$$

Using the estimated coefficients *A–D* from (7) the simulated model output p_{aw} can be calculated by (6) and substituted into the RHS of (7) in subsequent iterations. Equation (7) is solved again in terms of linear least squares. This process is repeated with re-simulated p_{aw} until a convergence criterion is fulfilled. The convergence tolerance for the residuals and parameter values were set to 10^{-6} for IIM and LMA. Finally, the patient-specific parameters R_1, C_1, R_2 and C_2 are regained by solving (5) by substitution leading to 1 of 2 possible solutions due to model symmetry.

$$\begin{aligned} R_1 &= \frac{4AC+2AD\sqrt{B^2-4AC}+B\sqrt{B^2-4AC}-B^2}{2(AD^2+BD+C)} \\ R_2 &= -\frac{(B+R_1D)\sqrt{{R_1}^2D^2-2R_1BD-8R_1C+B^2}+{R_1}^2D^2+2R_1(-C+BD)+B^2}{2(R_1D^2+BD+C)} \\ C_2 &= \frac{R_1-R_2}{(R_1+R_2)(B+R_2D)} \\ C_1 &= -\frac{R_1-R_2}{{R_1}^2D+B(R_1+R_2)+R_1R_2D} \end{aligned} \quad (8)$$

D. Evaluation

The IIM was applied to the 39 data sets and verified by the commonly used Levenberg-Marquardt Algorithm (LMA). To provide appropriate initial values for the LMA, the median of each parameter over all patients identified by the IIM were used as initial values for the LMA (R_1 = 0.218 mbar·s/mL, C_1 = 10.51 mL/mbar, R_2 = 0.015 mbar·s/mL, C_2 = 22.89 mL/mbar).

Finally, the resulting parameter values, Sum of Squared Error (SSE) and the Coefficient of Determination (CD) were compared. The CD is a measure for the goodness-of-fit of the

model, and takes a value from 1, which corresponds to a perfect fit, to 0, which means the model has no relation to the data whatsoever [10].

$$SSE = \sum\left(p_{aw,meas} - p_{aw}\right)^2 \tag{9}$$

$$CD = 1 - \frac{SSE}{\sum(p_{aw} - \bar{p}_{aw,meas})^2} \tag{10}$$

III. Results

The LMA converged to physiological plausible solutions in 36 out of 39 data sets and required a median of 5 iterations [IQR: 4-6] iterations and 0.30 ms [IQR: 0.25-0.36] per data set on a standard desktop PC (Intel Core 2 Duo, 2.80 GHz). The IIM found solutions with the same SSE as the LMA requiring a median of 14 iterations [IQR: 12-16] and 0.14 ms [IQR: 0.12-0.16]. Importantly, the IIM also returned physiological plausible values in those 3 data sets where the LMA converged to non-physiological negative values. The identified parameter values of both methods differ by median 1.37 % [IQR: 0.56-4.78]. The correlation of the parameters for which the LMA successfully converged are shown in Fig. 3.

TABLE I. Resulting Parameter Sets Of LMA and IIM Parameter Identification

Parameter	Set 1		Set 2	
	LMA	**IIM**	**LMA**	**IIM**
R_1 *(mbar·s/mL)*	0.276	0.272	0.096	0.084
C_1 *(mL/mbar)*	6.818	6.843	30.03	32.02
R_2 *(mbar·s/mL)*	0.008	0.008	0.042	0.044
C_2 *(mL/mbar)*	16.37	16.37	19.72	17.40
SSE ($mbar^2$)	539.17	539.23	3039.78	3043.76
CD	0.993	0.993	0.944	0.944

Exemplar parameter sets of parameter identification processes using the IIM and the LMA are shown in Table I. The corresponding pressure responses of the IIM solutions (Table I, Set 1 and Set 2) are illustrated in Fig. 2a and 2b.

IV. Discussion

In general, the resulting parameters of the IIM were consistently plausible and in accordance to the parameter values that were found by the LMA. The LMA was provided with the same initial values for all data sets, being the median parameter values over all patients. Nevertheless, the LMA iterated to negative parameter values in all three data sets of one patient. Hence, the population derived initial values started the convergence at an unsuitable position on the error plane for this participant's test data.

To achieve successful parameter identification using error-mapping methods patient-specific initial values could be derived hierarchically by identifying simpler models first [6].

The IIM was a factor 2x faster than the LMA, and found consistently physiological values. The IIM took advantage of

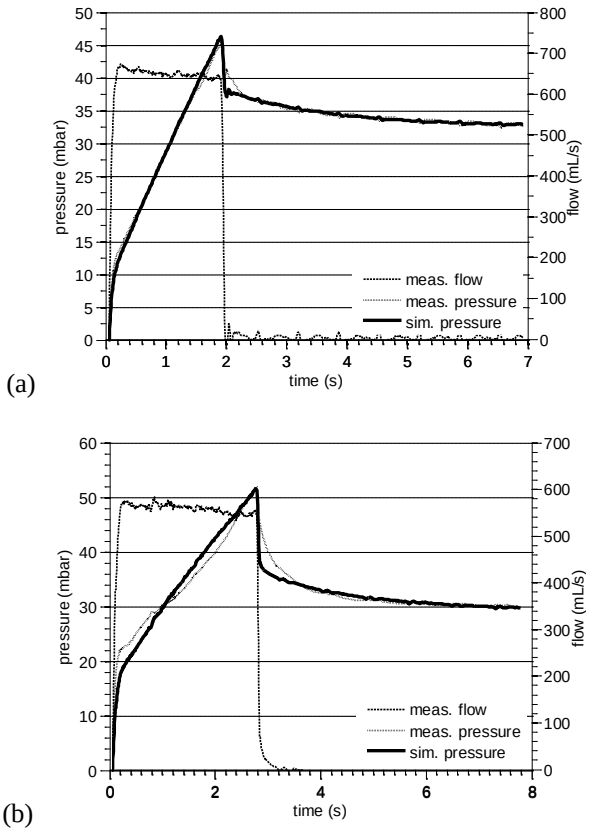

Figure 2. Measured flow rate and airway pressure and simulated pressure of the IHM. (Parameter values according to (a) Set 1 and (b) Set 2 Table I).

the mathematical structure of the model and did not require any initial values. The double integration in the derivation of the input-output relation (4) avoided the noise-amplifying effect of differentiation and assures numerical stability.

The minor differences in the resulting parameter of the IIM and LMA could be related to the amount of noise within the data. In data sets with low CD values (< 0.95), higher variance in the resulting parameters was found than in data sets with high CD values. The noise is related to cardiogenic-distortions and additional non-linear effects in respiratory mechanics, such as alveolar recruitment and distention effects or turbulent flow. This situation is illustrated in (Figure 2b) where the IHM is not sufficient to reproduce the characteristics during inspiration. Thus the IIM is better suited to typical, noisy patient data.

In this paper, the underlying dynamic effects in respiratory mechanics, captured in measured flow rate and airway pressure were assigned to inhomogeneity (Pendelluft) effects. The same measured characteristics could be assigned to viscoelastic tissue properties or time-depending recruitment according to Bates [13]. Therefore, different or additional measurements are necessary to distinct between these effects.

V. Conclusion

The IIM operates without the common initial value problem of LMA and provides robust parameter identification for 2nd order linear models of respiratory mechanics. The evaluation

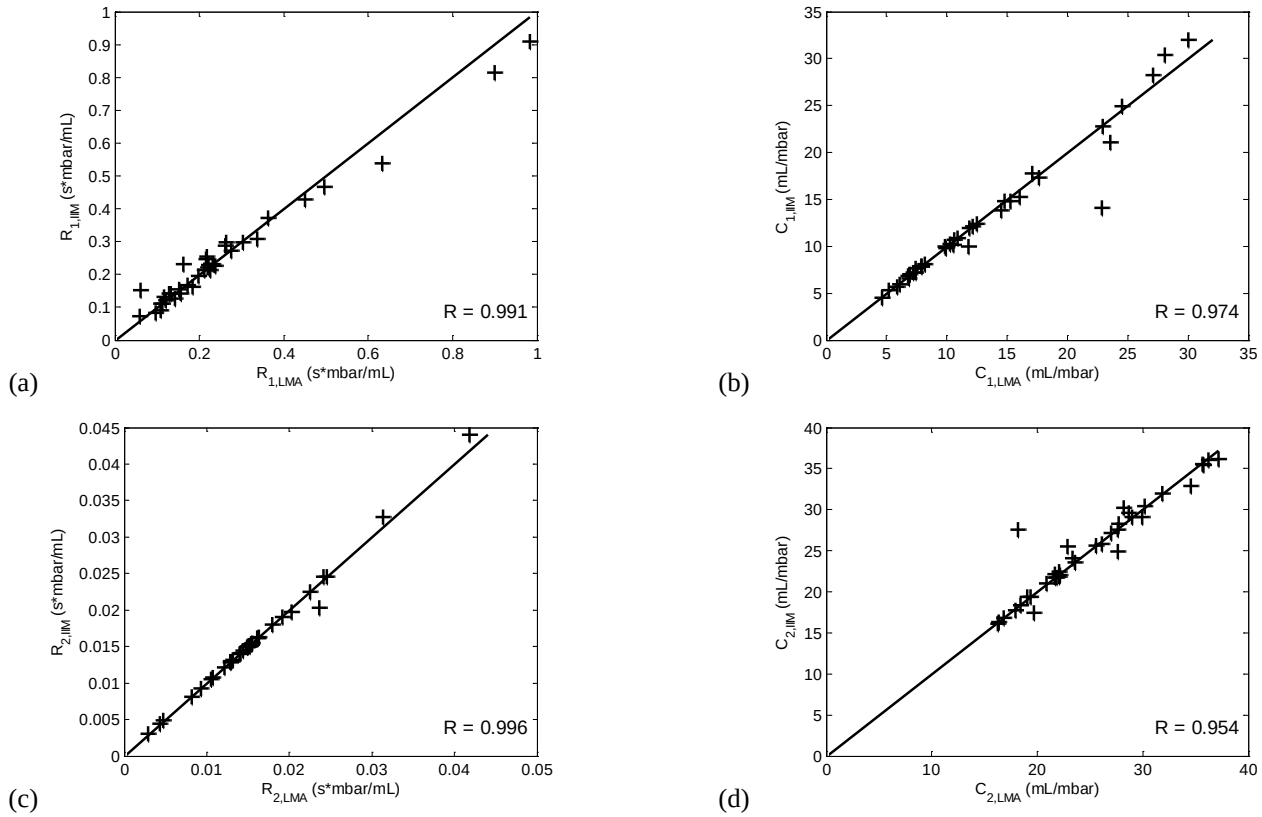

Figure 3. Correlation of the IHM parameter values (R_1, C_1, R_2, C_2) identified by the Levenberg-Marquardt Algorithm (LMA) and by the Iterative Integral-Based Method (IIM) of 36 data sets.

presented shows that the IIM also seems superior to error-mapping methods with respect to efficiency and thus shows potential to be implemented in real-time, patient-specific ventilation management.

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