A forward model for maximum expiration

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Abstract

The maximum expiratory flow–volume (MEFV) curve is a sensitive test of respiratory mechanics. Several mathematical models for forced expiration have been developed, but they suffer from various shortcomings. It is impossible to calculate the parts of the MEFV curve beyond the flow limiting conditions and computational algorithms do not allow a direct calculation of maximal flow. In the present work a complex, nonlinear forward model, including exciting signal and static recoil pressure–lung volume descriptions and 132 parameters, has been constructed. Direct determination of maximum flow is achieved by means of successive approximation algorithm. The model enables prediction of flow during forced expiration in the whole range of forced vital capacity. © 1998 Elsevier Science Ltd. All rights reserved.

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1. Introduction

The plot of maximum expiratory flow versus exhaled air volume in the whole range of forced vital capacity (FVC) of the lungs (the MEFV curve) is highly reproducible in a given subject and effort-independent for a wide range of FVC. It should be noted that FVC is a volume of air measured during expiration as deep and quick as possible, preceded by maximum expiration, in opposition to vital capacity (VC), measured in the similar circumstances with air exhaled quietly. (Usually FVC is a little bit smaller than VC, which is probably caused by airway collapsing during the last stage of expiration [1]). The MEFV
manoeuvre is a sensitive test of respiratory mechanics since its shape strongly depends on the physical properties of the airways and the lungs.

One of the first ways of MEFV curve prediction on the ground of its mathematical description was the model based on the differential equation of flow [2, 3]. At the beginning, the respiratory system was studied as a uniform elastic tube situated in a pressure environment, like that of the pleural pressure of the lungs, and afterwards the Weibel symmetrically branching model of the bronchial tree was utilized. The maximum airflow could be predicted from the physical properties of the flow-limiting segment, i.e. the bronchial tree cross-sectional area dependence on the transmural pressure and the position along the tree. Although the predicted values of maximum flow at high lung volumes were reasonable, at lower volumes the values of flow were too high. Similar, simplified models focusing on local mechanisms of flow limitation were also proposed later [4, 5]. Useful descriptive approaches were presented by Mead et al. [6] and Pride et al. [7]. The analyses were conceptually useful, but the former did not explain the exact mechanisms leading to flow limitation, and the latter did not allow to predict maximum flow. Shapiro [8] showed that flow limitation may occur in collapsible tubes by purely viscous dissipation and Dawson and Elliott [9] explained the mechanism limiting forced expiratory flow on the basis of the local speed of wave propagation at the point (called the choke point) in the intrathoracic airways. The predictions of the wave-speed theory were tested successfully by Hyatt et al. [10]. They showed that wave-speed is the mechanism for flow limitation at high and mid-lung volumes. This theory and the phenomenological description of pressure losses were used by Lambert et al. [11] to create the mathematical model of maximum expiratory flow. The expression for the pressure gradient in the airways was integrated along the bronchial tree from the alveoli to the end of the trachea for a given value of flow and the total area of all tubes of each generation. The model predictions agreed with published values of maximum flow dependence on gas density and viscosity. The authors concluded that at high and middle lung volumes, maximum flow is determined by the wave-speed mechanism, and at low volumes by the coupling of viscous pressure losses and airways’ mechanical properties.

In spite of the above achievements, the hitherto existing models suffer from various shortcomings. The first of them is lack of an exciting signal description, which makes it impossible to calculate the first and last part of the MEFV curve. The airway properties were usually treated as global features of a uniform tube without differentiation between separate canals, and all the airway generations were assumed to be surrounded by the lung parenchyma, although the trachea and a part of the first generation lie outside the pleura. Moreover, the computational algorithms did not allow a direct calculation of maximal flow, but the authors were reconstructing it on the basis of simulated iso-volume flow–pressure curves or graphically. Each generation of the airways is described by a few parameters and so are properties of the lung (i.e. the alveoli region and the parenchyma), etc. In effect the models include up to several dozen parameters. This is why they enable only prediction of flow on the basis of known parameters’ values (the forward problem) and do not allow to measure the parameters on the ground of the experimental data (the inverse problem).

The far-reaching purpose of the author’s investigation is solving the inverse problem in forced expiration, i.e. the elaboration of a noninvasive method for estimation of respiratory system properties on the ground of experimental data obtained during this test. A forward–inverse method [12] has been chosen to construct an identifiable and valid model of the
phenomenon under investigation. This methodology allows a simulative validation of the inverse model. It utilizes an extremely complex, usually nonlinear and unidentifiable model of the system to simulate measuring data and as a subject of further reduction. The present paper shows the creation of the complex model for maximal expiration as the first stage of the forward–inverse modelling.

2. Model formulation

2.1. Model for the driving pressure

The details of the driving pressure model have been described elsewhere [13, 14]. Briefly, a pneumatic model of the respiratory system composed of a cylinder, a piston with springs causing its movement and an outlet tube has been proposed. Classical mechanics and gas physics in quasistatic conditions have been used to derive the mathematical model for forced expiration. Neglecting accretion of expiratory muscle power, thorax inertia and compressibility of air, a linear relationship between airflow \( Q \) and lung volume \( V_L \) has been achieved. It results in exponential dependence of expired air volume \( V \) on time \( t \) [13], used also in former papers, e.g. [15].

Analysis of the three phenomena mentioned has revealed the importance of one of them only, i.e. the accretion of the expiratory muscle power [14]. Assuming that the muscle power increases exponentially (which can be deduced from data of Agostoni and Fenn [16]), the pressure \( P_e \) developed by the respiratory muscles is as follows:

\[
P_e(V) = \frac{P_m}{V_C} (1 - e^{-t/\tau})(V_C - V), \tag{1}
\]

where \( P_m \) is the maximal expiratory pressure that can be produced by muscles and elastic forces of the thorax, \( V_C \) is the vital capacity, \( \tau \) is the time constant. Eq. (1) is essentially the same as the one recently used by Barnea et al. [17]. The pressure \( P_e \) consists of two components: the driving pressure \( P_d \) (i.e. the difference between alveolar and barometric pressures) and pressure losses caused by respiratory tissue resistance \( R_T \) during airflow \( Q \)

\[
P_e = P_d + R_T Q. \tag{2}
\]

Finally, substituting Eq. (1) in Eq. (2) yields a formula for the driving pressure \( P_d \)

\[
P_d(V) = P_m(1 - e^{-t/\tau})\left(1 - \frac{V}{V_C}\right) - R_T \cdot Q. \tag{3}
\]

2.2. Model for airflow in a compliant tube

A unified mathematical model for steady airflow in a compliant tube (bronchi and bronchioli) during maximal expiration can be expressed as a dependence of lateral pressure gradient on the locus along the tube, and it takes into account dissipative pressure losses, the
relationship between tube cross-sectional area $A$ and transmural pressure $P_{tm}$ as well as the longitudinal variation of a tube neutral cross-sectional area $A_0$ [18] (the neutral cross-sectional area $A_0$ is an airway cross-sectional area at zero transmural pressure)

$$\frac{dP_{lt}}{dx} = \left\{ \frac{\rho q^2}{A^3(x)} \left( \frac{\partial A}{\partial A_0} \right) \frac{dA_0}{dx} - f(x) \right\} \div \left\{ 1 \left( \frac{\partial A}{\partial P_{tm}} \right) \right\}$$

where $f(x)$ is the dissipative pressure loss per unit of distance, $\rho$ is the gas density and $q$ the airflow in a tube. Function of the dissipative pressure loss, provided by Reynolds as a result of studies on expiratory flow in bronchial casts [19], is a sum of laminar and turbulent factors

$$f = \left( a + b \cdot \frac{2pq}{\mu \sqrt{\pi A}} \right) \cdot \frac{8\pi \mu q}{A^2},$$

where $a$, $b$ are proportionality coefficients and $\mu$ the gas viscosity.

The relationship between the cross-sectional area ($A$) and the transmural pressure ($P_{tm}$) was approximated by two nonlinear functions matching at zero transmural pressure. For $P_{tm} < 0$ Shapiro [8] and Lambert et al. [20, 11] proposed similar hyperbolae with a coefficient multiplied by $P_{tm}$ depending on this pressure and a constant exponent $n$, or the coefficient and the exponent varying with the generation number, respectively. The latter has been chosen in this work (Eq. (6)). For $P_{tm} > 0$ the exponential relationship has been used.

$$A = A_0 \cdot \left( 1 - \frac{\gamma}{n \cdot A_0} \cdot P_{tm} \right)^{-n} \quad P_{tm} < 0$$

$$A = A_m - (A_m - A_0) \cdot \exp \left( - \frac{\gamma}{A_m - A_0} \cdot P_{tm} \right) \quad P_{tm} \geq 0,$$

where $A_0$ is the neutral cross-sectional area and $A_m$ the maximal cross-sectional area of an airway. The neutral elementary compliance $\gamma$ defined as

$$\gamma = \left( \frac{\partial A}{\partial P_{tm}} \right)_{P_{tm}=0}$$

and has a value yielded by matching the slopes of the curves at $P_{tm} = 0$.

The assumption of constancy of the neutral cross-sectional area in a given bronchus ($dA_0/\ dx = 0$) was taken and Eq. (4) simplified to the form derived previously by Lambert et al. [11]

$$\frac{dP_{lt}}{dx} = \frac{-f(x)}{1 - \rho q^2/A^3(x)(\partial A/\partial P_{tm})^2}.$$

2.3. Model for lateral pressure drop along the bronchial tree

The idealized lung geometry of Weibel [21] is the anatomical basis for the model. The airways are assumed to form a symmetrically bifurcating tree with the generation number $g$ ranging from 0 at the trachea to 23 at the most peripheral bronchioli [22]. The pressure drop
along each of the airways from the generation $g$, $\Delta P_{lt}(g)$, can be calculated by integrating Eq. (8) on the airway length $L$. Because the neutral cross-sectional areas were assumed to be constant, there is a difference between the cross-sectional area of a mother tube and the sum of the daughters’ ones at the point of branching. The transition from one generation to the next takes place over such a short distance that dissipation is negligible, and the additional pressure drop $\Delta P_{lt}(g)$ arises from the convective losses only [11]

$$\Delta P_{lt}(g) = \frac{1}{2} \rho q^2(g) \cdot \left( \frac{1}{4} A_L^g(g + 1) - \frac{1}{4} A_0^g(g) \right),$$

where $A_L$ is the cross-sectional area at the end of the bronchus and $A_0$ the cross-sectional area at the beginning of the bronchus. The pressure losses due to branching may be neglected [5].

Since the glottis varies with airflow and lung volume, the pressure loss in the mouth $\Delta P_U$ has been estimated according to the experimentally derived formula [23, 24], used also by Pardaens et al. [5]

$$\Delta P_U = R_U Q',$$

where $R_U$ is an airflow resistance coefficient, $r$ is an exponent of value between 1.5 and 2.0, and $Q$ denotes flow in the mouth.

On the basis of Weibel’s anatomical model it is possible to sum pressure losses in the intrathoracic and extrathoracic airways, the mouth (the sum denoted as $\Delta P_{lt}$) and to equate it with the driving pressure $P_d$

$$\Delta P_{lt} = \sum_{g=23}^{0} \Delta P_{lt}(g) + \sum_{g=22}^{0} \Delta P_{lt}(g) = P_d. \quad (11)$$

2.4. Other dependencies

Other dependencies between physiological quantities of the respiratory system used in the model have been based on the published results. Intapleural bronchi lengths $L$ change with the cube root of lung volume $V_L$ [3, 25]

$$L(V_L) = L_{RV} \left( \frac{V_i + V_L}{V_i + RV} \right)^{1/3},$$

where RV is the residual volume of the lung, $L_{RV}$ the airway length at residual volume and $V_i$ the lung tissue volume.

Static recoil pressure of the lung is given as a logarithmic function of lung volume [26]

$$P_{st}(V_L) = \frac{V_m - V_0}{C_{L0}} \cdot \ln \left( \frac{V_m - V_0}{V_m - V_L} \right),$$

where $P_{st}$ is the static recoil pressure of the lung, $V_m$ and $V_0$ the maximal and minimal lung volume and $C_{L0}$ the lung compliance at zero recoil pressure. The relationship between instant lung volume $V_L$ and volume of expired air $V$ can be simply expressed (neglecting gas
compressibility) as follows [1]

\[ V_L = VC + RV - V. \] (14)

Airflow \( q \) in the tube of generation \( g \) in the dichotomous bronchial tree is calculated according to the formula

\[ q(g) = Q \cdot 2^{-g}. \] (15)

3. Computer implementation of the model

3.1. Forward algorithm

Calculation of airflow for \( N \) values of expired gas volume occurs according to a successive approximation scheme (Fig. 1). For each value of \( V \) an approximate value of airflow \((Q_{\text{approx}})\) is estimated (higher than a half of maximal possible flow at this lung volume) and Eq. (9) is solved at the entrance of each generation \((g < 23)\). Then Eq. (8) is integrated along

![Fig. 1. Scheme of the forward algorithm (see text for explanation and notation).](image-url)
each generation over its length by means of the fourth-order Runge–Kutta method with adaptive stepsize control [27] and Fehlberg coefficients, using the airway area and compliance for the local value of $P_{tm}$ at each point. This procedure of determining pressure is repeated for every generation to the end of the trachea and then the pressure loss in the mouth is added. Generations 2–23 were accounted for the intrapleural ones, thus transmural and lateral pressures are equal in generations 0 and 1.

If flow limitation (FL) is detected during computation, the value of airflow is decreased by one half in the next loop. Otherwise, it is checked if the difference between the driving pressure and instant lateral pressure drop in the airways is sufficiently small, or if the last change of flow is negligible. If not, the airflow value is increased or decreased by half depending on this pressure difference sign. With every next loop the airflow alteration is a half of the former value.

Detection of flow limitation during forced expiration is an essential function of the algorithm. Flow limitation may occur in two instances. The first one is when flow used in calculations exceeds the critical value of pressure disturbances wave speed in some point along the bronchial tree (Fig. 2). This is found during integration of the Eq. (8) when the second term of the denominator is higher than or equal to 1 (FL = TRUE). The second case relates to the junction between two generations. To compute the pressure loss $\Delta P_{lt}^{(g)}$ at this point, Eq. (9) has been transformed into the following shape

$$h(\Delta P_{lt}^{(g)}) = \frac{1}{2} \rho q^2(g) \cdot \left( \frac{1}{4 \cdot A_{1}^{1}(g+1)} - \frac{1}{A_{0}^{2}(g)} \right) - \Delta P_{lt}^{(g)}$$

and the roots of function $h$ are found by means of the Newton–Raphson method [27]. The curve $h$ may present one or two roots in the physiological range, depending on the flow rate (Fig. 3). The higher value of $\Delta P_{lt}^{(g)}$ corresponds to a stable condition [5] and is taken into account in calculations. When the sum of two cross-sectional areas of generation $g + 1$ is bigger than the cross-sectional area of generation $g$, the increasing flow results in bringing the two roots (stable and unstable) closer and they couple when the flow rate is critical. In the case

![Fig. 2. Lateral pressure drop along the 2nd generation bronchus for $P_{tm}=0$ at the beginning of the airway and different rates of flow: (A) $Q = 1$ l/s, (B) $Q = 5$ l/s, (C) $Q = 6$ l/s; flow limitation exists between 5 and 6 l/s.](Fig. 2.png)
in which there is no real solution, the flow rate used in calculations is considered to exceed the critical value (FL = TRUE).

Accuracy of flow calculations $e_q$ has been evaluated as corresponding to 1 bit resolution of a commonly used 12-bit analog-to-digital converter cooperating with a flow transducer of the range $20 \text{l/s}$

$$
e_q = 0.01 \text{l/s} \approx \frac{40 \text{l/s}}{212}$$

and pressure accuracy $e_p$ as a product of minimal respiratory resistance and $e_q$

$$
e_p = 200 \text{Pa l/s}, \quad e_q = 2 \text{Pa}.$$

### 3.2. Parameter values

During computer implementation of the model it was necessary to make a choice between a number of anatomical and physiological data.

The main point in selecting parameter values is a proper description of airway properties because they mostly influence the MEFV curve shape. The data of Lambert [20] was chosen for several reasons: he used airway parameter values basing on Hyatt’s data [10] for the central airways, Weibel’s data [21] for the more peripheral ones and Reynolds’s coefficients [19] for frictional losses of pressure; the elementary equations describing airflow in the bronchial tree were similar or the same as in the present study. His data was consistent with results of experiments. The airway properties were used in [20] for the case of one uniform tube standing for each generation. Since it was too general for our purposes, their values had to be divided by the amount of the tubes in a given airway generation. Simultaneously airway lengths were rescaled from 75% of total lung capacity (TLC = VC + RV) to RV value. Airway parameters

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![Fig. 3. Roots (→) of the function $h$ for the 9th airway generation with $P_{tm} = 500 \text{ Pa}$ at the end of a former generation and different rates of airflow: (A) $Q = 0.1 \text{ l/s}$, (B) $Q = 14 \text{ l/s}$, (C) $Q = 20 \text{ l/s}$; flow limitation exists between 14 and 20 l/s.](image-url)
beyond generation 16 were extrapolated using their exponential regression on generation number \((g = 10–16, \text{correlation coefficients lower than } -0.99)\).

The volume properties of the lungs (RV and VC) were taken from the CECA standard tables for a 25-year old man of 176 cm height (1.5 and 5.6 l, respectively), with FVC a little bit smaller than VC (5.5 l). Minimal lung volume ranges roughly between 15\% [11] and 25.5\% [5] of TLC and in this research it was assumed to be about 20\% of TLC (1.4 l). The data of Colebatch et al. [26] was used to evaluate maximal lung volume as approximately 106\% of TLC (7.5 l) and lung compliance at zero static recoil pressure \((5.7 \text{ l/kPa})\) was computed according to Eq. (13), assuming that \(P_{st} = 3 \text{ kPa}\) at \(V_L = 95\% V_m\).

Maximum expiratory pressure was designated by Aguilar et al. [28] as 24 kPa and the time constant of expiratory muscles constriction can be deduced from [16] (0.2 s). Lung tissue resistance was accepted on a 500 Pa/l/s level. The difference exists between proposed values for \(R_U\) and \(r\) [23, 24]. For calculations mean values were taken: \(R_U = 1.2E7\) and \(r = 1.68\) (pressure given in Pa and flow in m³). Air viscosity and density were taken for expired gas temperature \(34^\circ C\) [29]. The summary of the model parameters is given in Table 1.

### 3.3. Simulative investigations

The set of Eqs. (3), (5), (6) and (8)–(18) has been used to calculate airflow values for the given respiratory properties in the range of FVC (Fig. 4), according to the scheme shown in Fig. 1. Then the airway resistance has been computed for airflow \(Q = 1\) l/s and functional residual capacity of the lung \(FRC = 2.5\) l:

![Fig. 4. Simulated MEFV curve of the forward model.](image)
The validity of the model has been additionally checked by using it to make predictions concerning experimentally documented phenomena: influences of patient’s effort and external flow-resistance. In the first case alternation of expiratory muscle force has been simulated by simultaneous decreasing maximal pressure $P_m$ and increasing time constant $\tau$ (Fig. 5). In the second simulation the external, linear flow-resistance $R_0$ has been added at the mouth with remaining settings of the model being unchanged (Fig. 6).

\[
R_{aw} = \frac{\Delta P_R(FRC, Q)}{Q} = 0.24 \text{ kPa/l/s.}
\]  

(19)

Fig. 5. Influence of patient’s effort on MEFV curve: (A) $P_m=24$ kPa, $\tau = 0.2$ s, (B) $P_m=15$ kPa, $\tau = 0.3$ s, (C) $P_m=10$ kPa, $\tau = 0.4$ s.

Fig. 6. Influence of external resistance on MEFV curve: (A) $R_0=0$ kPa/(l/s), (B) $R_0=0.25$ kPa/(l/s), (C) $R_0=0.5$ kPa/(l/s).
4. Discussion

Construction of a complex model for maximum expiration and its computer implementation was the aim of this study. It should be mentioned that a number of simplifying assumptions have been used. The very general ones are: flow is steady and air is incompressible, thus the effects of energy accumulation and restoration due to airway and thorax compliance, tissue inertia and gas density variation are neglected; the bronchial tree is fully symmetrical, surrounded by uniform pleural pressure with the same air-temperature at every point, so no kind of inhomogeneities is taken into account. The first airway generation is assumed to be extrapleural, in spite of the fact that approximately one half of it lies inside parenchyma. Change of anatomical dead space with lung volume is not considered in the model either, though it may produce additional flow and expired air volume [5].

The forward model is characterized by some new properties in comparison to the former ones. The main features are: a mathematical description of the exciting signal, i.e. driving pressure dependence on lung volume and direct computation of MEFV curve instead of constructing iso-volume flow–pressure curves or graphical methods. The experimental relationship between lung volume and static recoil pressure is replaced with the algebraic formula. Airway generations 0–23 are taken into account with the trachea and main bronchi situated outside the pleura. This approach is more realistic than the previous ones, where only generations 0–16 were considered, all subject to the pleural pressure.

The basic model equations connected with flow limitation in the airways are the same or similar to those used by Lambert et al. [11]. The agreement between results of Lambert’s model and empirical data was good in case of density and viscosity dependency of maximum flow and static recoil pressure influence on maximal flow for different gases. The location of the equal pressure point (EPP) and the flow limiting segment (FLS) were in good coherence with the documented data, too. Thus validity of that model for maximum expiration was proved. Even in a simpler model, not incorporating wave-speed theory, the agreement between experimental results and model simulations (airway resistance–lung volume relationship, location of the EPP, influence of changes in inhaled gas density and viscosity) was generally satisfying [5]. The above provides validity of the forward model presented in this paper in the range of lung volumes, when airflow limitation occurs.

Additional predictions concerning influence of patient’s effort and external flow-resistance confirmed qualitative validity of the forward model also for low volumes of expired air, when flow limitation does not exist. Muscle power reduction changes only the first part of the MEFV curve, leaving the second half of FVC unchanged (Fig. 5), as it has been reported since the establishing this form of maximum expiration presentation by Hyatt et al. [30]. In a similar way, additional flow-resistance enlargement decreases maximum flow in the same part of the MEFV curve (Fig. 6), which was also presented in clinical conditions by Mead et al. [6]. Furthermore, airflow yielded by the model as well as the calculated value of the airway resistance (Eq. (19)) are also in good coherence with clinical data.
5. Summary

A complex, nonlinear forward model, based on acceptable data for gas physics and the anatomy and physiology of the lungs and including 132 parameters, has been constructed. Besides previously known quantitative relationships, it incorporates the exciting signal and static recoil pressure–lung volume descriptions, as well as the symmetrical model for the bronchial tree of 23 airway generations. The model enables prediction of flow during maximum expiration in the whole range of forced vital capacity. Its validity was shown for both ranges: when flow limitation occurs and when it does not. Direct determination of maximum flow for a given volume of expired air is an important feature of the forward model. It was achieved by means of successive approximation algorithm.

The next step in elaboration of a method for respiratory mechanical parameters estimation on the ground of forced expiration data, according to the forward–inverse modelling, is the complex model reduction. Several well-known techniques, as aggregation of parameters, simplification of mathematical formulas (i.e. their linearization) or acceptance of reported relationships between parameters, can be applied. The resulting reduced model should be identifiable and ought to be considered as still valid.

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References


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