Mathematical modelling and curve fitting for the study of respiratory system parameters

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Abstract
The target of this study was the development of mathematical models that best describe the behaviour of respiratory parameters.
First of all, we studied lung volume in relation to time both for normal and maximal inspiration/expiration by developing mathematical models. For the construction of these equations the exponential model was used.
Then we tried to study the flow-volume of a typical spirometer curve by dividing it into two parts: the first part reaches the Peak Expiratory Flow (PEF) point and the second follows until the volume reaches Vital Capacity (VC). For the first part we built an exponential equation; for the second part a number of existing prediction equations for the flow in various points of VC were used.
For the volume-pressure diagram, we built exponential equations that describe the volume-pressure relation below Vo (Vo: lung volume where pressure is zero). The equations were coupled for expiration and inspiration.

Keywords:
Mathematical models; curve fitting; respiratory system.

1. Introduction

Most parameters that describe the function of respiratory system are well defined but the number of the existing mathematical models is inadequate. The basis of this study is a number of mathematical models that were determined either by the completion of previous research work or by our team. So, the research findings of the near past about Caucasian subjects of all ages (the African and Asian origin subjects are not included in this study) helped us specify the value of many respiratory parameters [Hankinson (1999)], [Roberts (1991)], [Manzke (2001)], [Kapp (1988)], [Gibson (1979)], [Colebatch (1979)], [Wilson (1984)]. In combination to them, and in order to control the diagrams we constructed our own mathematical models.
Finally, the definitions of the main parameters used in this study should be added. According to American Thoracic Society (ATS), Vital Capacity (VC) is the maximal volume of air exhaled from the point of maximal inhalation, Forced Vital Capacity (FVC) is the maximal volume of air exhaled with maximally forced effort from a position of maximal inhalation, i.e., vital capacity performed with a maximally forced expiratory effort and Peak Expiratory Flow (PEF) is the largest expiratory flow achieved with a maximally forced effort from a position of maximal inspiration [American Thoracic Society (1995)]. Moreover, Total Lung Capacity (TLC) is the volume of gas in the lungs at the end of a maximal inspiration, Residual Volume (RV) is the volume remaining after a maximal inspiration, Functional Residual Capacity (FRC) is the lung volume at the end of a normal expiration and Tidal Volume (V_T) is the air volume a person inhale or exhale during a normal breath [Lumb (2000)]. The other parameters will be, briefly, explained in text.

2. Data structures and mathematical equations

For the implementation of the study numerous mathematical equations were used. As mentioned above, some of them were extracted from bibliography and our team developed the rest.
For the dynamic representation of lung volume in relation to time and for normal and maximal inspiration/expiration we developed our own equations. In both cases we made the assumption that inspiration and expiration last for a period of 4 seconds (15 breaths/minute) [Lumb (2000)]. For the construction of these equations the exponential model was used. The diagrammatic representation of an exponential model results to a curve that fits well to the curve proposed on various citations [American Thoracic Society (1995)], [Lumb (2000)] for the description of volume change during breath cycle. This is the reason we selected this mathematical method among others. The exponential model was applied in the case of normal inspiration/expiration:

$$V_I = FRC + V_T*(1 - e^{-t/0.5}) \quad (1)$$

$$V_E = FRC + V_T*e^{-t/0.5} \quad (2)$$

where V_I is the inspired and V_E is the expired lung volume at a particular time point of breath cycle, FRC is the functional residual capacity and V_T is the tidal volume. All volumes are measured in liters.
The same mathematical method was used to describe the lung volume behaviour during maximal inspiration/expiration:

$$V_I = FRC + (TLC - FRC)*(1 - e^{-t/0.5}) \quad (3)$$

$$V_E = RV+VC*e^{-t/0.5} \quad (4)$$

where V_I is the inspired and V_E is the expired lung volume at a particular time point of breath cycle, FRC is the functional residual capacity, TLC is the total lung capacity, RV is the residual volume and VC is the Vital Capacity. All volumes are measured in liters.
In both cases the time constant is equal to 0.5 [Lumb (2000)]. The equations used for the calculation of TLC, FRC and RV came up as previous research findings [Roberts (1991)], [Manzke (2001)] for Caucasian subjects of all ages; these equations are presented in “Table 1”. Additionally, VC is equal to TLC-RV and V_T is the 10% of total lung capacity [Cherniack (1992)].
The diagrammatic output of the mathematical equations appeared above is viewed in “Figure 1” and corresponds to a 20 years-old male person, of 170 centimetre height and 40 kilogram weight. In this figure, the curve loops that correspond to normal and to maximal inspiration/ expiration are clearly viewed.

Table 1
Prediction equations used for the calculation of lung volumes and capacities appeared in the second section of the system for the black race. TLC: Total Lung Capacity in liters, FRC; Functional Residual Capacity in liters, RV: Residual Volume in liters, h: height in meters, a: age in years, w: weight in kilograms

	TLC	FRC	RV
Men	7.956*h-6.948	7.502*h+0.009*a-0.033*w-7.608	3.380*h+0.020*a-0.014*w-3.927
Women	7.107*h-6.435	5.867*h+0.009*a-0.022*w-5.972	2.548*h+0.017*a-3.387
Boys	exp(-1.3191+ 1.7383*h)	exp(-1.8195+1.6779*h)	$0.0046+0.1473*h^3+2.8681/a$
Girl	exp(-1.2940+ 1.7021*h)	exp(-2.0159+1.7942*h)	$-0.2189+0.2042*h^3+3.6015/a$

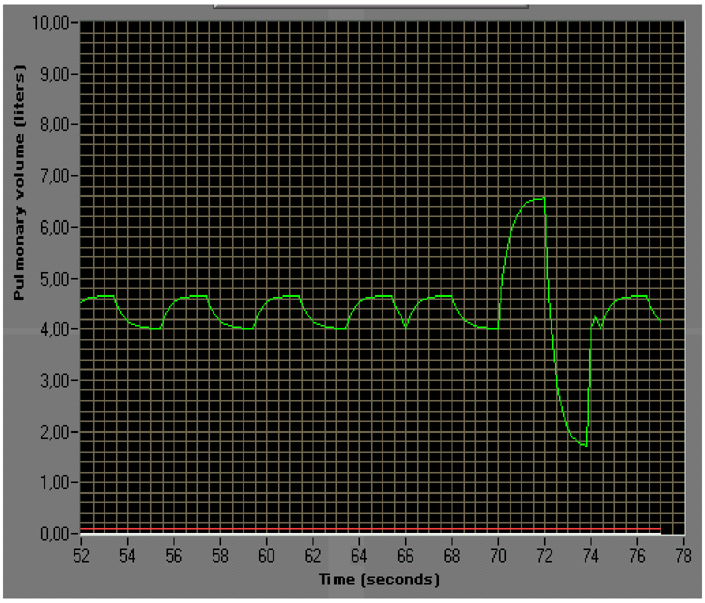

Figure 1: Lung (pulmonary) volumes in relation to time.

For the flow-volume diagram we tried to present it by the most coherent way. For this purpose, we analyzed the flow-volume curve of a typical spirometer and divided it into two parts: the first part reaches the Peak Expiratory Flow (PEF) point and the second follows until the volume reaches Vital Capacity (VC). PEF normally occurs the first 0,1 sec of the forced expiratory maneuver. So, according to "Equation (4)", if t = 0.1 sec, we get that PEF occurs when V = 0.18*VC. Considering this result, for the first part of the flow-volume curve we built an exponential equation:

$$\dot{V} = PEF*e^{-V/0.03*VC} \qquad (5)$$

where $\dot{V}$ is the instantaneous forced expiratory flow in liters/sec, PEF is the Peak Expiratory Flow in liters/sec, VC is the Vital Capacity in liters and V receives values until it is equal to the 18% of VC. The constant is the product of 0.03 multiplied by the absolute value of VC. VC is the difference TLC-RV, where TLC and RV are calculated using the equations mentioned above. The values of PEF are estimated using prediction equations, which were extracted from the Hankinson and coworkers [Hankinson (1999)] and Roberts and coworkers [Roberts (1991)] research efforts and are presented in "Table 2".

Table 2
Prediction equations used for the calculation of PEF appeared in the third section of the system. PEF: Peak Expiratory Flow in liters/sec, h: height in centimeters and a: age in years.

	PEF
Men	1.0523+0.08272*a-0.001301*a*a+0.00024962*h*h
Women	0.9267+0.06929*a-0.001031*a*a+0.00018623*h*h
Boys	-0.5262-0.12357*a+0.013135*a*a+0.00024962*h*h
Girls	-3.6181+0.60644*a-0.016846*a*a+0.00018623*h*h

Table 3
Prediction equations used for the calculation of flows parameters appeared in the third section of the system. $\dot{V}_x$: flow at a x point of Vital Capacity in liters/sec, a: age in years and h: height in cm

Flow	Men ≥ 25 years	Women ≥ 20 years	Men<25 years	Women<20 years
$\dot{V}_{25}$	-5.618-0.035*a+0.088*h	-0.132-0.025*a+0.043*h	-7.054+0.147*a+0.070*h	-3.365+0.144*a+0.044*h
$\dot{V}_{30}$	-5.492-0.029*a+0.084*h	0.605-0.023*a+0.037*h	-6.590+0.129*a+0.068*h	-3.514+0.131*a+0.046*h
$\dot{V}_{40}$	-5.643-0.018*a+0.077*h	0.952-0.017*a+0.031*h	-5.188+0.126*a+0.056*h	-3.480+0.094*a+0.046*h
$\dot{V}_{50}$	-5.400-0.015*a+0.069*h	-0.444-0.013*a+0.035*h	-4.975+0.081*a+0.051*h	-2.531+0.120*a+0.034*h
$\dot{V}_{60}$	-3.152-0.015*a+0.050*h	0.083-0.013*a+0.027*h	-4.385+0.053*h	-1.522+0.123*a+0.023*h
$\dot{V}_{70}$	-4.650-0.011*a+0.050*h	0.808-0.014*a+0.017*h	-2.980+0.039*h	0.757+0.166*a
$\dot{V}_{75}$	-4.143-0.012*a+0.044*h	3.042-0.014*a	-2.455+0.032*h	0.692+0.139*a
$\dot{V}_{80}$	-3.205-0.013*a+0.035*h	2.610-0.015*a	-3.098-0.052*a+0.039*h	0.643+0.114*a
$\dot{V}_{90}$	-3.031-0.008*a+0.026*h	1.632-0.012*a	-2.120-0.054*a+0.027*h	-0.626

For the second part of the curve a number of prediction equations by Roberts and coworkers [Roberts (1991)] for the flow in various points of VC were used and are presented in "Table 3". In this table flow is denoted by $\dot{V}$ and the numeric indices (25, 30, 40 etc.) below $\dot{V}$ denote the VC point. This part of the curve is constructed if we connect the points that have as y-coordinate the value of flow at a specific VC point (x-coordinate). Finally, another parameter that is used for the study of the diagram is angle β that was proposed by Kapp and coworkers for the assessment of a patient status [Kapp (1988)]:

$$\beta = 180^o - \tan^{-1}\frac{PEF - TLC*0.5}{1/2*FVC} + \tan^{-1}\frac{TLC*0.5}{1/2*FVC} \quad (6)$$

where PEF (Peak Expiratory Flow) and TLC (Total Lung Capacity) are calculated as mentioned above and FVC (Forced Vital Capacity) is equal to VC [American Thoracic Society (1995)].
The diagrammatic output of the mathematical equations regarding flow-volume diagram is viewed in "Figure 2" and corresponds to a 40 years-old male person, of 170 centimetre height and 60 kilogram weight.
For the volume-pressure diagram, we followed the structure of the exponential equations developed by researchers for volumes up to Vo (Vo is the lung volume where pressure is zero) [Gibson (1979)], [Colebatch (1979)]. Using the same basis we built exponential equations that describe the relation volume-pressure below Vo. The equations are coupled for expiration and inspiration. So, for expiration and above Vo we used the equation developed by Gibson and coworkers [Gibson (1979)]:

$$V_E = TLC - (TLC - Vo)*e^{-Ke*P} + RV \quad (7)$$

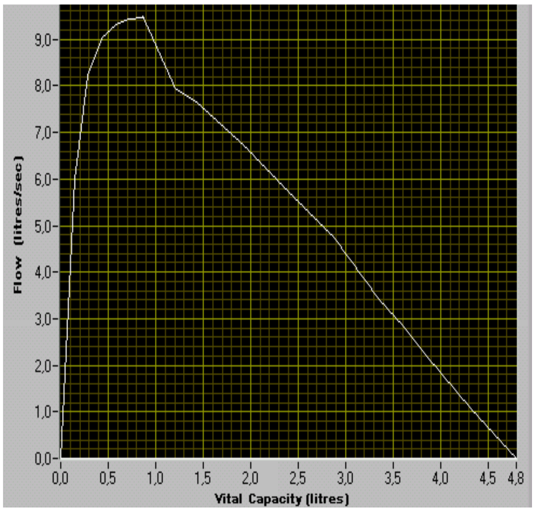

Figure 2: Flow in various points of Vital Capacity

In order to describe expired lung volume in relation to pressure and below Vo, we followed the same methodology:

$$V_E = Vo*e^{Ke*P} + RV \quad (8)$$

In both "Equation (7)" and "Equation (8)", V_E is the expired lung volume in liters, Vo is the lung volume (where pressure is zero) in liters, Ke is an expiration constant in cmH_2O^{-1}, TLC is the total lung capacity in liters, RV is the residual volume in liters and P is the pressure at any lung volume in cmH_2O. P gets its maximal value when lung volume is equal to TLC and its minimum when lung volume is equal to RV. These pressure values are calculated according to equations that will be mentioned below. Vo and Ke are calculated, again, by Gibson and coworkers equations [Gibson (1979)]:

$$Vo = TLC*(0.601*a - 8.49) \quad (9)$$
$$Ke = 6.64*10^{-4}*a + 0.082 \quad (10)$$

where a: is the age in years.
In the case of inspiration the "Equation (7)" and "Equation (8)" are repeated but V_E and Ke are replaced with V_I (inspired lung volume) and Ki (K inspiration). Ki was calculated in Gibson and coworkers research [Gibson (1979)]:

$$Ki = 6.64*10^{-4}*a + 0.050 \quad (11)$$

where a: is the age in years. For Vo in inspiration Colebatch and coworkers developed a set of equations for females and males, accordingly [Colebatch (1979)]:

$$Vo = TLC - TLC*(1.04 - 0.00517*a) \quad (12)$$

$$Vo = TLC - TLC*(1.17 - 0.00624*a) \quad (12)$$

where a: is the age in years. The TLC and RV quantities are calculated from the same equations appeared in "Table 1".
As mentioned above, for the completion of the diagram the estimation of maximal and minimum pressures (inspiratory and expiratory) is required. The maximal pressures were calculated by Wilson and coworkers [Wilson (1984)] and are presented in "Table 4". The minimums are, usually, negative and are equal to the 1/3 of maximal ones [Cherniack (1992)].

Table 4
Prediction equations used for the calculation of maximal pressures appeared in the third section of the system. $Pi_{(max)}$: maximal inspiratory pressure in cmH_2O, $Pe_{(max)}$: maximal expiratory pressure in cmH_2O, h: height in centimeters, a: age in years and w: weight in kilograms.

	$Pi_{(max)}$	$Pe_{(max)}$
Men	142-(1.03*a)	180-(0.91*a)
Women	-43+(0.71*h)	3.5+(0.55*h)
Boys	44.5+(0.75*w)	35+(5.5*a)
Girls	40+(0.57*w)	24+(4.8*a)

Finally, the diagrammatic output of the mathematical equations regarding volume-pressure diagram is viewed in "Figure 3" and corresponds to a 40 years-old male person, of 170-centimetre height and 60 kilogram weight. In this figure the white curve corresponds to expiration phase and the green curve to the inspiration phase.

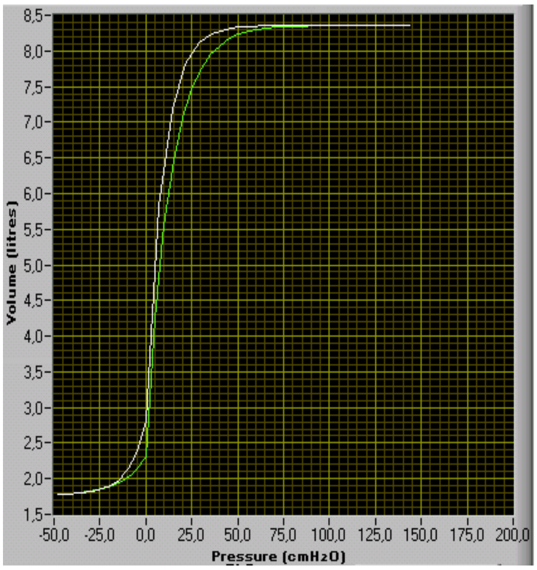

Figure 3: Volume-pressure diagram

3. Discussion

The mathematical modelling of various physiological systems empowered their study [Rideout (1991)]. Among them the respiratory system modelling led to solutions that covered, in a way, the gap between theory and practice.

The mathematical models that were developed in accordance to the existing mathematical equations could be implemented in a computer program and presented by the most dynamic way to the public.
The exponential models we developed are not the only approach that could describe the respiratory functions, but other solutions could be suggested, too. Though, after studying various physiology sources [American Thoracic Society (1995)], [Lumb (2000)] and the related diagrams appeared there, we concluded that the parameters' behaviour was best described through these equations.
This study provides a tool for a deep review of the respiratory parameters and a dynamic representation of its properties, as well. The diagrams that were constructed with the equations mentioned above led to curves that fit well to the respiratory parameters behaviour. Especially, the volume-pressure diagram was a suggestion of a pneumologists group who are part of KAT Hospital (located in Athens, Greece) workforce; their willing was to have a curve in their deposit that best describes this relation.
Finally, another point that should be mentioned is the selection of Caucasian origin subjects for our study. The criteria for this selection were the great amount of data that came up from previous research and the numerous mathematical models that have been developed, so far, for Caucasians. On the other hand, the provided material for the other two origins (African and Asian) was not enough to support our study. Though the models we developed could be well applied to them; the problem was concentrated on some of the quantities appeared in our equations. So, the final decision was to exclude them, for the moment, from our study.

4. Conclusions

At present, we tried to study the respiratory functionality in two directions. The first one presents the dynamic change of lung volume in relation to the cycle of breathing and the second describes lungs' mechanical properties. For these applications we used existing models and developed some more after the extensive study of respiratory physiology and related previous research findings.
Furthermore, we concluded that the developed models could offer new potentials in the description of respiratory parameters. The diagrammatic representation of these models led to curves that describe the parameters behaviour quite well.
The lessons learned from the development of these mathematical models led us to specify some future goals for the further exploitation of the current effort. Concentrating on what we developed, we plan to enrich it by studying pathological situations and how they affect the parameters and the respiratory functionality. The mathematical modelling and the curve fitting for pathological conditions is the next step. Moreover, there is the intention to study more factors that, possibly, affect the respiratory system. Another future plan is the inclusion of data for Asians and Africans, as soon as the research findings allow us to do so. Finally, revisions will take place in periods determined by innovations in the field and by remarks mentioned by the scientific community.

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