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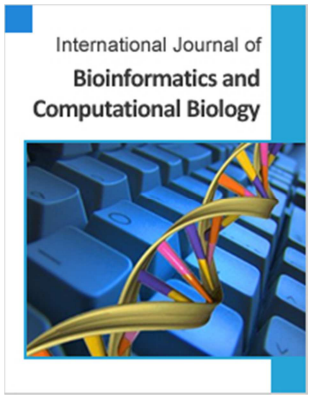

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Chaotic Lung Airway Scaling Using Verhulst Dynamics

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Abstract
The contribution introduces an airway scaling procedure, which assumes (a) a fractal anatomy of the human lung and (b) a generation-related variability of bronchial morphometry in a chaotic fashion. Basic scaling of the branching system was conducted by application of an inverse power-law including the fractional dimension of the anatomic object. Simulation of intrasubject diversity of the measurements, on the other side, was realized by using a normalized and repeatedly corrected variant of the logistic equation primarily introduced by Verhulst. Two morphometric data sets were theoretically approximated with the help of the scaling procedure, thereby assuming a morphometric diversity covered by a 60%-range. In both cases, excellent prediction of experimental data was provided.

1. Introduction

Based upon numerous morphological studies conducted in the past century [1-5] the human tracheobronchial tree is known as progressively branching structure. Preliminary theoretical models described the lung architecture in terms of a symmetric construct, within which each parent tube bifurcates into two equally sized daughter tubes from the trachea to the terminal bronchioles. As a consequence of that, all airway tubes belonging to a certain order or generation (z) of the dichotomous branching tree are characterized by exactly the same physical dimensions [1, 2]. Assumption of ideal dichotomy also enables the calculation of the number of branch segments (N) in each generation according to $N = 2^z$.

In the meantime, it is a well-known fact that the daughter airways arising at a given bifurcation commonly differ in their measurements (diameter, length). In addition, they are usually marked by different bifurcation angles with regard to the parent tube. All these peculiarities result in a highly asymmetric architecture of the human lung [6-8]. From a theoretical point of view, branching asymmetry has been modelled in terms of two approaches hitherto: In the stochastic model airway dimensions of a given generation are randomly varied by application of related probability density functions [9, 10]. By using fractal concepts, on the other side, the lung is regarded as an object, which lacks a characteristic scale and is distinguished by its self-similarity [11, 12]. However, consideration of the tracheobronchial tree either as a probabilistic construct or as an anatomic fractal requires the availability of morphometric measurements carried out on human lung casts [1, 2, 13].

Within the human lung mean airway diameter and length in a given generation are subject to a decrease with respect to the preceding generation. According to classical approaches downward scaling of the airway tubes from the trachea to the terminal bronchioles follows an exponential function and uses a single order-related scaling factor (α). Hence, mean dimension (diameter and length) of the branches in a selected

generation z may be obtained from the formula

$$S(z) = S(0) \cdot \alpha^z, \quad (1)$$

Where $S(0)$ denotes the respective tracheal dimension. By setting the scaling factor to $0.67 < \alpha < 0.73$ a good approximation of the morphometric data presented by Weibel [1, 2] is provided. In order to consider the above stated complexity of the lung architecture, the single scale presented in Eq. (1) is replaced by a multiplicity of scales [14, 15]. This is achieved by definition of a probability function $P(\alpha)$ including a distribution of scaling functions [15-17]. As outlined by Nelson and co-workers [17], application of multiple scales results in a modification of $S(z)$ to $S(z/\alpha)$ due to the dependence of airway dimensions on the the z/α^{th} generation. The relationship between $S(z)$ and $S(z/\alpha)$ is then given by

$$S(z) = \int_0^\infty S(z/\alpha) P(\alpha) d\alpha, \quad (2)$$

with $P(\alpha)$ representing the functional form of the size distribution. If, for instance, probabilistic scaling is assumed, $P(\alpha)$ adopts the form of a Gaussian normal distribution. If, on the other hand, $P(\alpha)$ is only represented by a single point, a deterministic structure is generated and Eq. (1) becomes valid again (Figure 1). Based upon Eq. (2) West and co-workers [12] argued that airway dimensions better decline as an inverse power-law of the following form:

$$S(z) = z^{\mu} A(z). \quad (3)$$

In the equation noted above μ denotes the power-law index, which may be related to the fractional dimension. The term $A(z)$ is a function reflecting harmonic periodicity and is expressed by the equation

$$A(z) = \sum_{n=-\infty}^{\infty} A_n \exp\left[\frac{2\pi i n \ln(z)}{\ln(\lambda)}\right], \quad (4)$$

where λ describes the overall range of scales, whilst A_n denote the relative weights of the harmonic terms used for the data fit. It could be demonstrated that the lung-morphometric data provided by Raabe and co-workers [13] can be adequately modelled with the assumptions summarized in Eq. (3) and (4).

Although assumption of harmonic periodicity has been pointed out as an appropriate step for the mathematical description of realistic lung structures, it also bears some disadvantages. First, natural constructs such as the human lung are characterized by a morphology, where no structural element is completely equal to another one. In this case a non-periodic (chaotic) concept represents a good alternative for scaling purposes. Second, the tracheobronchial architecture, on the one side, exhibits a certain amount of intrasubject variability, which can be covered by harmonic functions to a certain degree, but, on the other side, also shows high intersubject variability. Hence, excellent fit of one morphometric dataset does not force the high-quality fit of another. In this contribution a non-harmonic and non-periodic scaling procedure is introduced, which may be applicable to a wider range of morphometric data. The concept of chaotic scaling, whatsoever, is based on the so-called logistic equation originally defined by Pierre François Verhulst in the year 1837 [18].

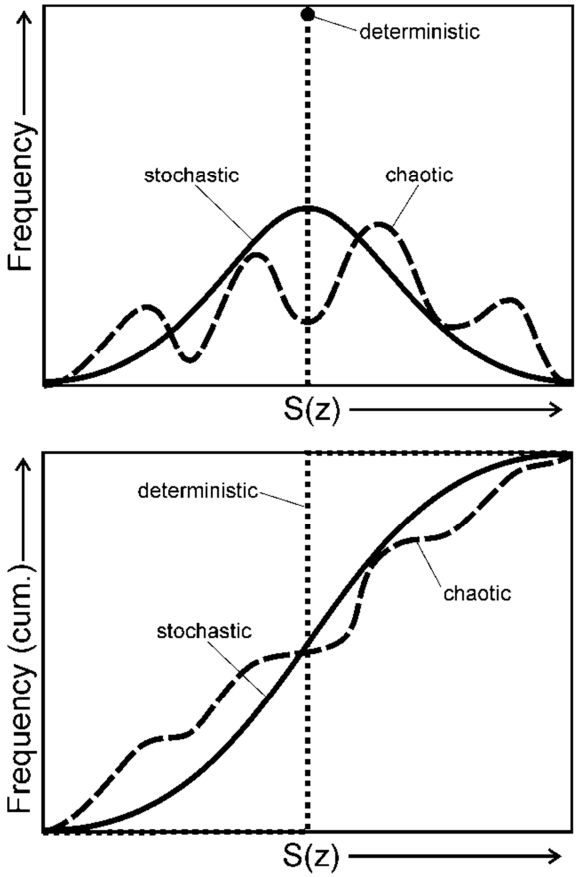

Figure 1. *(a) Different functions describing the distribution of scaling factors over a predefined range. In the case of a deterministic lung structure only a single scaling factor occurring with 100% probability is provided. (b) Cumulated distribution functions depicting the probability density. Here, the chaotic distribution of scales deviated significantly from the probabilistic approach.*

2. Methodology

2.1. Brief Description of the Logistic Equation

The logistic formula represents an excellent example of how complex chaotic behaviour can arise from simple non-linear equations. Although largely used in population ecology, the equation has found lots of scientific and non-scientific applications during the past decades. In general, the equation can be written as

$$x_{n+1} = r \cdot x_n \cdot (1 - x_n), \quad (5)$$

where x_0 denotes the initial value, whereas r is a constant. If the constant adopts a value between 0 and 1, x rapidly tends to zero. For 1 < r < 2, x monotonously approximates the value 0.3, whilst for 2 < r < 3, x approaches the value 0.6 in an alternating fashion. In the case of 3 < r < 3.57 the mathematical sequence alternates between 2, 4, 8, 16, 32, etc. frequency points. For r > 3.57 the sequence starts to become chaotic, whereby any periodicity gets lost with further increase of the constant (Figure 2).

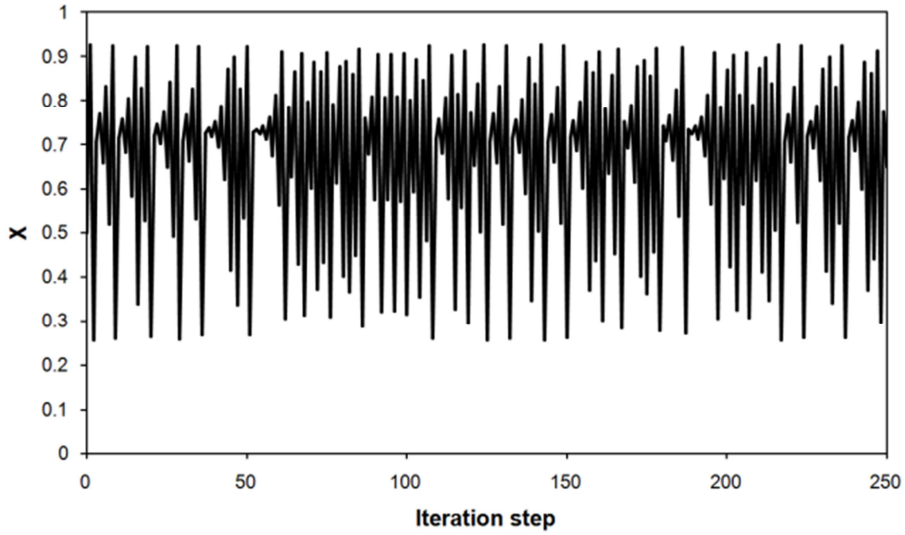

Figure 2. *Graphic presentation of the logistic equation and its typical chaotic behaviour. In the concrete case the initial value was set to 0.5, whereas the constant adopts a value of 3.7.*

2.2. Application of the Logistic Equation to Airway Scaling

In the mathematical approach presented here airway scaling is principally based upon a modified version of the inverse power-law described in Eq. (3). The new formula writes as

$$\mathrm{S}(z,n) = z^{\mu} \cdot \mathrm{F}(z,n), \tag{6}$$

where F(z,n) denotes a specific function used for an optimal fit of morphometric data. This generation-related function expresses intrasubject variability of airway scaling by adopting the following form:

$$\mathrm{F}(z,n) = \mathrm{F}(0) \cdot \mathrm{V}(z,n). \tag{7}$$

In the equation noted above F(0) has to be regarded as Null-function fitting the mean values of the studied morphometric measurements, whereas V(z,n) represents a normalized function including the Verhulst dynamics. It commonly writes as

$$V(z,n) = \frac{[r \cdot x_n \cdot (1 - x_n)] \cdot \mathrm{N}(z)}{\sum_{n=1}^{\mathrm{N}(z)} r \cdot x_n \cdot (1 - x_n)}, \tag{8}$$

with N(z) denoting the number of airway tubes in generation z. In order to obtain higher accuracy of the mathematical model, the function V(z,n) is submitted to two separate correction processes. The first one generates higher symmetry of the chaotic distribution around the mean value, thereby generating a new function V*(z,n) of the form

$$\mathrm{V}^*(z,n) = \mathrm{V}(z,n) + \mathrm{d}(z,n) - \mathrm{k}(z,n) \cdot (\mathrm{V}(z,n) - \mathrm{MIN}(z,n)), \tag{9}$$

where

$$\mathrm{d}(z,n) = 2 \cdot \left[\frac{\sum_{n=1}^{N(z)} r \cdot x_n \cdot (1 - x_n)}{\mathrm{N}(z)} \right] - (\mathrm{MIN}(z,n) + \mathrm{MAX}(z,n)) \tag{10}$$

and

$$\mathrm{k}(z,n) = \frac{\mathrm{d}(z)}{\mathrm{RANGE}(z,n)}. \tag{11}$$

In Eq. (9)–(11) MIN(z,n), MAX(z,n), and RANGE(z,n) represent the minimum, maximum, and range of the data set generated for a given airway generation z. A second correction procedure allows the new adjustment of the range covered by the values of the distribution. For this purpose, a new function V**(z,n) of the form

$$V^{**}(z,n) = MIN^{*}(z,n) + \frac{RANGE^{*}(z,n)}{RANGE(z,n)} \cdot (V^{*}(z,n) - MIN(z,n)) \tag{12}$$

is defined, where MIN*(z,n) and RANGE*(z,n) denote the newly constituted values for the minimum and the range of the data. Finally, V(z) in Eq. (7) has to be simply substituted by V**(z,n) generated with the help of Eq. (8)–(12). Preliminary application of the fractal scaling model including chaotic dynamics for the description of intrasubject variability of generation-related airway morphometry was carried out by simulation of the morphometric data sets of the human lung published by Weibel [1, 2] as well as Raabe and co-workers [13].

3. Results

According to the results of lung scaling provided in Figures 3 and 4 the theoretical model assuming a fractal basic structure and chaotic behavior with regard to intrasubject variability generates a plausible close-to-reality architecture of the tracheobronchial system. Both airway diameter and airway length are subject to a continuous decrease after an inverse power-law function. Thereby, inaccuracy produced by the chaotic approach also declines permanently with rising generation. This phenomenon may be regarded as result of the increasing number of bronchial tubes included in more distal generations, which improves the significance of the statistical computations.

For an appropriate validation of the model two morphometric data sets [1, 2, 13] were simulated. With regard to the morphometric lung data provided by Weibel and co-workers [1, 2], differences between theoretical approach and real measurements are mainly observable for generations 3 to 5, where a slight overestimation of data by the model is given. In the case of the airway diameters all experimental data points plot within the SD-intervals of the related theoretical predictions. Differences of mean values are commonly on the order of several percent, but may increase to > 20% in exceptional cases. A more complex situation is given for the airway lengths, because airways of generation 3 represent a statistical outlier, which cannot be satisfactorily explained by the model (discrepancies > 30%). For the other generation good correspondence between reality and model can be reported again.

Simulation of the morphometric data set provided by Raabe and co-workers [13] provides a similar picture as already reported for the Weibel-lung. Regarding the airway diameters, differences between mathematical approach and reality range from several percent in the proximal and central lung areas to > 30% in generations 3 to 5 as well as in the most peripheral lung regions. For the airway lengths, the same difficulty as observed for the Weibel-lung can be recognized, with maximal discrepancies between model and reality again exceeding 30%.

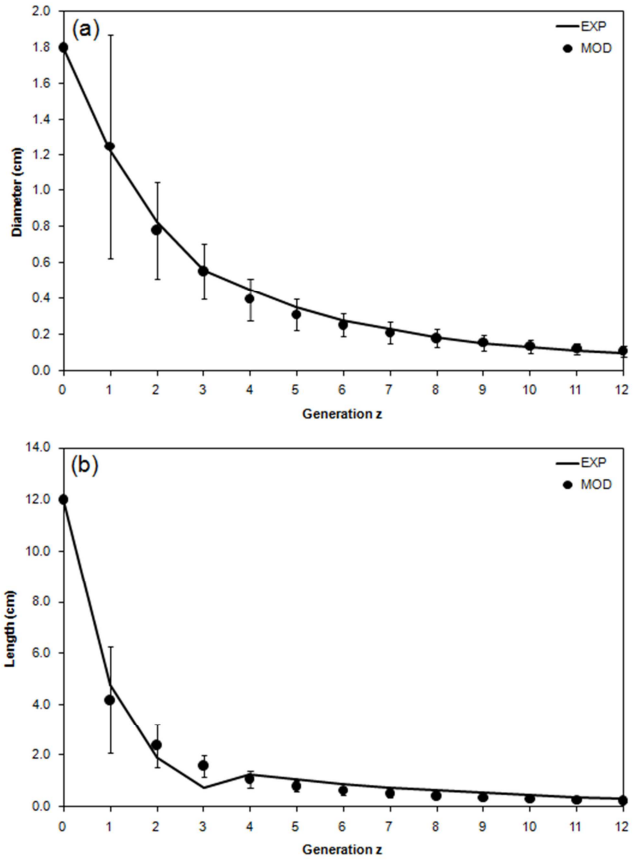

Figure 3. *Simulation of morphometric lung data provided by Weibel and co-workers [1]: (a) airway diameters, (b) airway lengths.*

4. Discussion

The current study could clearly demonstrate that chaotic distributions such as those produced with the logistic equation [18] are of great value for the description of morphometric variability occurring in single airway generations. Based upon various morphometric data sets [1, 2, 13], order-related ranges of single airway dimensions (diameter, length) are highly significant in part, with small respiratory bronchioles and much larger segmental bronchioles being present in the same generation. As argued by Nelson and co-workers [17], this intrasubject variability may be best described by harmonic (periodic) scaling functions, which develop around a mean value. Detailed statistical analysis of the morphometric data set provided by Raabe and co-workers gave rise to an alternative hypothesis, according to which any kind of lung-morphometric diversity is ideally covered by normal-distributions [19-28]. These

mathematical functions, whatsoever, reflect a symmetric and well predictable distribution of data and, thus, only find occasional realization in natural systems. Since the ground-breaking studies of Benoît Mandelbrot it has to be regarded as given fact that predictability of most natural constructs is partly restricted due to their highly chaotic behaviour [11].

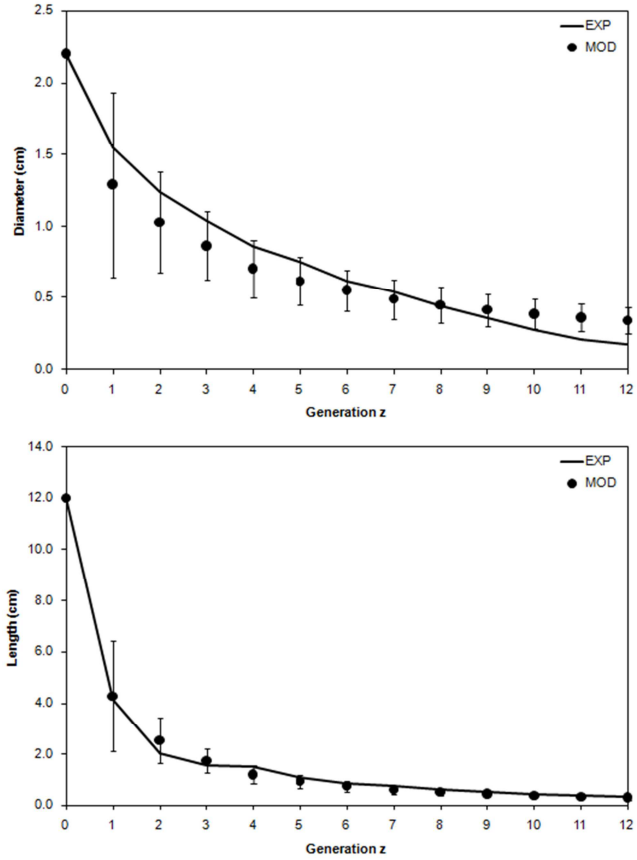

Figure 4. *Simulation of morphometric lung data provided by Raabe and co-workers [15]: (a) airway diameters, (b) airway lengths.*

As clearly shown in the results section, fit of lung-morphometric data by application of fractal scaling and chaotic functional dynamics is marked by high success. Depending upon the scaling range covered by the logistic equation, experimental data can be more or less reliably predicted by the theoretical model. In the concrete case, a range of the produced distribution covering a 60%-interval around the mean already enables the prediction of high morphometric diversity. It has to be clearly mentioned in this context that generation of a hypothetical branching system with the help of Eq. (6)−(12) represents a rather simple procedure, which can be programmed by using any basic software (e.g., MS-Excel, Matcad, Matlab, Mathematica). Compared to the stochastic lung model [23-28] the calculation routines are characterized by much lower expenditure but significantly higher variability.

The high variability of the current concept is provided insofar as it enables the construction of a deterministic branching system (for $1 < r < 3$), an architecture characterized by respective periodicities ($3 < r < 3.57$), and a tracheobronchial tree including a highly non-periodic and non-harmonic morphometry ($r > 3.57$). In this context, further applicability of the scaling model has to be briefly discussed. The approach is primarily thought to provide the lung architecture for future particle transport and deposition models [19-23]. Particle behaviour in a fractal lung with realistic intrasubject variability of airway morphometry has been already discussed in numerous publications, but has not been realized hitherto.

5. Conclusion

Based on the data presented here it can be concluded that fractal lung models are able to describe realistic morphometric scenarios in the meantime. The phenomenon of morphometric variability within a given generation can be solved in different ways. One of these solution procedures includes the application of chaotic systems, among which the logistic equation is conspicuous due to its simplicity on the one hand and its adjustability in the other. Future studies will provide a more detailed insight into the multiplicity of applications provided for this innovative concept.

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