On the Fractality of the Biological Tree-like Structures

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The fractal tree-like structures can be divided into three classes, according to the value of the similarity dimension D_s: $D_s < D$, $D_s = D$ and $D_s > D$, where D is the topological dimension of the embedding space. It is argued that most of the physiological tree-like structures have $D_s \geq D$. The notion of the self-overlapping exponent is introduced to characterise the trees with $D_s > D$. A model of the human blood-vessel system is proposed. The model is consistent with the processes governing the growth of the blood-vessels and yields $D_s = 3.4$. The model is used to analyse the transport of passive component by blood.

Keywords: Fractals, Blood-vessels, Tree-like structures, Similarity dimension, Advective diffusion

I INTRODUCTION

The fractal tree-like systems are very common objects, and have been attracted a lot of attention, c.f. Mandelbrot (1983), West (1990), Bassingthwaighte *et al.* (1994). The most obvious examples are ordinary trees. The physiological tree-like structures – such as a blood-vessel system, a lung, nerve tissues, a lymphatic system – are not exceptions. Unlike the ordinary trees, the physiological "trees" are "hidden" by tissues. For this reason, it is quite a complicated task to study the fractal properties of them. The constituent parts of these tree-like systems (single blood vessels, neurons and bronchial tubes) have been studied for a long time and the physical properties of them are known in great details. Meanwhile, the global properties of the respective "trees" have been the object of systematic studies only during the last decade.

In what follows we show that the fractal tree-like structures can be meaningfully divided into three classes, according to the value of the similarity dimension D_s: $D_s < D$, $D_s = D$ and $D_s > D$, where D is the topological dimension of the embedding space. In Section II we argue that most of the physiological tree-like structures belong to the second and third classes ($D_s \geq D$). Section III is devoted to the fractal trees with $D_s = D$ and to the model of lung in particular. In Section IV we discuss the case of $D_s > D$ on the example of blood-vessel system. Section V is devoted to the trees with $D_s < D$ and Section VI to the analysis of the transport of passive scalar in the blood-vessel system.

II THE PHYSIOLOGICAL TREE-LIKE STRUCTURES

A fractal model of a biological tree-like structure should satisfy the following rather generic criteria:

(a) it should be in accordance with the simplest physical laws, such as the flow continuity and the Poiseuille law in the case of the blood-vessel system;

(b) it should satisfy certain physiological requirements, e.g. ensure a complete (homogeneous) blood supply of the organism;

(c) it should be in accordance with our knowledge about the processes governing the growth and formation of the "trees";

(d) it should be self-similar within a wide range of scales;

(e) the result of many iterations of a generation-to-generation relation specifying the model should not be very sensitive to the subtleties of the model;

(f) the model should not contradict empirical data.

Some comments are needed here. First, adopting the criterion (d) we disregard the possibility of a multifractal or a non-scale-invariant behaviour. As discussed above, in some cases these effects can be significant. The simplest way would be to assume that there is a transition scale between two different self-similar regions. However, in Section IV we shall argue that at least for a considerable range of scales, the self-similarity of the blood-vessels can be a consequence of the dynamical growth mechanisms of the vascular tree. In order to shed more light into the problem of scale-invariance, detailed three-dimensional experimental data would be needed.

Second, the consequence of the item (b) is that in the case of physiological vascular networks, the spatial distribution of the branches of the tree should be quasi-homogeneous, i.e. the tree should be space-filling. Indeed, in the case of the blood-vessel system the "holes" are not admittable, since all the cells need a blood supply. In the case of lung the alveoli fill almost all the space of the lung.

Perhaps in a lesser extent this is true for a neural network; however, within distinct regions of the organism, the distribution of neurons is also quasi-homogeneous. If there would be a true fractality of the vascular network, the fractal dimensions could not be less than the topological dimension (three in most cases and two for effectively two-dimensional structures), because the fractional values less than the dimension of the embedding space would mean that the structure is sparse, with "holes".

The models of the blood-vessel system have been developed in several papers (cf. Spaan, 1991; Family et al., 1989; Masters, 1994; VanBeek et al., 1989; Kalda, 1993); main subject has been the geometrical arrangement of the blood-vessels. Special attention has been paid to the essentially two-dimensional structures, such as subcutaneous arteriovenous networks (Gazit et al., 1995), human retinal vessels (Family et al., 1989) and vessels of the avian chorioallantoic membrane (Kurz et al., 1993). Three-dimensional analysis has been attracted much less attention; one can mention NMR-computer tomography-based analysis of the pig kidney arteries, where the box-counting fractal dimensions have been calculated (Sernetz et al., 1992).

There is also a considerable number of papers devoted to the airway tree of a lung (cf. West, 1990; Kitaoka and Takahashi, 1993; Weibel, 1991). They include extensive experimental measurements and concern mainly the geometrical arrangement of the bronchial tubes (particularly characterised by the box-counting dimension). Also, mathematical models have been proposed to match the experimental data.

According to the arguments given above, these models cannot be applied to the blood-vessel system (or to the lung) as a whole, particularly because the reported fractal dimensions were less than the topological dimension of the embedding space. The fractional values of the box-counting dimension should be attributed to the limited range of scales and can be treated as an evidence of the lack of global self-similarity. In order to avoid misinterpretations, these fractional values could be referred to as the local scaling exponents.

III TREES WITH $D_s = D$. THE MODEL OF BRONCHIAL TREE

A characteristic feature of the fractal trees with $D_s = D$ is that

(a) the structure is space-filling,
(b) a distinct branch (together with its sub-branches) forms a compact structure, so that overlapping of different branches of the same generation is insignificant.

Bronchial tree is a typical example of this kind of trees: the bronchial tubes and alveoli are packed tightly and there are no major regions between them filled by tissues of other organs. The tomographic images of lung indicate that the condition (b) is satisfied, as well. By Kitaoka and Takahashi (1993), a simple regular three-dimensional model of lung has been suggested. According to that model, all the bronchial tubes are similar to each other; each tube branches into two smaller tubes which are perpendicular both to the given tube and to the tube of the previous generation. Sometimes a confusion has been caused by the fact that the experimental dependencies are not power laws (as would be expected in the case of self-similarity). Thus, it has been pointed out by West (1990) that the plot of the logarithm of the average diameter of the bronchial tubes versus the generation number differs notably from the straight line. It has been shown that the experimental curves can be modelled fairly well, if we take into account the presence of the small-scale cut-off at the alveoli size (Kalda, 1993). Indeed, for real lung, the two branches of a bronchial tube are always of different sizes. Thus we can modify the model of Kitaoka and Takahashi (1993) by introducing the distribution function of the diameter ratio of the branches. Due to such an unequal branching, the generation number of the alveoli (the alveoli are assumed to be approximately of the same size) can vary several times. The power laws can be expected only by the generation numbers, smaller than the smallest generation number among the alveoli.

Another example (though not biological) of the trees with $D_s = D$ is the river networks. The network is space-filling, if we assume that the sources are distributed quasi-homogeneously. The compactness is caused by the limitations of two-dimensional topology: two branches cannot intersect.

IV TREES WITH $D_s > D$. THE BLOOD-VESSEL SYSTEM

To begin with, let us make a rough estimate of the similarity dimension of the blood-vessel tree. Here we can use the following empirical data: the length of the capillaries (i.e. the vessels of the last generation) $\lambda \approx \lambda_0 \approx 0.5\,\mathrm{mm}$ (cf. Hoppe et al., 1978), the length of the largest vessels (aorta) $l_0 = 0.5\,\mathrm{m}$ and the total length of capillaries, $L \approx \lambda_0 N \approx 100{,}000\,\mathrm{km}$. The total number of capillaries N can be expressed via the effective number of generations n_{eff} as $N = 2^{n_{\mathrm{eff}}}$. Being guided by the assumption of self-similarity, we can express the similarity factor a as $a = (\lambda_0/l_0)^{1/n_{\mathrm{eff}}}$. Using the definition of the similarity dimension we can easily find

$$D_s = -1/\log_2 a \approx 3.4. \tag{1}$$

The seemingly curious fact that the similarity dimension exceeds the topological dimension can be explained as follows. It is easy to show that the Hausdorff–Besicovitch and box-counting dimensions of a space-filling fractal set D_{HB} and D_b are always equal to the topological dimension of the embedding space D. As for the similarity dimension, it is generally accepted (cf. Mandelbrot, 1983) that D_s coincides with the Hausdorff–Besicovitch dimension D_{HB}. Thus it may seem that always $D_s \leq D$. However, the equality $D_s = D_{\mathrm{HB}} = D_b$ can be applied only if all the dimensions are less than the dimension of the embedding space. Indeed, one can imagine that the fractal tree was originally embedded into a space of dimensionality $D_{\mathrm{in}} > D_s$ and then projected into the space of dimensionality $D < D_s$, see Fig. 1. As a result of such a projection, the dimensions D_{HB} and D_S become equal to the new value of D, whereas the similarity dimension will evidently remain unchanged. The similarity
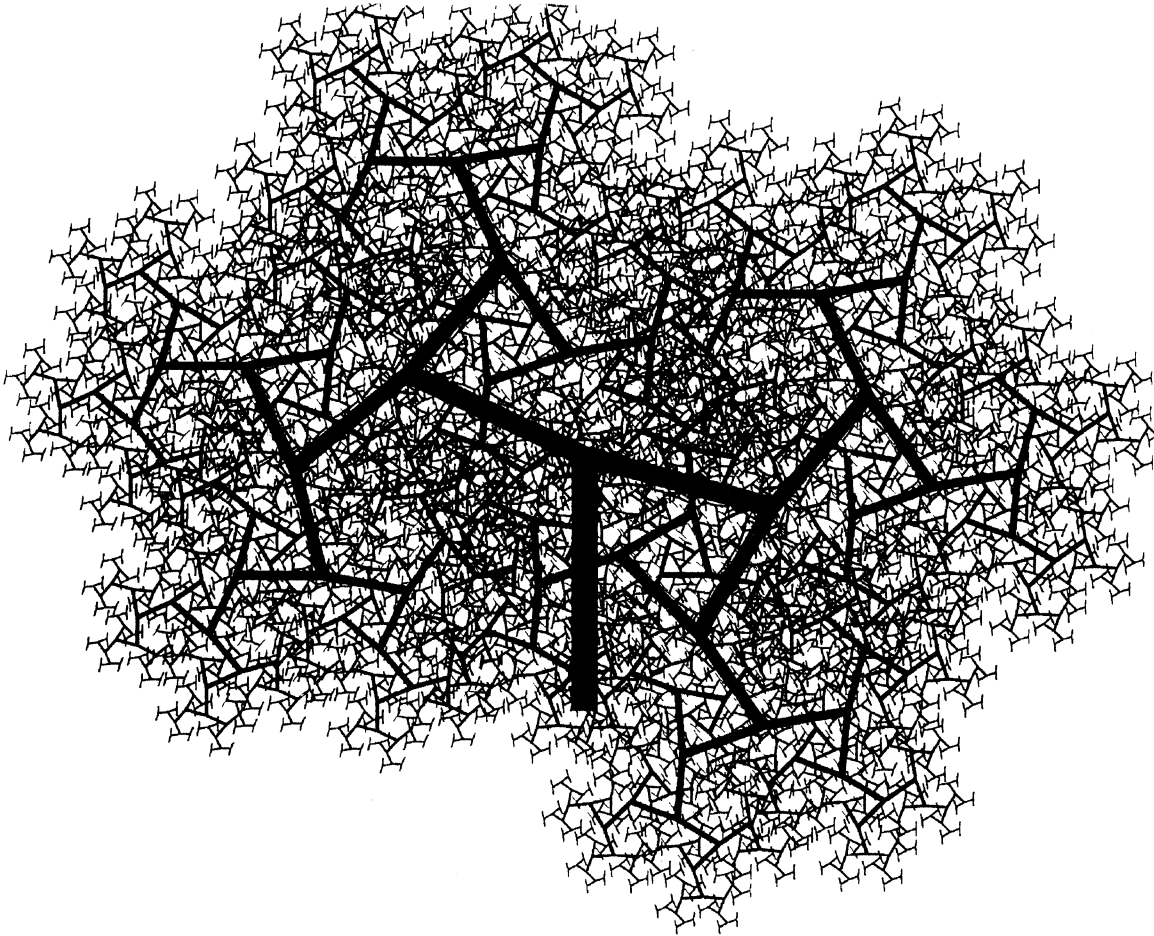
FIGURE 1   Example of a fractal tree with the similarity dimension exceeding the dimensionality of the embedding space: $D_s \approx 2.53$, $D = 2$.

dimension exceeds the topological dimension if the ratio δ_n/l_n of the average distance between the branches of nth generation δ_n and average length of them l_n vanishes towards higher generation numbers n, i.e. towards smaller values of l_n. This is possible in two cases:

(a) the tree is not self-similar, but instead, self-affine;
(b) the branches of the same generation number have significant overlapping regions.

Finally, let us note that in order to provide an homogeneous blood supply of the organism, the distance between capillaries should be less than the

effective diffusion radius $\delta_{diff} \approx 100 \,\mu m$: the relative distance between capillaries is somewhat smaller than between large vessels. So, it is rather natural that the similarity dimension of the blood-vessel system does exceed the dimension of the embedding space.

The self-similar model of the spatial arrangement of the blood-vessels is, in fact, a generalisation of the Scheidegger's model of rivers (Scheidegger, 1967). The Scheidegger's model can be outlined as follows: tree-like network is generated by trajectories of particles ("droplets") randomly jumping from site-to-site on n-dimensional square lattice (in our case $n = 2$). In the $n + 1$-dimensional space (time-axis added) the trajectories follow the edges
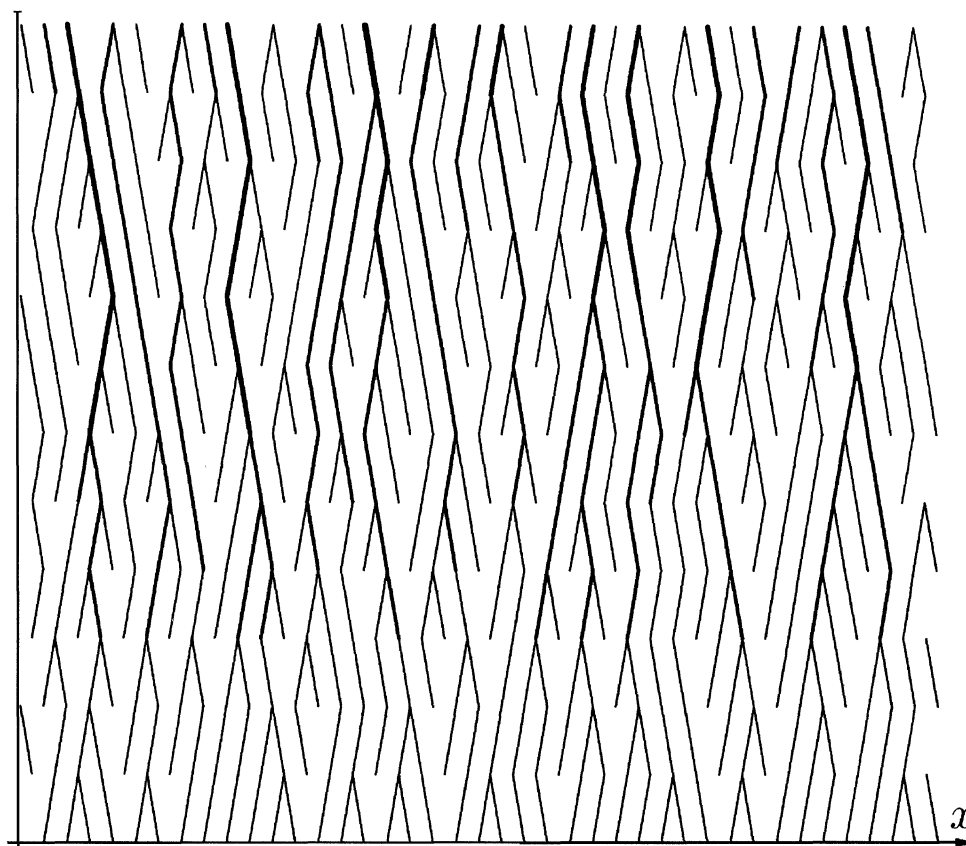
FIGURE 2   Scheidegger's rivers. This picture arises as a pattern of particle trajectories. At each time step, a particle is born at every integer value of x; the particles move with constant velocity and random direction along the x-axis through a unit length; the colliding particles coalesce.

of the parallelepiped-shaped grid and coalesce from time-to-time forming larger particles, see Fig. 2.

The Scheidegger's model has been chosen as a starting point because the underlying parallelo-piped-shaped grid gives us a convenient way to ensure a quasi-homogeneous distribution of the capillary vessels (i.e. of the vessels of the smallest size). Alternatively, we could use the generators of fractals to construct trees similar to that of depicted on Fig. 1. The latter method can also be randomised (cf. Mandelbrot, 1983) and as it can be seen on Fig. 1, the resultant distribution of the capillary vessels is quasi-homogeneous, too. However, the model based on Scheidegger's rivers has still the advantage that it has more control parameters which can be used to adjust the model to the empirical data.

The modified Scheidegger's model is given by the following rules of the dynamics of the "droplets":

(i)   The time t is discrete with the unit time step.
(ii) At each time step, each coordinate of a particle changes randomly and independently of the other coordinates and other particles but correlates with its previous history so that the resulting motion is fractional Brownian with the Hurst exponent H (the average rms displacement of a particle is proportional to t^H); the coordinate is increased or decreased by one.
(iii) Colliding particles coalesce with the probability of 1 if both of the following conditions are fulfilled: (a) the mass ratio lies between 1/2 and 2; (b) the interaction cores of the particles

overlap. Otherwise, the particles continue their motion without interaction. The radius of the interaction core is defined by the mass of the particle as follows:

$$r_m \approx r_0 m^\rho, \quad \rho > 0. \tag{2}$$

(iv) At each time step and at each lattice site, a new particle of unit mass is added. As compared with the original Scheidegger's model, in item (ii) now a non-locality in time is assumed; in item (iii) now two particles can coalesce at a non-zero distance and the coalescence of particles which are very different in size is prohibited.

Further we have to tie the parameters of the model with the physical observable quantities of the blood-vessel tree. Evidently, the mass of the "droplets" corresponds to the flux of blood through the vessels. In order to derive the expression for the average length of vessels l via the average flux through them, it is convenient to introduce the mass doubling time t_m of the "droplets" – the average time needed for a particle of mass m to double its mass. Besides, let l_m denote the average spatial distance between the "m"-particles (which we define as the particles of masses within the interval $[m, 2m]$).

The problem of finding the mass doubling time of a "droplet" is similar to the problem of finding the kinetic constants of a chemical reaction. There are two possibilities: first, the anti-correlation in time is weak enough, so that the "m"-particles behave as a gas. Then the area covered by the interaction core of an "m"-particle during a typical coalescence time t_m should be equal to the average area per one "m"-particle:

$$r_m t_m \approx l_m^2, \quad \text{if } r_m t_m < t_m^{2H}. \tag{3}$$

The other possibility is that process becomes "diffusion-limited": Eq. (3) is no longer valid since the self-overlapping of the particle's trajectory cannot be neglected. Instead, the time t_m can be assessed as the time needed for a particle to "diffuse" to the distance l_m:

$$t_m^{2H} \approx l_m^2, \quad \text{if } r_m t_m > t_m^{2H}. \tag{4}$$

Suppose the system of "droplets" has been evolved for a long time, then a stationary regime should have been established. Specifically, the spectral flux of mass per unit area (towards large masses) has to be constant over the whole spectrum of masses:

$$\frac{m}{l_m^2 t_m} = const. \tag{5}$$

Solving the system (2)–(5) for t_m and l_m, we find

$$l_m \approx m^\lambda, \quad t_m \approx m^\tau, \tag{6}$$

where

$$\lambda = \frac{1+\rho}{4}, \quad \tau = \frac{1-\rho}{4}, \quad \text{if } 2H > \frac{1+\rho}{1-\rho},$$

$$\lambda = \frac{H}{2H+1}, \quad \tau = \frac{1}{2H+1}, \quad \text{if } 2H < \frac{1+\rho}{1-\rho}. \tag{7}$$

Note that our arguments can be repeated without changing the original Scheidegger's model, as well. In that case a logarithmic factor should be added to take into account the effect of self-overlapping of the trajectories; the relevant expressions of papers by Takayasu (1989) and Huber (1991) can be easily recovered.

Now let us recall that in the case of blood-vessel system, m is the flux of blood, l_m is the average distance between the vessels and t_m is the length of vessels. Due to the continuity condition, the total flux through all the vessels of a given size is constant, thus the number of "m"-vessels $N_m \propto m^{-1}$. On the other hand, the number of vessels scales with their length as $N_m \propto t_m^{-D_s}$. Further, if we take into account Eqs. (5) and (6) we find

$$2\lambda = 1 - 1/D_s. \tag{8}$$

Comparing Eqs. (1), (7) and (8), it is easy to see that there are solutions,

$$\rho = 0.4, \quad H > 1.2, \tag{9}$$

$$\rho > 0.4, \quad H = 1.2. \tag{10}$$

The first solution corresponds to the case, when the capillaries fed by a fixed artery form a sparse system and in a vicinity of every capillary there are capillaries fed by other arteries. We shall show somewhat later that this situation is more realistic than the opposite one (corresponding to Eq. (10)) when the capillaries fed by a fixed artery form a dense system.

To conclude with the model, let us discuss it from the evolutionary point of view. The growth of the vascular network is controlled by several chemical mechanisms. The generally accepted model (cf. Gazit *et al.*, 1995; Nekka *et al.*, 1996) of this process can be outlined as follows. In the growing organism, the tissue cells grow at a certain rate and sub-divide when a maximum size is reached. The existing vascular structure grows with all the other tissues. The distance between capillaries grows as well; this can cause ishemia of the most distant cells. Ishemic cells generate chemical substances – angiogenic factors (AF) – which lead to angiogenesis. The particles of AF diffuse in all the directions. These particles can be captured by blood vessels; when captured, they cause a new vessel sprouting towards the ishemic cell (actually, towards the higher concentration of AF). Some purely perfused vessels undergo regression and disappear.

Despite the fact that diffusion plays an important role in such a model, it seems that in most cases the growth is not diffusion-limited. Instead, diffusion is faster than the growth of the tissues: the time between the subsequent emergence of two ishemic regions is longer than the characteristic diffusion time. Such a growth model leads to a space-filling statistically self-similar vascular tree. If we assume that the average distance between the capillaries is constant during all the growth process and that the regression of vessels is negligible, there would be a fractal tree of $D_s = 3$ with slightly overlapping branches. Besides, the relative distance between the large vessels would be equal to the relative distance between capillaries.

If we admit that the regression of vessels can be significant, we obtain a tree with $D_s > 3$. The higher the regression rate is, the higher the similarity

dimension will be. Such an inequality has two observable consequences. First, the relative distance between vessels increases with the size of vessels. Second, there will be a significant overlapping of the same-generation branches. This is rather important from the physiological point of view: the damage of a vessel will not lead to the complete cease of the blood supply, in a vicinity of every cell fed by a capillary belonging to the damaged branch there are capillaries belonging to healthy branches. In order to describe this effect quantitatively, we introduce the overlapping exponent of a fractal tree. Let us draw around a branch of size l a sphere of diameter l. We repeat this procedure with all these branches which satisfy the condition $L < l < 2L$. Further, let the maximum number of spheres of non-zero intersection scale with size L as

$$N_{\max} \propto L^{-\beta}. \qquad (11)$$

Then we say that β is the overlapping exponent. It is easy to see that if the tree is self-similar (i.e. not just self-affine),

$$\beta = D_s - D. \qquad (12)$$

Indeed, in the case of vascular system the average distance between the vessels of size l with $L < l < 2L$ can be calculated as $d \approx [l_0^3/(2^m L)]^{1/2}$. Here m denotes the effective generation number of the vessels of given size; it can be eliminated using the expression for the similarity factor $a = (L/l_0)^{1/m} = 2^{-1/D_s}$. Finally, the number of overlapping spheres can be assessed as $N_{\max} \approx L^3/(d^2 L) \approx (l_0/L)^{D_s - 3}$.

Due to the lack of experimental data, it is impossible to check directly the applicability of our model. In fact, it is a very difficult technical task to make three-dimensional measurements of vascular tree and cover a wide range of scales. However, detailed data are available concerning the correspondence between blood pressure, flux of blood and diameters of the vessels. Particularly, the diameter of the vessels scales with the flux w of blood as $d \propto w^{1/\alpha}$, $\alpha \approx 2.7$ (see Takayasu, 1990). According to our model and Poiseuille law, this scaling law corresponds to the dependence

$p(d) = p_0 - cd^\gamma$ with $\gamma \approx -0.5$ (the exponent γ can be expressed via α and D_s), where $p(d)$ denotes the average blood pressure in the vessels of diameter d (for details see Kalda, 1993). This dependence is in accordance with the experimental data (cf. Hoppe *et al.*, 1978) and can be considered as an indirect argument supporting our model.

It should be emphasised that the model described above cannot be used equally well for all the scale-lengths. The experimental data (Kurz *et al.*, 1993; Sernetz *et al.*, 1992) indicate that for some scale-lengths the vascular tree can be notably non-self-similar: the exponent of the local fit to a power-law revealed a significant dependence on space-scale. Further experimental data are needed to determine the range of applicability of the model.

V   TREES WITH $D_s < D$

Most of the ordinary trees fall into this category. Typically, the fractal dimension of them is something between two and three. The trees with $D_s < 2$ are very "transparent" the shade of such a tree (even with leaves) has significant holes. On the other hand, the trees with $D_s \geq 3$ are very thick: it is impossible to climb on these trees, because all the space of the heads of the trees is filled with branches.

Despite the fact that the ordinary trees can be easily accessed and measured, it is rather difficult to calculate the fractal dimension of them. This is caused by the three-dimensional geometry. One possible solution is to measure the length l_i and mass M_i of each branch and find the similarity dimension as the minimum of the function

$$F_{D_s} = \sum_i (l_{1i}^{D_s} + l_{2i}^{D_s} + l_{3i}^{D_s})^2 / l_{3i}^{2D_s}. \tag{13}$$

In fact, we can do the measurements even on two-dimensional photographic images, assumed that trees have lost their leaves and all the branches can be distinguished (the other methods would fail here and yield $D = 2$). For instance, using the images of several birch trees we obtained $D \approx 2.6$.

VI   CONVECTION OF PASSIVE COMPONENT BY BLOOD

In this section we outline a simple implementation of the model of vascular tree (Kalda, 1996). We consider the transport of a passive admixture through the blood-vessel system. It is assumed that the admixture has been injected into tissues and fills a certain region between the vessels. Besides, the following assumptions are made:

(a) outside the vessels, the propagation of the admixture is diffusive, of molecular diffusivity D_0;

(b) the admixture particles can penetrate the walls of the vessels;

(c) the presence of the admixture around and inside the vessels does not affect substantially the blood flow in these vessels. However, a small change (by a factor of the order of two) in the rate of the blood flow is admitted;

(d) a vessel is called to be of size L, if its length is between L and $2L$. The vessels of size L form an homogeneous network;

(e) the transport is accomplished in the venous half of the blood-vessel tree. In fact the admixture is convected also by the arterial flow, but this is the convection towards the capillaries and the transport distance in the arterial tree is limited by the size of the vessel where the injection was made;

(f) the blood flow in vessels is laminar (cf. Hoppe *et al.*, 1978).

The analysis is based on two "integrals of motion". The first one is the expression for the total volume of the whole body:

$$V = N(L)L\lambda(L)^2, \tag{14}$$

where (L) denotes the average distance between the neighbouring vessels of size L and $N(L)$ – the total number of vessels of size L.

The second one is the estimate of the total flux of blood through the heart:

$$Q = N(L)v(L)d(L)^2. \tag{15}$$

Here $v(L)$ denotes the characteristic velocity of the blood in a vessel of size L and $d(L)$ – the diameter of the vessel of size L. These equations are valid for any value of L. Sometimes it is more convenient to use the combined and hence a dependent "integral of motion":

$$V/Q = \frac{L\lambda(L)^2}{v(L)d(L)^2} \approx 1000 \, \text{s}. \qquad (16)$$

Here the numerical value 1000 s was obtained by substituting $V = 70 \, \text{dm}^3$ and $Q = 70 \, \text{cm}^3/\text{s}$.

Let us assume that inside the tissues there is a spot of passive admixture which diffuses into the blood vessels and will be carried into the other parts of the organism by blood. The admixture can be an injection, a venom of an insect or of a snake or something else. The character of propagation depends on the seed diffusivity D_0 and on the initial size of the spot r. It can be shown that there are four qualitatively different regimes of propagation.

The admixture propagates in the form of a "sausage" around the vessel stretching out of the initial spot. The diameter of it can be assessed as $\sqrt{D_0 t}$ and the "stretching" velocity of the "sausage" as

$$v_{\text{eff}} \approx \frac{d(L)^2}{D_0 t} v(L). \qquad (17)$$

If the spot is large and diffusivity low, the admixture fills the vascular system approximately during one rotational cycle of blood, $\tau \approx W/Q \approx 1 \, \text{min}$, W being the total volume of the blood.

Otherwise the convection is slowed down by diffusion inside the tissues. It can be shown that in this case the characteristic time of invading the whole organism is given by $\tau = V/Q \approx 100 \, \text{s}$.

VII CONCLUSION

The values of the similarity dimension D_s and the dimension of the embedding space D can be used to divide the fractal tree-like structures into three classes. Most of the ordinary trees belong to the class of sparse trees with $D_s < D$. Most of the physiological tree-like structures are quasi-homogeneous with $D_s \geq D$. The compact self-similar structures with non-overlapping branches (such as a lung) have $D_s = D$. The dense structures with $D_s > D$ (such as a blood-vessel system) can be additionally characterised by the self-overlapping exponent. If the tree is self-similar (i.e. not just self-affine), the exponent $\beta = D_s - D > 0$; this implies a significant overlapping of branches.
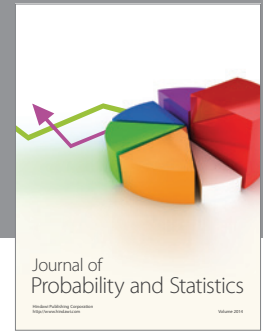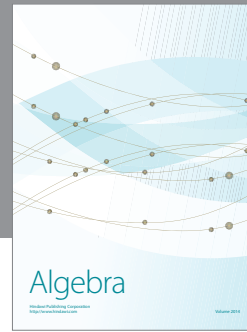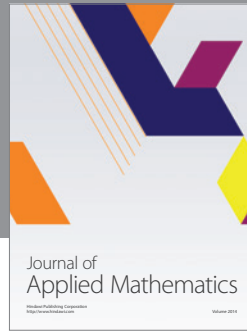
We have constructed a self-similar model of blood-vessel system, which is in agreement with the modern understanding of the processes governing the growth of the vascular network. Our basic assumptions were: (a) the tree can be considered to be self-similar; (b) variations of the blood consumption rate of the body cells are not significant. The similarity dimension of the model $D_s \approx 3.4$. On the basis of this model, we have analysed the transport of passive component by blood. Depending on the diffusivity of the passive component, the characteristic time of invading the whole vascular tree can vary from one to twenty minutes.

It should be stressed that the applicability of the assumption of self-similarity itself is not quite clear and deserves further studies. On the one hand, it is supported by the dynamical growth model of the blood-vessel system; on the other hand, several papers have been reported that the fractal box-counting dimension of the effectively two-dimensional structures – retinal and subcutaneous vascular networks – is close to $D_b \approx 1.7$ (Family $et\ al.$, 1989; Masters, 1994; Gazit $et\ al.$, 1995). These results could be treated as an evidence of the lack of self-similarity for wider inertial range of scales. However, it should be noted that the effectively two-dimensional structures constitute only a negligible part of the whole body. One should also bear in mind that the uncertainties of the box-counting dimensions can be easily underestimated, especially if the available range of scales is limited.

References

Bassingthwaighte, J.B., Liebovitch, L.S. and West, B.J. (1994). *Fractal Physiology.* Oxford Univ. Press, New York.

Family, F., Masters, B.R. and Platt, D.E. (1989). Fractal pattern formation in human retinal vessels. *Physica* **D38**, 98–103.

Gazit, Y., Berk, D.A., Leunig, M., Baxterand, L.T. and Jain, R.K. (1995). Scale-invariant behavior and vascular network formation in normal and tumor tissue. *Phys. Rev. Lett.* **75**, 2428–2431.

Hoppe, W., Lohmann, W., Markl, H. and Ziegler, H. (Eds.) (1978). *Biophysik*. Springer, Berlin, p. 554.

Huber, G. (1991). Scheidegger's rivers, Takayasu's aggregates and continued fractions. *Physica* **A170**, 463–470.

Kalda, J. (1993). Fractal model of blood vessel system. *Fractals* **1**, 191–197.

Kalda, J. (1996). Fractality of blood-vessel system and lung. *Med. Biol. Eng. Comp.* **34**, 375–376.

Kitaoka, H. and Takahashi, T. (1993). Relationship between the branching pattern of airways and the spatial arrangement of pulmonary acini – a re-examination from a fractal point of view. In, *Fractals in Biology and Medicine* (T.F. Nonnenmacher, G.A. Losa, E.R. Weibel, Eds.). Berlin, pp. 116–131.

Kurz, H., Wilting, J. and Christ, B. (1993). Multivariate characterization of blood vessel morphogenesis in the avian chorioallantoic membrane (CAM): cell proliferation, length density and fractal dimension. In, *Fractals in Biology and Medicine* (T.F. Nonnenmacher, G.A. Losa, E.R. Weibel, Eds.). Berlin, p. 132.

Mandelbrot, B.B. (1983). *The Fractal Geometry of Nature*, Freeman, San Francisco.

Masters, B.R. (1994). Fractal analysis of normal human retinal blood vessels. *Fractals* **2**, 103–110.

Nekka, F., Kyriacos, S., Kerrigan, C. and Cartilier, L. (1996). A model of growing vascular structures. *Bullet. Math. Biol.* **58**, 409–424.

Scheidegger, A.E. (1967). *Bull. Int. Assoc. Sci. Hydrol.* **12**, 15.

Sernetz, M., Wübbeke J. and Wlczek, P. (1992). Three-dimensional image analysis and fractal characterization of kidney arterial vessels. *Physica* **A191**, 13–16.

Spaan, J.A.E. (1991). *Blood Flow*, Kluwer Academic Publishers, Dordrecht, p. 40.

Takayasu, H. (1989). Steady-state distribution of generalized aggregation system with injection. *Phys. Rev. Lett.* **63**, 2563–2567.

Takayasu, H. (1990). *Fractals in the Physical Sciences*, Manchester University.

VanBeek, J.H.G.M., Roger, S.A. and Bassingthwaighte, J.B. (1989). Regional myocardial flow heterogeneity explained with fractal networks. *Am. J. Physiol.* **26**, H1670–H1680.

Weibel, E.R. (1991). Fractal geometry: a design principle for living organisms. *Am. J. Physiol.* **261**, L361–369.

West, B.J. (1990). *Fractal Physiology and Chaos in Medicine*. World Scientific, Singapore.

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