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MAGIC TREES IN MAMMALIANS RESPIRATION OR WHEN EVOLUTION SELECTED CLEVER PHYSICAL SYSTEMS

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Abstract

The respiratory system of mammalians is made of two successive branched structures with different physiological functions. The upper structure, or bronchial tree, is a fluid transportation system made of approximately 15 generations of bifurcations leading to the order of $2^{15} = 30,000$ bronchioles with a diameter of order 0.5 mm in the human lung.[1] The branching pattern continues up to generation 23 but the structure and function of each of the subsequent structures, called the acini, is different. Each acinus is made of a branched system of ducts surrounded by alveolae and play the role of a diffusion cell where oxygen and carbon dioxide are exchanged with blood across the alveolar membrane.[2] We show in this paper that the bronchial tree presents simultaneously several optimal properties of totally different nature. It is first energy efficient;[3–6] second, it is space filling;[7] and third it is "rapid" as discussed here. It is this multi-optimality that is qualified here as magic. The multi-optimality physical characteristic suggests that, in the course of evolution, an organ selected against one criterion could have been later used for a totally different reason. For example, once energetic efficiency for the transport of a

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viscous fluid like blood has been selected, the same genetic material could have been used for its optimized rapidity. This would have allowed the emergence of mammalian respiration made of inspiration–expiration cycles. For this phenomenon to exist, the rapid character is essential, as fresh air has to reach the gas exchange organs, the pulmonary acini, before the start of expiration.

Keywords: Evolution; Respiration; Mammals; Optimal Systems; Fractals.

1. INTRODUCTION

The ubiquity of branched distribution systems in living organisms has been the subject of many queries since about two centuries.[8,9] These structures are found in various organs: arteries, kidney and lungs where they perform different functions. Owing to ubiquity of such systems, there exist many studies that are not referred here that the reader can find in the above references or on the web of science.

They are then common but other types of networks do exist in living systems, such for example brain connections. All these structures are "space filling" in the sense that they feed the entire volume of an organ. However tree structures (loopless networks) permit to connect a small source to a volume[10] for example the heart to the body, of the mouth or nose to the volume of the thoracic cage. Reciprocally, they permit to connect a volume, like that of the mammary gland to a small exit, the papilla. In contrast, brain connections are more of the nature of what is called complex networks connecting a volume to itself.

Here we concentrate on the respiratory system of mammalians and more precisely on the tracheobronchial tree. In the upper part of lung airway system of mammalians, starting with the trachea and down to generation 5 to 6 in the human lung, the transport of air is governed by the Navier-Stokes equation which also accounts for inertial effects.[11–16] Going deeper into the tree, as the total cross-section increases the air velocity decreases to the point that the approximation of Stokes flow can be used to describe the aerodynamics of the tree from typical generation range 5 to 15. The entire tracheobronchial transport system is made of approximately 15 generations of bifurcations leading to the order of $2^{15} = 30,000$ terminal bronchioles with a diameter of order 0.5 mm.

Our purpose here is to draw attention to some special physical properties of the intermediate tree from typical generation range 5 to 15. Typical examples are shown in Fig. 1. This is the very

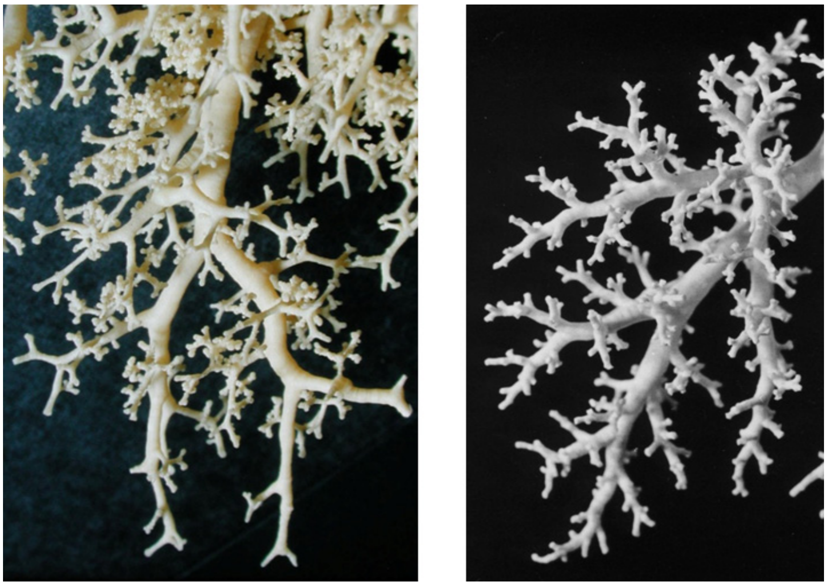

Fig. 1 Real cast of intermediate bronchial trees; left, human; right, rat (courtesy of E. R. Weibel).

system that exhibits simultaneously the three types or properties that can be considered as constituting a "magic" ensemble. The magic lies in the fact that a system optimized against one criterion happens to be also optimized for a *totally different criterion*. The three different types of optimality that are simultaneously observed are

- energetic efficiency in fluid transport,
- geometry efficiency, and
- flight time efficiency.

Curiously this last question has not been discussed in the past.

2. ENERGETIC EFFICIENCY

We recall briefly the formal argument to find the best energy saving tree.[16] We consider a symmetric dichotomous tree as schematized in Fig. 2. The effect of airway geometry on ventilation can be developed as follows. Assume that from generation $(p-1)$ to generation p the diameter and the length of the airway segments are reduced by a homothetic factor h_p. This means that the bronchia shape is maintained through generations. Calling R and V the resistance and volume of a given duct, the h homothetically reduced duct has a resistance R/h^3 since this resistance is proportional to the duct length L and inversely proportional to the fourth power of the duct diameter d. (Although the length over diameter ratio of the intermediate bronchia are only of the order of 3 and end effects cannot be neglected, this is a reasonable approximation[16]). In contrast, the volume is multiplied by a factor h^3 at each generation. After p generations, the sizes are reduced by a factor $h_1 \times h_2 \times \cdots \times h_{p-1}$ so that the total resistance and volume of a tree with $N+1$ generations (indexed 0 to N) can be written

$$R_N = R_0 + \sum_{p=1}^{N} \frac{1}{2^p} \frac{R_0}{(h_1 \times h_2 \times \cdots \times h_p)^3}$$

$$V_N = V_0 + \sum_{p=1}^{N} 2^p (h_1 \times h_2 \times \cdots \times h_p)^3 V_0.$$

If Φ is the global airflow, the total pressure drop is $\Delta P_N = R_N \Phi$ and the total dissipation can be written $\Phi \Delta P_N$. This power loss can be minimised relative to $(h_1, \ldots, h_{N-1})$ on the surface defined by the constraint $V_N = \Omega$. The minimum of R_N on $V_N \leqslant \Omega$ is characterised by the existence of a Lagrange multiplier μ such that $\nabla(R_N) = \mu \nabla V_n$. This leads to $h_1 = [(\Omega V_0)/(2NV_0)]^{1/3}$ and $h_i = (1/2)^{1/3}$ for i in $\{2, \ldots, N\}$. Note that the factor $h_i = (1/2)^{1/3}$ is known for a long time under the name of the Hess-Murray law. Note also that what is really optimized here, is the energy expense per volume which is the important criterion as such branching trees are only feeding systems and not acting systems, the acting system being the muscles in the body or the acini in the mammalian lungs. The volume of the bronchial tree is called the dead space volume in physiology (of order 200 ml in the human lung), as it plays no role in gas exchanges. Note that is has been also shown that cylindrical pipes are more efficient energetically than elliptic pipes.[17] In summary the best *energy saving* symmetric dichotomic tree is self-similar with a constant scaling ratio independent of the generation. This is a clear indication that evolution has selected self-similarity for efficiency.

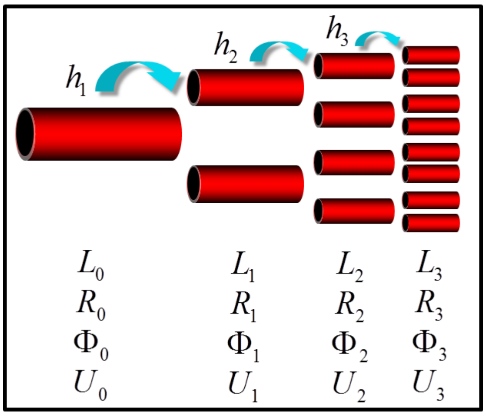

Fig. 2 Schematic constitution of a general symmetric dichotomic tree. Each generation is characterized by the lengths L_n and diameters that are reduced by an homothety factor h_n. The flux in each individual branch is divided by 2 at each bifuration, and the velocity of the fluid is U_n.

3. GEOMETRIC EFFICIENCY

Consequently, the best energetic tree is a self-similar fractal with a fractal dimension equal to $D = \ln 2/\ln(1/h)$ or $D = 3$. It is interesting to note that anatomy measurements of the real bronchial tree has given value for h close to 0.85, not far from the optimum.

But, reciprocally, the fractal dimension of a tree structure is given by $D = \log N/\log h$ where N is the number of branches at each bifurcation (or degree of the tree) and h the scaling ratio of the branches. So the scaling ratio that guarantees that for $N = 2$ the dimension is equal to 3 is such that

$3 = \ln 2/\ln(1/h)$ or $h = (1/2)^{1/3}$. And then, under the only hypothesis that a dichotomous tree must be space-filling one finds that it must be the best energy saving tree.

Note that what is called “space filling” does not imply that the total bronchial volume is equal to the lung volume. It means precisely that any point chosen arbitrarily in the lung volume is close to a small bronchiole.

4. FLIGHT TIME EFFICIENCY

A third “magic” property of this best tree is that it exhibits optimal rapidity in providing the shortest time for the air to travel through. This can be seen in the following steps as follows. Let us call $t_0, t_1, t_2, \ldots, t_n$, the time for the flow to travel across generation $0, 1, 2, 3, \ldots, n, \ldots$. See Fig. 2. We search for the smallest total time $T = t_0 + t_1 + t_2 +, \ldots, +t_n + \cdots$. The first step is to use a collage argument to ensure that the fastest tree is obtained when all these transit times are equal. For this, suppose that they different, then there is one that is the smallest. One can substitute all the longer times by the shortest and the total time will be minimized. So, the fastest (best tree for two way respiration) tree is *isochronous*.

Now, call L_n and, L_{n+1} the bronchia lengths at generation n and $n + 1$ and U_n, and $U_{n+1}, \ldots$ the associated air velocities. One has $t_n = L_n/U_n$ and we want $t_{n+1} = L_{n+1}/U_{n+1} = t_n = L_n/U_n$. The flux in a generation n branch is Φ_n is proportional to $U_n(d_n)^2$ or $U_n(L_n)^2$. The conservation of the flux at each branching implies $\Phi_n = 2\Phi_{n+1}$. Searching for the homothety factor h that satisfies these equations one obtains, here again: $h = (1/2)^{1/3}$. In summary the above facts indicate that there exists what can be called a “best best” tree structure that obeys simultaneously different criteria. From this, one can suggest that during the course of evolution, natural selection has met the one among these criteria that was of critical importance for survival given the external circumstances.

For instance, the fact to be an energy saving distribution system was probably of primary importance for the circulation of a viscous fluid like blood whereas viscous dissipation in the aerial bronchial tree of mammalian is only a small part of the work for breathing in air due to the very small air viscosity as compared to that of blood. If primordial animals with one-way blood circulation were aquatic, there arterial system could have evolved towards energetic efficiency creating the basis for a subsequent aerial cyclic respiration. Note that if the bronchial tree has a short flight time for respiration at rest it will also be efficient for respiration at exercise where the velocity of air is 10 times higher than at rest.[2]

Note also that for a given pressure drop, if the structure is blown up by a constant factor the flight time will diminish but this is at the expense of the dead space volume. So the optimization of the flight time is a specific constrain by itself.

Another specific property of such a magic tree is that the hydrodynamic resistance between successive bifurcations is constant, such that the pressure drop between bifurcations is also constant.

5. SOME REMARKABLE PROPERTIES OF THE MAMMALIAN RESPIRATORY ACINUS AND WHY DO MAMMALIANS NEED A DISTRIBUTION TREE FEEDING SMALL ACINI

Each termination of the bronchial tree, called a bronchiole, feeds an acinus, the gas exchange unit for respiration but also a mini-pump for air. This in itself could also be qualified as magic as two totally different functions, gas exchange and mechanical pumping, are provided by the same organ.

But as, for mechanical reasons, the membrane must have a minimal strength then a minimal thickness and consequently a finite resistance for gas diffusion.[18] The acinus surface must then be large enough to provide enough oxygen to the blood. A human acinus is shown in Fig. 3. Several parameters govern the global oxygen uptake: air velocity at the acinus entry, oxygen diffusivity in air, alveolar membrane permeability, blood hemoglobin content and its reaction rate with oxygen, and, last but not least, the morphology of the system plays an essential role.[19] So, the proximal acinar regions receive fresh air through the terminal bronchioles. But the more distal acinar regions, those that contain the major exchange surface that are deeper than the location of the convection/diffusion transition, are fed only by diffusion. These regions may then be submitted to diffusion limitations or screening. Qualitatively, diffusion screening is the consequence of the fact that, when O_2 molecules diffuse

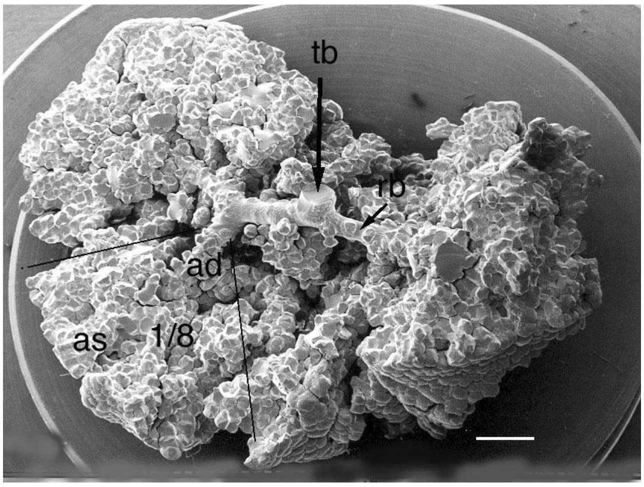

Fig. 3 Human pulmonary acinus (courtesy of E. R. Weibel). The scale marker is 1 mm. The acinus entry is the end of the transitory bronchiole (tb) and one can observe the first alvedae on the respiratory bronchiole (rb).

inside the acinus, they may hit the alveolar membrane and may be trapped by the blood. The gas may then be progressively depleted from its oxygen content due to diffusion screening. This problem has been solved in Ref. 19.

The flux depends on the relative values of two lengths: Λ, and the so-called "surface perimeter" L_p. The length Λ is the ratio D/W of the diffusion coefficient of oxygen in air, D by the membrane permeability, W.[20] It is of purely physicochemical nature and its value is around 28 cm in the human lung. The "surface perimeter" L_p is the ratio of its area S by its diameter, the diameter being that of the smallest sphere embedding the irregular surface. If Λ is larger than L_p the surface works uniformly whereas when L_p is larger than Λ, oxygen cannot reach the less accessible regions and the surface is only partially active. The morphometric study of the human acinus yields a value of $L_p \approx 30\,\text{cm}$ for a 1/8 sub-acinus a remarkable agreement also found for the acini in several mammalian species.[19] It strongly suggests that screening plays a role in mammalian respiration and that lung design is adjusted to cope with this problem. But, at the same time, it indicates that too large acinus, in which $L_p \gg \Lambda(O_2)$, would be poorly working and this is *the reason why the lungs are not made of a single very large acinus* but are instead constituted of the 30,000 small acini in the human lung,[21] all supplied by the efficient branched conducting airways described above.

6. TREE OPTIMALITY IN REAL LIVING SYSTEMS?

One should first discuss the fact that real structures are found to be somewhat different from the ideal structures presented above. This has been documented in the case of the human intermediate bronchial tree where the scaling ratio is more, when averaged, of the order of 0.85 than the optimal value 0.79. In that sense this part of the bronchial tree has a slightly too large dead space volume at the benefit of a better conductance robustness towards geometrical variability.[7] This also constitutes a protection against mild forms of asthma. In the strict sense, its fractal dimension is then larger than 3 but this is permitted because the tree is finite. From the point of view of the transit time, the value 0.85 would increase significantly the transit time if the real splitting was exactly dichotomous.

This is however compensated by the fact that for the upper branches h is smaller than 0.79. Also, it is known that the real geometrical splitting is not symmetric,[22–24] giving rise to a smaller daughter with $h < 0.79$ and a large daughter with $h > 0.79$ or a more rapid and a more slow branch at each bifurcation. It has been shown in Ref. 7 that this could be at the benefit for the global conductance, which is less sensitive to bronchia constriction than the symmetric tree. This indicates that the "averaged" value of 0.85 does not describe properly the complicated effects of succession of rapid and slow bronchia.

In the case of the arterial blood system, it is the opposite; the scaling ratio is a little smaller at the benefit of the quantity of blood.[25] The quantity of blood was the criterion driving Hess and Murray in their derivation of the optimal value $h = (1/2)^{1/3}$. This value has been found to be a good descriptor of the hierarchy of vessels in plants when their role is uniquely to transport water and do not play simultaneously a mechanical role.[26]

One should also comment that real bronchial trees are generally found to be asymmetric, probably as a consequence of their growth in a natural non-symmetric environment.[24–26]

There are other consequences of the magic of these tree structures. First, their performances strongly depend critically on the h value.[16] Second, the extreme sensitivity of the final distribution to defects. This is for instance the question of the final distribution of a given air flux entering the tree if the dichotomic splitting of the flux is not strictly equal to 1/2 and 1/2 but for instance $1/2+\alpha$ and $1/2-\alpha$. Let us suppose that at the next bifurcation a similar splitting occur. Then, between the four daughter branches, one will find fluxes as $(1/2+\alpha)^2$ and $(1/2-\alpha)(1/2+\alpha)$ twice and $(1/2-\alpha)^2$ and so on. This is a multiplicative process and it provides after n bifurcations a strongly uneven distribution of the flux between $(1/2+\alpha)^n$ and $(1/2+\alpha)^n$ with fractal correlations in space. Such a distribution is called multifractal[27,28] and its main characteristic is the strong unevenness of the fluxes reaching the final branches. In other words it is inherent to a tree distribution system to create unequal distribution of the fluxes. This means that, to really be efficient distributive systems these "magic" trees have to be regulated. This is known for arteries. In the lung, it could be the role of the smooth muscle found around the bronchia. There is then, along with the physical performances of these magic trees, the necessity of an adapted physiological control of its functioning.

7. A PHYLOGENETIC POINT OF VIEW INDUCED BY PHYSICS, WHAT CAME FIRST?

A first observation that one can draw from the above facts is that the same system may favour simultaneously different types of use because it is efficient for different properties. And an obvious question is: during evolution, what came first?

Before suggesting an answer one should mention that several systems have been already found to be used by living systems for very different functions. The general idea is the role of tinkering in evolution.[29] One example is the RuBisCO enzyme that is used for sulfur metabolism.[30] An other example is the crystallin genes issued from chaperone-like proteins.[31] Such findings have been developed in recent years as a concept called "the book as a paperweight" by Danchin.[32] The same processes are also known as gene sharing[33] or acquisitive evolution.

Here, we discuss the purely physical properties of the bronchial tree and try to answer the question: what came first between energy, geometry, and time performances? We suggest that, between these, space-filling geometry came first. In life there are essentially two transport mechanisms, diffusion and forced convection. Diffusive transport is effective at small scales like cellular scales for diffusion in liquids. But at the scale of an organ, and even more at the scale of an animal, diffusion is far too slow to bring nutrients at the speed necessary to support life. On the other hand, it is the volume of the organs that have to be fed. The transport system has then to be space filling. There are only two types of space-filling geometries: a network, or a tree. Both exist but the tree is more efficient from the energetic point of view. So, the suggestion is that tree distribution systems have been selected together with the growth of multi-cellular systems or animals.

To have an energy saving distribution system was probably of primary importance for the circulation of a viscous fluid-like blood. In primordial aquatic animals with one-way blood circulation, the arterial system would have necessarily evolved towards energetic efficiency.

In contradistinction, under normal conditions, the viscous dissipation in the aerial bronchial tree of mammalian is only a small part of the work for breathing in aerial respiration because the viscosity of air is negligible as compared to the viscosity of blood. But once the genetic material was available it could have been used for creating the basis for a subsequent aerial, two-way respiration, i.e. mammalian respiration. So the phylogenesis that physics suggests starts from space filling, and then follows energetic efficiency to be finally used for the aerial respiration of mammals.

Although this does not constitute a proof, the visual observation of Fig. 4 suggests that the same genetic material could have been at work in the growth of arteries and bronchia.

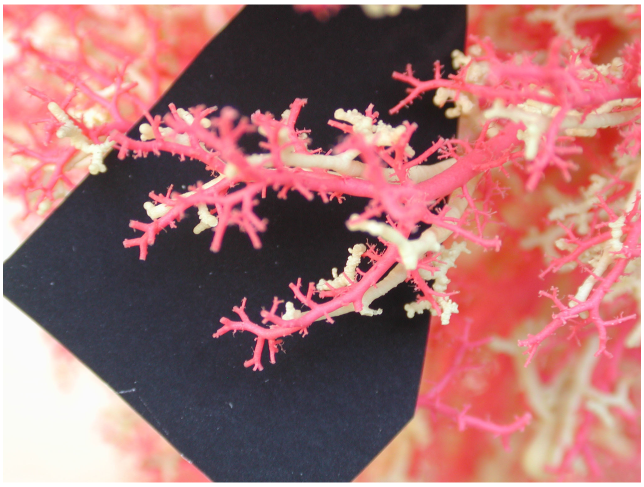

Fig. 4 Small bronchia and bronchioles and pulmonary arteries in the human lung. The pulmonary arteries transport veinous blood but here they have been coloured in red. (Courtesy of E. R. Weibel).

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