

Optimisations and evolution of the mammalian respiratory system^{*}

A suggestion of possible gene sharing in evolution

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Abstract. The respiratory system of mammals 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 about $2^{15} = 30,000$ terminal bronchioles with a diameter of approximately 0.5 mm in the human lung. The branching pattern continues up to generation 23 but the structure and function of each of the subsequent structures, called *acini*, is different. Each acinus consists in a branched system of ducts surrounded by alveoli and plays the role of a diffusion cell where oxygen and carbon dioxide are exchanged with blood across the alveolar membrane. We show here that the bronchial tree simultaneously presents several different optimal properties. It is first energy efficient, second, it is space filling and third it is also “rapid”. This physically based multi-optimality suggests that, in the course of evolution, an organ selected against one criterion could have been used later for a totally different purpose. For example, once selected for its energetic efficiency for the transport of a viscous fluid like blood, the same genetic material could have been used for its optimized rapidity. This would have allowed the emergence of atmospheric respiration made of inspiration-expiration cycles. For this phenomenon to exist, rapidity is essential as fresh air has to reach the gas exchange organs, the pulmonary acini, before the beginning of expiration. We finally show that the pulmonary acinus is optimized in the sense that the acinus morphology is directly related to the notion of a “best possible” extraction of entropic energy by a diffusion exchanger that has to feed oxygen efficiently from air to blood across a membrane of finite permeability.

1 Introduction: Physical constraints to feed living systems and the properties of arborescent tree structures

The metabolism of living systems requires cells and organs to be efficiently fed. This means that the entire volume of a living organ has to be supplied by a “space-filling transport mechanism”. Only two mass transport mechanisms fulfill this requirement: convective transport through a space-filling network, and diffusion. But these mechanisms have very different velocities. Typical diffusion coefficients in water are of order 10^{-6} to 10^{-5} cm²/s. The diffusion velocity to cross a distance ℓ in a medium with diffusion coefficient D is about D/ℓ , and the time to cross this distance is ℓ^2/D . The diffusion time to cross a distance $\ell \approx 10 \mu\text{m}$ in water is therefore about several

seconds. This time increases as the square of the distance and is already of order 10^4 seconds for $\ell \approx 1$ mm. This is why diffusion is an efficient feeding mechanism at small spatial scales like that of cellular or small multi-cellular systems, but is not found at the scale of an entire organ, even less for a complete animal or plant whose size ranges from several centimeters to tens of meters. There exists therefore a threshold length ℓ below which nutrients or oxygen can be transported by diffusion, and above which mass transport has to be achieved through a space-filling network of “pipes” (which can be capillaries, vessels, or bronchi). By “space-filling” we mean that any point chosen at random in a living system is never distant from a fluid transport element by more than about ℓ .

Two types of geometry commonly found in biological systems satisfy this space-filling condition: i) lattice-type grids (perhaps random) as for instance the capillary bed in muscles or in the alveolar membrane of mammals, and ii) tree-like structures similar to that of the arterial or bronchial tree of mammals. In order to better understand the emergence of transport architectures in living systems

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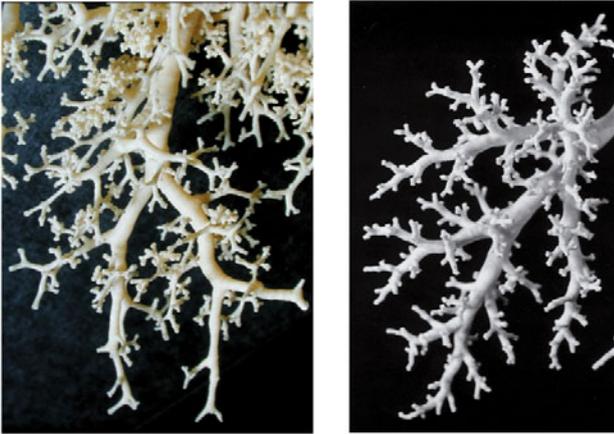


Fig. 1. Real cast of intermediate bronchial trees; left, human; right, rat (courtesy of E.R. Weibel).

at different scales, one has then to compare the properties of arborescent systems with that of other space-filling networks. This will be addressed in the next section.

2 Properties of tree distribution systems

The ubiquity of branched distribution systems in living organisms has been the subject of many studies for about two centuries [1–4], and the object of recent interest [5–9]. Tree structures such as veins, arteries, or bronchi are found in various organs (kidney, liver, lung, ...) where they perform transport, transfer, distribution or filtering functions. All these networks are “space-filling” in the sense that they feed the entire volume of an organ. Other types of space-filling networks do exist in living systems such as for example brain connections. But the brain connection network is more of a type volume to volume, similar in that to a complex network.

A specificity of tree structures (or loopless networks) is that they permit connecting a small source to a volume in order to perform distribution functions [10–12]. For instance blood is distributed from the heart to the entire body through the arterial tree, and air from the mouth and the nose to the volume of the thoracic cage through the tracheobronchial tree. Conversely, trees can also connect a volume like that of the mammary gland to a small exit, the papilla. In this paper, we focus on the respiratory system of mammals, and more precisely on the intermediate tracheobronchial tree [13, 14].

The reason for this choice is that the aerodynamics can be described in this part of the bronchial tree using the Stokes equation only (generations 5 to 15 in the human lung). On the opposite, in the upper part of the mammalian lung airway system (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 [15–19].

Our purpose here is to draw attention on a very peculiar property of the intermediate tree, whose typical examples are shown in fig. 1. This system simultaneously exhibits three types of properties that can be seen as con-

stituting a “magic” ensemble. The “magic” here 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 simultaneously observed in fluid transport are

- energetic efficiency,
- geometric efficiency,
- transit time efficiency.

2.1 Energetic efficiency

We briefly recall the formal argument to find the best energy-saving tree [8]. 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 bronchus aspect ratio 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 bronchi in the intermediate tree are only of the order of 3, which means that end effects cannot be totally neglected, this is a reasonable approximation [8].) In contrast, the volume is multiplied by a factor h^3 at each generation. After p generations, the sizes are reduced by a factor $h_1 \times h_2 \times \dots \times h_{p-1}$ so that the total resistance R_N and total volume V_N of a tree with $(N + 1)$ generations (indexed from 0 to N) can be written as

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

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

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 minimized relative to (h_1, \dots, h_{N-1}) under the constraint $V_N = \Omega$. The minimum of R_N on $V_N = \Omega$ is characterized by the existence of a Lagrange multiplier μ such that $\Delta(R_N) = \mu \Delta(V_N)$. This leads to $h_1 = [(\Omega - V_0)/(2NV_0)]^{1/3}$ and $h_i = (1/2)^{1/3}$ for i in $\{2, \dots, N\}$. Note that the value of the factor $h_i = (1/2)^{1/3}$ is known for a long time as the “Hess-Murray law”. Note also that what is really optimized here is the energy expense per volume which is the important criterion, since such branching trees are only passive transport systems, the active 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 150 mL in the human lung [13]) as it plays no role in gas exchanges. Moreover, cylindrical pipes with circular cross section have been shown to be

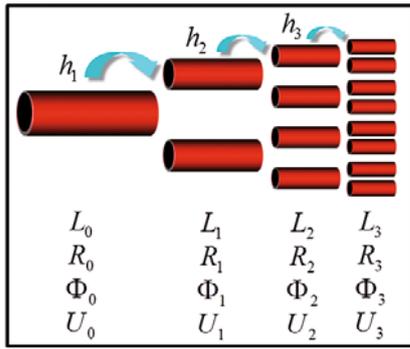


Fig. 2. Schematic constitution of a general symmetric dichotomous tree. Each generation is characterized by the lengths L_n and diameters that are reduced by a homothety factor h_n , the resistances R_n , the flux in each individual branch is divided by 2 at each bifurcation, and the velocity of the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

more energetically efficient than elliptic pipes [20]. In summary the best energy-saving symmetric dichotomous tree is self-similar with a constant scaling ratio independent of the generation.

This could be an indication that evolution has selected self-similarity for energetic efficiency. This statement has however to be toned down. Because air viscosity is small, the viscous losses are only a small part of the “work for breathing” whereas they are dominant for blood circulation in the arterial tree. This remark will be part of our later suggestion on phylogenesis.

2.2 Geometric efficiency

As we just saw, the best energetic tree is a self-similar fractal with a fractal dimension equal to $d_F = \ln 2 / \ln(2^{1/3})$ or $d_F = 3$. It is interesting to note that anatomy measurements of the real bronchial tree have given a value for h close to 0.85 [8], not far from the optimum. But, reciprocally, the fractal dimension of a tree structure is given by $d_F = \min(3, \ln(m) / \ln(1/h))$, where m is the number of branches at each bifurcation (or degree of the tree) and h the scaling ratio of the branches across generation. So the smallest scaling ratio that guarantees that for $m = 2$ the dimension is equal to 3 is such that $3 = \ln 2 / \ln(1/h)$, in other words $h = (1/2)^{1/3}$. Therefore, under the only hypothesis that the dichotomous tree must be space-filling, one finds that the one with the smallest scaling ratio is also 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 that any point chosen arbitrarily in the lung volume is “not far” from a small bronchiole or any point chosen arbitrarily in a muscle is “not far” from a small arteriole. For instance, the bronchial tree is known to occupy only about 4-5% of the total lung volume. On a mathematical point of view it means that the tree skeleton has a fractal dimension equal to 3.

2.3 Transit time efficiency

A third “magic” property of this best symmetric tree is that it exhibits optimal rapidity in providing the shortest time for the air to travel for a given energy dissipation. This rapidity is particularly important in pulsatile trees such as the pulmonary airway system in which the oxygen delivery has to be achieved in a limited time.

Let us call $t_0, t_1, t_2, \dots, t_N$, the time for the flow to travel across generation $0, 1, 2, 3, \dots, N$, see fig. 2. We search for the smallest total time $T = t_0 + t_1 + t_2 + \dots + t_N$. Since there are 2^p branches at generation p , the flow rate crossing each bronchus at generation p is $\Phi_0 / 2^p$. The transit time across generation p is then the volume of one bronchus divided by the flow rate crossing this bronchus

$$t_p = \frac{\pi}{4} D_p^2 L_p \times \frac{2^p}{\Phi_0}. \tag{3}$$

Hence the total transit time is the sum of the volume of all bronchi

$$T = t_0 + \dots + t_N = \frac{1}{\Phi_0} \left(\sum_{p=0}^N 2^p \frac{\pi}{4} D_p^2 L_p \right) = \frac{V_N}{\Phi_0}. \tag{4}$$

The total transit time across the tree is thus directly determined by the volume of the tree. As a consequence, the best compromise between energy dissipation and volume, described in subsect. 2.1, also corresponds to the best compromise between energy dissipation and transit time. And this best compromise corresponds to the smallest scaling ratio for which the tree is also space-filling. Note that $t_0 = t_1 = t_2 = \dots = t_N$ so that the tree is also isochronal.

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 against selection pressure.

For instance, 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, their arterial system could have evolved towards energetic efficiency, thus creating the basis for a subsequent aerial cyclic respiration. Note that if the bronchial tree has a short transit time for respiration at rest, it will also be efficient for respiration at exercise where the air velocity is 10 times higher than at rest [14].

Another specific property of such a magic tree is that the aerodynamic resistance between successive bifurcations is constant, such that the pressure drop between bifurcations is also constant. This remark is to be used below in the comparison between tree resistance and what would be the “lattice resistance”.

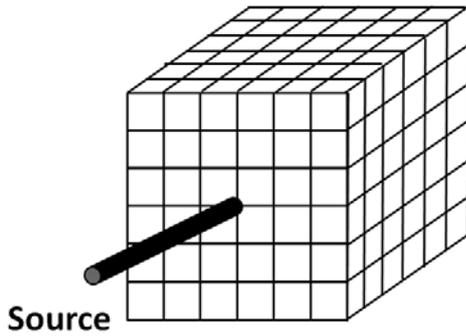


Fig. 3. Schematic representation of a space-filling lattice linking a source, on the left, to a sink uniformly distributed in $(L/\ell)^3$ diffusion cells of lateral size ℓ .

2.4 Space-filling networks: loops or trees?

In this section we compare the energies dissipated in an ordinary network and in the magic “tree” of the same macroscopic size L , both distributing nutrients down to an “equivalent” cell size ℓ (below this size, passive diffusion is assumed to be the efficient transport mechanism). We consider a volumic structure similar to the cubic lattice shown in fig. 3. Suppose we have a source on the left surface and there exists a volumic sink uniformly distributed in the volume where the nutrients are consumed. Each line in fig. 3 represents a micro-pipe, each of these micro-pipes feeding a “cell” whose volume is proportional to ℓ^3 . Let us call r the resistance to feed one micro-pipe. The global lattice resistance from the source to the opposite face of the cube is the individual resistance multiplied by the number (L/ℓ) of “cells” per line and divided by the number of lines $(L/\ell)^2$ per face. As a consequence, the global lattice resistance is proportional to $r\ell/L$.

Now consider the optimized tree structure described in the previous subsection. Since the tree is space-filling, the number of terminal branches to feed the entire volume is of order $(L/\ell)^3$. Now the resistance of the last generation is equal to the individual branch resistance r divided by the number of branches in that generation. This last generation equivalent resistance is then of order $r(\ell/L)^3$. Each generation of the tree exhibiting the same resistance, the global resistance is $Nr(\ell/L)^3$, where N is the total number of generations needed to go down from a branch size about L to the order of ℓ . As a consequence, N satisfies $h^{-N} = L/\ell$ or $2^{N/3} = L/\ell$. Finally the space-filling tree resistance R_{tree} is of order

$$R_{\text{tree}} \approx 3(\ln(L/\ell)/\ln(2))(r(\ell/L)^3). \quad (5)$$

To feed a volume L^3 with nutrients, a global flow rate Φ proportional to L^3 is necessary. The hydrodynamic power P_{hydro} dissipated in the flow is proportional to $\Phi \cdot \Delta P$ where $\Phi = \Delta P/R_{\text{tree}}$ and ΔP is the pressure drop between the entry of the system and each elementary sink. This pressure ΔP is determined by the very biological process. Finally the hydrodynamic power P_{hydro} is proportional to $(R_{\text{tree}})^{-1}$, in others words essentially proportional to

the volume L^3 (see eq. (5)), if one forgets the logarithmic factor which is of order of a few units.

The gain in resistance between the lattice network and the tree structure is then of order G

$$\frac{R_{\text{lattice}}}{R_{\text{tree}}} \approx G = \frac{\left(\frac{L}{\ell}\right)^2}{3 \ln\left(\frac{L}{\ell}\right) \ln(2)}. \quad (6)$$

For an organ in which $L = 20$ cm and $\ell = 200 \mu\text{m}$ (these are the typical values corresponding to the human lung for instance), G is of order $3 \cdot 10^4$! In summary, only small multi-cellular systems can be fed efficiently by diffusion, larger organs *have* to be fed by tree structures.

The above comparison is valid whatever the fluid. Note also that a diffusion time of order of 1 second is close to the drift time of air from the human mouth or nose to the volume of the lung and comparable to the time of the heart beat. In parallel, vascular plants have vascular tissues which circulate resources through the plant. This feature allows vascular plants to evolve to a larger size than non-vascular plants, which lack these specialized conducting tissues and are therefore restricted to relatively small sizes.

3 Tree optimalities in real living systems?

Can one observe in real systems this tree structure which seems to simultaneously optimize several independent criteria? 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 an increased robustness of the conductance towards geometrical variability [8]. This also constitutes a protection against mild forms of asthma. In a loose sense, its fractal dimension is larger than 3, but this statement corresponds to the fact that the infinite tree would not fit within a finite 3D volume. This situation is allowed in reality only 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 symmetric.

This increased scaling ratio in the intermediate tree is compensated by a scaling ratio smaller than 0.79 in the central airways [14, 21]. 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 larger daughter with $h > 0.79$, in other words a rapid and a slow branch at each bifurcation. This indicates that the “averaged” value of 0.85 does not properly describe the complicated effects of a succession of rapid and slow bronchi.

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]. Optimizing the amount of blood for a given energy dissipation was the criterion driving Hess and Murray in their derivation of the optimal value $h = (1/2)^{1/3}$. This value has also 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 on the branching asymmetry in real bronchial trees. It is probably a consequence of their growth in a natural non-symmetric environment [24–26]. It has been shown that this could benefit the global conductance which is less sensitive to bronchus constriction than in the symmetric tree [8].

There are however drawbacks to the “magical” combined optimal efficiency of these tree structures. First, their performances strongly depend on the h value [8]. Secondly, the flow distribution at the ends might exhibit an extreme sensitivity to defects. This can occur for instance in the end distribution of fresh air entering the pulmonary airway tree if the flow is not strictly divided into $1/2$ and $1/2$ at each dichotomous bifurcation, but into $1/2 + \alpha$ and $1/2 - \alpha$. Let us suppose that a similar splitting occurs at the next bifurcation. Then the flow will be divided among the 4 grand-daughter branches according to $(1/2 + \alpha)^2$, $(1/2 - \alpha)(1/2 + \alpha)$ twice and $(1/2 - \alpha)^2$. This is the start of a multiplicative process which provides after N bifurcations a strongly uneven distribution of the flow, ranging from $(1/2 - \alpha)^N$ to $(1/2 + \alpha)^N$ 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 an inherent feature of a tree-like system to create unequal distribution of the flows. This means that, for a given flow rate imposed at the entrance, these “magic” trees have to be regulated in order to be efficient even distributive systems. This is the case for arteries that are classically known to be active, but it is a general fact that a rigid tree with many generations would not be an efficient distribution system because of its extreme sensitivity to defects.

So the question arise of why we are breathing normally through an asymmetric tree. The reason is that the hydrodynamic motor is not at the tree entrance, the mouth or the nose in humans. It is constituted by the 30,000 acini that simultaneously breath and impose comparable flow rates at each of the 30,000 terminal bronchioles of the tracheobronchial tree. The asymmetry has however a direct consequence: the transit time for external air to reach each of the individual acini is not unique. Oxygenation times are distributed among the various acini [21, 29]. This avoids a simultaneous arrival of fresh air inside the whole lung and provides instead a more steady supply of oxygen.

The above remarks give a simple but fundamental reason why positive and negative pressure artificial ventilations work differently. In the case of positive pressure artificial ventilation, it is the external pressure at mouth-nose, imposed by a respirator, which drives the system and in this case, the tendency to heterogeneity will in principle

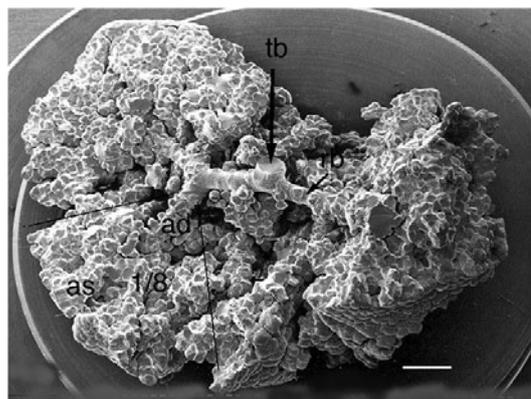


Fig. 4. Human pulmonary acinus (courtesy of E.R. Weibel). The scale marker is 1 mm. The acinus entry is the end of the transitory bronchiole (tb) and one can observe the first alveolae on the respiratory bronchiole (rb).

prevail. This might have severe medical consequences. On the opposite, in the case of negative pressure artificial ventilation driven by electric stimulation of the diaphragm, the final distribution will be more uniform, as in normal ventilation [30].

4 Some remarkable properties of the mammalian respiratory acinus and why do mammals need a distribution tree feeding small acini

Each termination of the bronchial tree, called a terminal bronchiole, feeds an acinus which is the gas exchange unit for respiration (shown in fig. 4). This acinus is at the same time a mini-pump for air. So once again, one finds that two totally different functions, gas exchange and mechanical pumping, are achieved by the same organ. To resist the hydrodynamic pressure difference, the membrane must have a minimal strength which means a minimal thickness and consequently a finite resistance for gas diffusion [31]. The acinus surface must then be large enough to supply the required amount of oxygen to the blood. 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 which plays an essential role [32]. The proximal acinar regions receive fresh air through the terminal bronchioles, but the more distal acinar regions, located deeper than the convection/diffusion transition region and containing the major exchange surface, are only fed by diffusion. These regions are therefore submitted to diffusion limitations also called *diffusion screening* [33]. Qualitatively, diffusion screening is the consequence of the fact that, when O_2 molecules diffuse inside the acinus, they may hit the alveolar membrane and be trapped by blood. Consequently, air is progressively depleted from its oxygen content as it progresses deeper into the acinar airway tree [32].

The oxygen flow rate across the acinar alveolar membrane 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 over the membrane permeability W [33]. This length Λ is of purely physico-chemical nature and its value is around 28 cm in the human lung. The “surface perimeter” L_p of an irregular membrane is the ratio of its area S by its diameter, the diameter being that of the smallest sphere embedding the irregular surface of the membrane. If Λ is larger than L_p the surface works uniformly. On the other hand, 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 $L_p \approx 30$ cm for a 1/8 sub-acinus. This remarkable agreement between the values of Λ and L_p is also found in the acini of several mammalian species [32]. It strongly suggests that diffusion screening plays an essential role in mammalian respiration, and that lung design is adjusted to cope with this problem. At the same time, it also indicates that too large acini in which L_p would be much larger than Λ_{O_2} would be poorly working. This is the reason why lungs are not made of a single very large acinus but are instead constituted of 30,000 small acini found in the human lung [34], all supplied by the efficient branched conducting airways described in the previous sections.

It is also interesting to consider the acinus functioning in terms of energetic efficiency. The potential energy that is used for oxygen transfer is the entropic term in the chemical potential. In the case of an ideal solution, the chemical potential per particle (here O_2 molecule) can be written as

$$\mu = \mu_0 + k_B T \ln C, \quad (7)$$

where k_B is the Boltzmann factor, T is the temperature, and C is the oxygen concentration. The driving potential for oxygen diffusion between alveolar gas and blood is the oxygen chemical potential difference between air and venous blood. Blood is a complex fluid in which oxygen is essentially trapped in hemoglobin molecules. However, blood as a whole can be considered in first approximation as an equivalent fluid in which the oxygen solubility is the same as the oxygen solubility in the gas. This is justified by the fact that at equilibrium, or in other words for identical oxygen partial pressures, one liter of air contains approximately the same quantity of oxygen than one liter of blood. So the drop of chemical potential between alveolar gas and venous blood can be expressed as

$$\Delta\mu = k_B T \ln \left(\frac{C_{\text{alv}}}{C_v} \right), \quad (8)$$

where C_{alv} and C_v respectively are the oxygen concentration in the averaged alveolar gas and in the venous blood. If the solubilities are approximately the same, then $\ln(C_{\text{alv}}/C_v) = \ln(P_{\text{alv}}/P_v)$, where P_{alv} and P_v are the oxygen partial pressures. Typical values are $P_{\text{alv}} \approx 100$ mm Hg and $P_v \approx 40$ mm Hg, which implies that $\Delta\mu \approx 0.9 k_B T$ or 23 meV. This means that the irreversible transfer from gas to blood uses an energy of entropic origin of order of $k_B T$ (≈ 1 eV per particle). Note that this

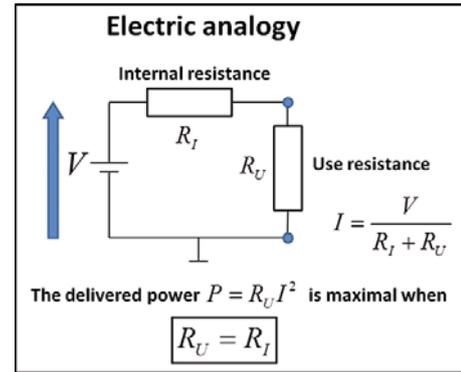


Fig. 5. Acinus-equivalent electric circuit for the oxygen exchange between the alveolar gas and blood. In the equivalence V stands for the chemical potential per particle of order $k_B T$, the generator internal resistance R_I stands for the access diffusion resistance $(DL)^{-1}$ and the useful resistance R_U stands for the membrane resistance (WS^{-1}) .

energy is only a small part of the total chemical energy transported by an oxygen molecule that is contained in the term μ_0 of the chemical potential of the order of 1 eV.

Now one can ask the following question: what are the exchanger conditions to make a better use of the entropic energy of oxygen in air? The problem can be formulated as a standard electric problem in which a source with an electric potential V and an internal resistance R_I feeds a “useful” resistance R_U , see fig. 5. The used power is $R_U I^2$ and its maximum can easily be obtained from Ohm’s law: it is found to be maximum when $R_U = R_I$. This is a classical result in electric network theory. Here the problem is similar, provided that one uses $k_B T$ for V , $(DL)^{-1}$ for the internal resistance and (WS^{-1}) for the “useful” resistance R_U . So the equality condition between the diffusion resistance and the permeation resistance corresponds to the best configuration to extract the maximum power from a purely entropic generator. In that sense, evolution has selected the best entropic machine. To our knowledge, this is a type of optimization that has never been mentioned in the past.

Under the same criterion, one should consider the case of the respiration of fishes in water. A general expression for the permeability of a membrane of thickness δ is $W = D_{O_2, H_2O} / \delta$ where D_{O_2, H_2O} is the diffusion coefficient of oxygen in water. Then, for fishes, the length is equal to $D_{O_2, H_2O} / (D_{O_2, H_2O} / \delta) = \delta$. And indeed the gills are arranged in a simple linear manner with a length of order $50 \mu\text{m}$ and the membrane thickness, in fishes, is of the order of $40 \mu\text{m}$ [35]. In that sense, oxygen exchangers in both mammals and fishes obey the same “best entropic machine” optimization.

5 A phylogenetic point of view induced by physics, what came first?

In summary the respiration of mammals obeys different types of optimalities: best use of mechanical energy in



Fig. 6. Small bronchi, bronchioles (in white) and pulmonary arteries and veins in the human lung. The pulmonary arteries transport venous blood but they have been coloured here in red while veins are coloured in blue (Courtesy of E.R. Weibel).

the tracheobronchial tree and best use of entropic energy in the acini systems to capture oxygen. But the mammalian lung tracheobronchial tree presents also geometric and kinematic optimization. Since this system is the result of natural selection, the obvious question arises: during evolution, what came first?

The general idea behind our suggestion is, following F. Jacob, that of the role of “tinkering” in evolution [36]. This means that a genetic system selected for one specific property can be used later for a different property if both combined properties are simultaneously “optimal”. Several systems have already been found to be used by living organisms for very different functions. One example is the RuBisCO enzyme that is used for sulfur metabolism [37]. Another example is the crystallin genes issued from chaperone-like proteins [38, 39]. Such findings have been expressed as the concept of “the book as a paperweight” by Danchin [40]. The same processes are also known as gene sharing [41] 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? In fact, space-filling is a prerequisite because the volume of a living system has to be fed. As we recalled, diffusive transport is effective at small scales and diffusion is itself space filling. But larger systems could not emerge without the emergence of distributive tree structures. 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. The transport system has then to be space-filling.

In Nature, there are two large classes of space-filling geometry: networks with loops or trees. Both could exist but the tree is, as discussed above, much more efficient from the energetic point of view [11]. So, our suggestion is that tree distribution systems have been selected together with the growth of large multi-cellular systems and later

the emergence of animals. Having an energetically efficient 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, their arterial system would therefore have necessarily evolved by natural selection towards energetic efficiency.

In contradistinction, in normal conditions, the viscous dissipation in the aerial bronchial tree of mammalian is only a small part of the work for breathing 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 pulsatile respiration, *i.e.* mammalian respiration. So the phylogenesis that physics suggests starts from space-filling and then proceeds to energetic efficiency to be finally used for the aerial respiration of mammals. Although this does not constitute a proof, the visual observation of fig. 6 suggests that the same genetic material could have been at work in the growth of arteries, veins and bronchi.

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