A General Model for the Origin of Allometric Scaling Laws in Biology

Geoffrey B. West, James H. Brown,* Brian J. Enquist

Allometric scaling relations, including the 3/4 power law for metabolic rates, are characteristic of all organisms and are here derived from a general model that describes how essential materials are transported through space-filling fractal networks of branching tubes. The model assumes that the energy dissipated is minimized and that the terminal tubes do not vary with body size. It provides a complete analysis of scaling relations for mammalian circulatory systems that are in agreement with data. More generally, the model predicts structural and functional properties of vertebrate cardiovascular and respiratory systems, plant vascular systems, insect tracheal tubes, and other distribution networks.

Biological diversity is largely a matter of body size, which varies over 21 orders of magnitude (1). Size affects rates of all biological structures and processes from cellular metabolism to population dynamics (2, 3). The dependence of a biological variable Y on body mass M is typically characterized by an allometric scaling law of the form

\[ Y = Y_0 M^b \]  

where b is the scaling exponent and Y0 a constant that is characteristic of the kind of organism. If, as originally thought, these relations reflect geometric constraints, then b should be a simple multiple of one-third. However, most biological phenomena scale as quarter rather than third powers of body mass (2–4). For example, metabolic rates B of entire organisms scale as M^{3/4}; rates of cellular metabolism, heartbeat, and maximal population growth scale as M^{1/4}; and times of blood circulation, embryonic growth and development, and life-span scale as M^{1/4}. Sizes of biological structures scale similarly: For example, the cross-sectional areas of mammalian aortas and of tree trunks scale as M^{1/4}. No general theory explains the origin of these laws. Current hypotheses, such as resistance to elastic buckling in terrestrial organisms (5) or diffusion of materials across hydrodynamic boundary layers in aquatic organisms (6), cannot explain why so many biological processes in nearly all kinds of animals (2, 3), plants (7), and microbes (8) exhibit quarter-power scaling.

We propose that a common mechanism underlies these laws: Living things are sustained by the transport of materials through linear networks that branch to supply all parts of the organism. We develop a quantitative model that explains the origin and ubiquity of quarter-power scaling; it predicts the essential features of transport systems, such as mammalian blood vessels and bronchial trees, plant vascular systems, and insect tracheal tubes. It is based on three unifying principles or assumptions: First, in order for the network to supply the entire volume of the organism, a space-filling fractal-like branching pattern (9) is required. Second, the final branch of the network (such as the capillary in the circulatory system) is a size-invariant unit (2). And third, the energy required to distribute resources is minimized (10); this final restriction is basically equivalent to minimizing the total hydraulic resistance of the system. Scaling laws arise from the interplay between physical and geometric constraints implicit in these three principles. The model presented here should be viewed as an idealized representation in that we ignore complications such as tapering of vessels, turbulence, and nonlinear effects. These play only a minor role in determining the dynamics of the entire network and could be incorporated in more detailed analyses of specific systems.

Most distribution systems can be described by a branching network in which the sizes of tubes regularly decrease (Fig. 1). One version is exhibited by vertebrate circulatory and respiratory systems, another by the “vessel-bundle” structure of multiple parallel tubes, characteristic of plant vascular systems (11). Biological networks vary in the properties of the tube (elastic to rigid), the fluid transported (liquid to gas), and the nature of the pump (a pulsatile compression pump in the cardiovascular system, a pulsatile bellows pump in the respiratory system, diffusion in insect
tracheae, and osmotic and vapor pressure in the plant vascular system). In spite of these differences, these networks exhibit essentially the same scaling laws.

For convenience we shall use the language of the cardiovascular system, namely, aorta, arteries, arterioles, and capillaries; the correspondence to other systems is straightforward. In the general case, the network is composed of N branches from the aorta (level 0) to the capillaries (level N, denoted here by a subscript c) (Fig. 1C). A typical branch at some intermediate level k has length l_k, radius r_k, and pressure drop Δp_k (Fig. 1D). The volume rate of flow is \( Q_k = \pi r_k^2 u_k \) where \( u_k \) is the flow velocity averaged over the cross section, and, if necessary, over time. Each tube branches into \( n_k \) smaller ones, so the total number of branches at level k is \( N_k = n_k n_{k-1} \cdots n_1 \). Because fluid is conserved as it flows through the system

\[
\dot{Q}_0 = N_0 \dot{Q}_k = N_c \pi r_k^2 \bar{u}_k = N_k \pi r_k^2 \bar{u}_k
\]

which holds for any level k. We next introduce the important assumption, the second above, that the terminal units (capillaries) are invariant, so \( r_k \), \( l_k \), \( \bar{u}_k \), and, consequently, \( \Delta p_k \) are independent of body size. Because the fluid transports oxygen and nutrients for metabolism, \( \dot{Q}_0 \propto B \); thus, if \( B \propto M^a \) (where a will later be determined to be 3/4), then \( \dot{Q}_0 \propto M^3 \). Equation 2 therefore predicts that the total number of capillaries must scale as B, that is, \( N_c \propto M^3 \).

To characterize the branching, we introduce scale factors \( \beta_k = r_{k+1}/r_k \) and \( \gamma_k = l_{k+1}/l_k \). We shall prove that in order to minimize the energy dissipated in the system in the sense of the third principle above, the network must be a conventional self-similar fractal in that \( \beta_k = \beta \), \( \gamma_k = \gamma \) and \( n_k = n \), all independent of k (an important exception is \( B_0 \), in pulsatile systems). For a self-similar fractal, the number of branches increases in geometric proportion (\( N_k = n^k \)) as their size geometrically decreases from level 0 to level N. Before proving self-similarity, we first examine some of its consequences.

Because \( N_c = n^N \), the number of generations of branches scales only logarithmically with size

\[
N = \frac{a \ln(M/M_o)}{\ln n}
\]

where \( M_o \) is a normalization scale for \( M (13) \). Thus, a whale is 10^7 times heavier than a mouse but has only about 70% more branchings from aorta to capillary. The total volume of fluid in the network ("blood volume" \( V_b \)) is

\[
V_b = \sum_{k=0}^{N} N_k V_k = \sum_{k=0}^{N} \pi r_k^2 l_k^k
\]

where the last expression reflects the fractal nature of the system. As shown below, one can also prove from the energy minimization principle that \( V_b \propto M^3 \). Because \( n \beta^3 < 1 \) and \( N \gg 1 \), a good approximation to Eq. 4 is \( \dot{Q}_k = V_b/(1 - n \gamma^2) = V_b (\gamma^2)^{-1/N} \)

\[
Q_k = \frac{(n \gamma^{1/N})^{-N} - 1}{(n \gamma^{1/N}) - 1} n^N V_c
\]

where \( \gamma^2 = 1 \) and \( \gamma \) is independent of \( \beta \). From our assumption that capillaries are invariant units, it therefore follows that \( (\gamma^2)^{-1/N} \propto M \). Using this relation in Eq. 3 then gives

\[
a = - \frac{\ln n}{\ln(\gamma^2)}
\]

To make further progress requires knowledge of \( \gamma \) and \( \beta \). We shall show how the former follows from the space-filling fractal requirement, and the latter, from the energy minimization principle.

A space-filling fractal is a natural structure for ensuring that all cells are serviced by capillaries. The network must branch so that a group of cells, referred to here as a "service volume," is supplied by each capillary. Because \( \gamma_k \ll 1 \) and the total number of branchings \( N \) is large, the volume supplied by the total network can be approximated by the sum of spheres whose diameters are that of a typical kth-level vessel, namely \( 4/3 \pi (l_k/2)^3 N_k \). For large \( N \) (but \( n \), this estimate does not depend significantly on the specific level, although it is most accurate for large k. This condition, that the fractal be volume-preserving from one generation to the next, can therefore be expressed as \( 4/3 \pi (l_k/2)^3 N_k \approx 4/3 \pi (l_{k-1}/2)^3 N_{k-1} \). This relation gives \( \gamma_k^3 = (l_k/l_{k-1})^3 \approx N_k/N_{k-1} = 1/n_k \), showing that \( \gamma_k \approx n^{-1/3} \approx \gamma \) must be independent of k. This result for \( \gamma_k \) is a general property of all space-filling fractal systems that we consider.

The 3/4 power law arises in the simple case of the classic rigid-pipe model, where the branching is assumed to be area-preserving, that is, the sum of the cross-sectional areas of the daughter branches equals that of the parent, so \( \pi r_k^2 = \pi r_{k+1}^2 \). Thus, \( \beta_k = r_{k+1}/r_k = n^{-1/3} = \beta \), independent of k. When the area-preserving branching relation, \( \beta = n^{-1/3} \), is combined with the space-filling result for \( \gamma \), Eq. 5 yields \( a = 3/4 \), so \( B \propto M^{10} \). Many other scaling laws follow. For example, for the aorta, \( r_0 = \beta^{-1/3} l_0 = N_0^{-1/3} r_0 \) and \( l_0 = \gamma^{-1} l_0 = N_0^{1/3} l_0 \), yielding \( r_0 \propto M^{10/3} \), and \( l_0 \propto M^{10/3} \). This derivation of the \( a = 3/4 \) law is essentially a geometric one, strictly applying only to systems that exhibit area-preserving branching. This property has the further consequence, which follows from Eq. 2, that the fluid velocity must remain constant throughout the network and be independent of size. These features are a natural consequence of the idealized vessel-branch structure of plant vascular systems (Fig. 1B), in which area-preserving branching arises automatically because each branch is assumed to be a bundle of \( n^{N-k} \) elementary vessels of the same radius (11). Pulsatile mammalian vascular systems, on the other hand, do not conform to this structure, so for them, we must look elsewhere for the origin of quarter-power scaling laws.

Some features of the simple pipe model remain valid for all networks: (i) The quantities \( \gamma \) and \( \beta \) play a dual scaling role; they determine not only how quantities scale from level 0 (aorta) to N (capillary) within a single organism of fixed size, but also how a given quantity scales when organisms of different masses are compared. (ii) The fractal nature of the entire system as expressed, for example, in the summation in Eq. 4 leads to a scaling different from that for a single tube, given by an individual term in the series. These network systems must therefore be treated as a complete integrated unit; they cannot realistically be modeled by a single or a few representative vessels. (iii) The scaling with \( M \) does not
depend on the branching ratio \( n \).

We next consider the dynamics of the network and examine the consequences of the energy minimization principle, which is particularly relevant to mammalian vascular systems. Pulsatil flow, which dominates the larger vessels (aorta and major arteries), must have area-preserving branching, so that \( \beta = n^{-1/2} \), leading to quarter-power scaling. The smaller vessels, on the other hand, have the classic “cubic-law” branching (10), where \( \beta = n^{-1/3} \), and play a relatively minor role in allometric scaling.

First consider the simpler problem of nonpulsatile flow. For steady laminar flow of a Newtonian fluid, the viscous resistance of a single tube is given by the well-known Poiseuille formula

\[
R_k = \frac{8 \mu L_k}{\pi r_k^4},
\]

where \( \mu \) is the viscosity of the fluid. Ignoring small effects such as turbulence and nonlinearities at junctions, the resistance of the entire network is given by

\[
Z = \sum_{k=0}^{N-1} R_k = \sum_{k=0}^{N-1} \frac{8 \mu L_k}{\pi r_k^4} = \frac{1}{(1 - n \beta^2 / \gamma)^{3/2}}
\]

(6)

Now, \( n \beta^2 / \gamma < 1 \) and \( N \gg 1 \), so a good approximation is

\[
Z \approx R_b = (1 - n \beta^2 / \gamma) N_c.
\]

Because \( R_b \) is invariant, \( Z \propto N_c^{-1} \propto M^{-3/2} \), which leads to two important scaling laws: blood pressure \( \Delta p = Z Q \) must be independent of body size and the power dissipated in the system (cardiac output) \( W = Q \Delta p \propto M^0 \), so that the power expended by the heart in overcoming viscous forces is a size-independent fraction of the metabolic rate. Neither of these results depends on detailed knowledge of \( n, \beta, \) or \( \gamma \); in contrast to results based on \( V_0 \propto M \), such as Eq. 5, \( a = 3/4 \), and \( r_s \propto M^{1/8} \).

From Eq. 2, \( Q_0 = \pi r_s^2 h_0 \), which correctly predicts that the velocity of blood in the aorta \( \bar{u}_s \propto M^{3/4} \). However, an area-preserving scaling relation \( \beta = n^{-1/2} \) also implies by means of Eq. 2 that \( \bar{u}_s = \bar{u}_0 \) for all \( k \). This relation is valid for fluid flow in plant vessels (because of the vascular bundle structure) (11, 15) and insect tracheae (because gas is driven by diffusion) (16); both therefore exhibit area-preserving branching, which leads to 3/4 power scaling of metabolic rate. Branching cannot be entirely area-preserving in mammalian circulatory systems because blood must slow down to allow materials to diffuse across capillary walls. However, the pulsatile nature of the mammalian cardiovascular system solves the problem.

Energy minimization constrains the network for the simpler nonpulsatile systems. Consider cardiac output as a function of all relevant variables: \( W(t_k, \lambda_k, n_k, M) \). To sustain a given metabolic rate in an organism of fixed mass \( M \) with a given volume of blood \( V_0(t_k, \lambda_k, n_k, M) \), the minimization principle requires that the cardiac output be minimized subject to a space-filling geometry. To enforce such a constraint, we use the standard method of Lagrange multipliers (\( \lambda_k, \lambda_\beta \), and \( \lambda_\lambda \)) and so need to minimize the auxiliary function

\[
F(t_k, \lambda_k, n_k) = W(t_k, \lambda_k, n_k, M) + \lambda V(t_k, \lambda_k, n_k, M) + \sum_{k=0}^{N-1} \lambda_\beta N_k n_k + \lambda_\lambda M
\]

(7)

Because \( B \propto Q_0 \), and \( W = Q_0^2 Z \), this problem is tantamount to minimizing the impedance \( Z \), which can therefore be used in Eq. 7 in place of \( W \). First, consider the case where \( n_k = n \), so that we can use Eqs. 4 and 6 for \( V_k \) and \( Z_k \), respectively. For a fixed mass \( M \), the auxiliary Lagrange function, which incorporates the constraints, must be minimized with respect to all variables for the entire system \( (t_k, \lambda_k, n_k) \). This requires \( \delta F/\delta \lambda = \delta F/\delta t_k = \delta F/\delta n_k = 0 \), which straightforwardly leads to \( \beta_k = n_k^{-1/3} \). More generally, by considering variations with respect to \( n_k \), one can show that \( n_k = n \), independent of \( k \). The result, \( \beta_k = n_k^{-1/3} \), is a generalization of Murray’s finding (17), derived for a single branching, to the complete network. Now varying \( M \) and minimizing \( F \) in Eq. 7 (\( \delta F/\delta Q = 0 \) leads to \( V_0 \propto M \), which is just the relation needed to derive Eq. 5. Although the result \( \beta_k = n_k^{-1/3} \) is independent of \( k \), it is not area-preserving and therefore does not give \( a = 3/4 \) when used in Eq. 5; instead, it gives \( a = 1 \). It does, however, solve the problem of slowing blood in the capillaries: Eq. 2 gives \( n_k = n \), so \( \bar{u}_k = \bar{u}_0 \). For humans, \( N_c = 10^{10} \), \( n_k = 10^{-3} \), in reasonable agreement with data (18). On the other hand, it leads to an incorrect scaling law for this ratio: \( \bar{u}_k / \bar{u}_0 \propto M^{-1/4} \). Incorporating pulsatile flow not only solves these problems, giving the correct scaling relations (\( a = 3/4 \) and \( \bar{u}_k / \bar{u}_0 \propto M^0 \)), but also gives the correct value for \( \bar{u}_k / \bar{u}_0 \).

A complete treatment of pulsatile flow is complicated; here, we present a simplified version that contains the essential features needed for the scaling problem. When an oscillatory pressure \( \rho \) of angular frequency \( \omega \) is applied to an elastic (characterized by modulus \( E \)) vessel with wall thickness \( h \), a damped traveling wave is created: \( \bar{p} = p_0 e^{i(\omega t - 2 \pi z / \lambda)} \). Here, \( t \) is time, \( z \) is the distance along the tube, \( \lambda \) is the wavelength, and \( p_0 \) is the amplitude averaged over the radius; the wave velocity \( c = 2 \pi a \lambda \). Both the impedance \( Z \) and the dispersion relation that determines \( c \) are derived by solving the Navier-Stokes equation for the fluid coupled to the Navier equations for the vessel wall (19).

In the linearized incompressible-fluid, thin-wall approximation, this problem can be solved analytically to give

\[
\frac{c^2}{g} = \frac{l_j^{(1/2)}}{g^{(1/2)}} \quad \text{and} \quad Z \approx \frac{c^2 g}{p^2} \tag{8}
\]

Here \( \alpha = (\omega p / \mu)^{1/2} \) is the dimensionless Womersley number (13), and \( c_0 = (E h / 2 \rho)^{1/2} \) is the Korteweg-Moens velocity. In general, both \( c \) and \( Z \) are complex functions of \( \omega \), so the wave is attenuated and disperses as it propagates. Consider the consequences of these formulas as the blood flows through progressively smaller tubes: For large tubes, \( \alpha \) is large (in a typical human artery, \( \alpha \approx 5 \)), and viscosity plays almost no role. Equation 8 then gives \( c = c_0 \) and \( Z = c_0 \rho / 4 \pi^2 \); because both of these are real quantities, the wave is neither attenuated nor dispersed. The \( \tau \) dependence of \( Z \) has changed from the nonpulsatile \( \tau^{-4} \) behavior to \( \tau^{-2} \). Minimizing energy loss now gives \( h / \bar{r}_k \) (and, therefore, \( c_k \)) independent of \( k \). For large \( k \), area-preserving flow dominates; but, because both of these are real quantities, the wave is neither attenuated nor dispersed. The \( \tau \) dependence of \( Z \) has changed from the nonpulsatile \( \tau^{-4} \) behavior to \( \tau^{-2} \). Minimizing energy loss now gives \( h / \bar{r}_k \) (and, therefore, \( c_k \)) independent of \( k \), and, most importantly, an area-preserving law at the junctions, so \( \beta_k = n_k^{-1/3} \). This relation ensures that energy-carrying waves are not reflected back up the tubes at branch points and is the exact analog of impedance matching at the junctions of electrical transmission lines (18). As \( k \) increases, the sizes of tubes decrease, so \( \alpha \to 0 \) (in human arterioles, for example, \( \alpha \approx 0.05 \)), and the role of viscosity increases, eventually dominating the flow. Equation 8 then gives \( c \approx \omega p / \mu \), in agreement with observation (18). Because \( c \) and, consequently, \( \lambda \) now have imaginary parts, the traveling wave is heavily damped, leaving an almost steady oscillatory flow whose impedance is, from Eq. 8, given by the Poiseuille formula; that is, the \( \tau^{-4} \) behavior is restored. Thus, for large \( k \), corresponding to small vessels, \( \beta_k = n_k^{-1/3} \). We conclude that for pulsatile flow, \( \beta_k \) is not independent of \( k \) but rather has a step-like behavior (Fig. 2).

Fig. 2. Schematic variation of the Womersley number \( \omega \) and the scaling parameters \( \beta_k \) and \( \gamma_k \) with level number \( k \) for pulsatile systems. Note the step-like change in \( \beta_k \) at \( k \) from area-preserving pulse-wave flow in major vessels to area-increasing Poiseuille-type flow in small vessels.
is well supported by empirical data (18, 20, 21). The crossover from one behavior to the other occurs over the region where the wave and Poiseuille impedances are comparable in size. The approximate value of \( k \) where this occurs (say, \( \overline{k} \)) is given by \( \frac{r_f}{r_o} \approx 8 \mu_p / p_o \), leading to \( N = \overline{k} = N = \ln(8 \mu_p / p_o \kappa) / \ln \rho \), independent of \( M \). Thus, the number of generations where Poiseuille flow dominates should be independent of body size. On the other hand, the crossover point itself grows logarithmically: \( \overline{k} \propto N \propto \ln M \). For humans, with \( n = 3 \) (21), \( N \approx 15 \) and \( N \approx 22 \) (assuming \( N \approx 2 \times 10^{4} \)), whereas with \( n = 2 \), \( N \approx 24 \) and \( N \approx 34 \). These values mean that in humans Poiseuille flow begins to compete with the pulse wave after just a few branchings, dominating flow after about seven. In a 3-g shrew, Poiseuille flow begins to dominate shortly beyond the aorta.

The derivation of scaling laws based on \( k \) derived from Eqs. 7 and 8 (Fig. 2) leads to the same results as before. For simplicity, assume that the crossover is sharp; using a gradual transition does not change the resulting scaling laws. So, for \( k > \overline{k} \), define \( \beta_0 = \beta_\infty = n^{-1/3} \) and, for \( k < \overline{k} \), \( \beta_0 = \beta_\infty = n^{-1/2} \). This predicts that area preservation only persists in the pulsatile region from the aorta through the large arteries, at most until \( k = \overline{k} \). First consider the radius of the aorta, its scaling behavior is now given by \( r_o = r_0 \beta_0 \approx r_0 n^{-1/3+1/6} = r_0 n^{-1/2} \), which gives \( r_o \approx M^{1/3} \) and, for humans, \( r_0 \approx 10^{-4} \), in agreement with data (2). Using Eq. 3 we obtain, for the ratio of fluid velocities in the aorta to that in the capillary, \( \frac{V_o}{V_c} = N \frac{r_o}{r_c} \approx n^{4/3} \frac{r_0}{r_c} \approx 250 \), independent of \( M \), again in agreement with data. Because \( \gamma \) reflects the space-filling geometry, it remains unchanged, so we still have \( \gamma \approx M^{3/4} \). Blood volume \( V_b \), however, is more complicated

\[
V_b = \frac{V_c}{(\beta_\infty)^2} \left( \frac{\beta_0}{\beta_\infty} \right)^2 \frac{1 - (n \beta_\infty^2 \gamma)^n}{1 - (n \beta_\infty^2 \gamma)^k} + \frac{1 - (n \beta_\infty^2 \gamma)^n}{1 - (n \beta_\infty^2 \gamma)^{1/2}} \right) \]

This formula is a generalization of Eq. 4 and is dominated by the first term, which represents the contribution of the large tubes (aorta and arteries). Thus, \( V_b \propto n^{4/3} k \) \( \propto n^{4/3} M \), because it must scale as \( M \), leads, as before, to \( a = 3/4 \). As size decreases, the second term, representing the cubic branching of small vessels, becomes increasingly important. This behavior predicts small deviations from quarter-power scaling (\( a \approx 3/4 \)), observed in the smallest mammals (2). An expression analogous to Eq. 9 can be derived for the total impedance of the system \( Z \). It is dominated by the small vessels (arterioles and capillaries) and, as before, gives \( \Delta \rho \) and \( \rho c \propto M^2 \).

In order to understand allometric scaling, it is necessary to formulate an integrated model for the entire system. The present model should be viewed as an idealized zeroth-order approximation: it accounts for many of the features of distribution networks and can be used as a point of departure for more detailed analyses and models. In addition, because it is quantitative, the coefficients, \( V_c \) of Eq. 1, can also, in principle, be derived. It accurately predicts the known scaling relations of the mammalian cardiovascular system (Table 1); data are needed to test other predictions. For example, the invariance of capillary parameters implies \( N_c \propto M^{1/4} \) rather than the naive expectation \( N_c \propto M \), so the volume serviced by each capillary must scale as \( M^{1/4} \), and capillary density per cross-sectional area of tissue, as \( M^{-1/2} \).

A minor variant of the model describes the mammalian respiratory system. Although pulse waves are irrelevant because the tubes are not elastic, the formula for \( Z \) is quite similar to Eq. 8. The fractal bronchial tree terminates in \( N_A \propto M^{3/4} \) alveoli. The network is space-filling, and the alveoli play the role of the service volume accounting for most of the total volume of the lung, which scales as \( M \). Thus, the volume of an alveolus \( V_A \propto M^{3/4} \), its radius \( r_A \propto M^{1/4} \), and its surface area \( A_A \propto r_A^2 \propto M^{1/2} \), so the total surface area of the lung \( A_L = N_A A_A \propto M^{1/2} \). This explains the paradox (22) that \( A_A \) scales with an exponent closer to 1 than the 3/4 seemingly needed to supply oxygen. The rate of oxygen diffusion across an alveolus, which must be independent of \( M \), is proportional to \( D_{O2} \sqrt{A_A / \rho} \). Thus, \( D_{O2} \propto M^{-1/4} \), which must be compensated for by a similar scaling of the oxygen affinity of hemoglobin. Available data support these predictions (Table 1).

Our model provides a theoretical, mechanistic basis for understanding the central role of body size in all aspects of biology. Considering the many functionally interconnecting parts of the organism that must obey the constraints, it is not surprising that the diversity of living and fossil organisms is based on the elaboration of a few successful designs. Given the need to redesign the entire system whenever body size changes, with empirical observations. Observed values of exponents are taken from (2, 3); ND denotes that no data are available.

### Table 1. Values of allometric exponents for variables of the mammalian cardiovascular and respiratory systems predicted by the model compared with empirical observations.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cardiovascular Exponent</th>
<th>Respiratory Exponent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta radius ( r_o )</td>
<td>3/8 = 0.375</td>
<td>Tracheal radius</td>
</tr>
<tr>
<td>Aorta pressure ( \Delta p_o )</td>
<td>0 = 0.00</td>
<td>Interpleural pressure</td>
</tr>
<tr>
<td>Aorta blood velocity ( u_o )</td>
<td>0 = 0.00</td>
<td>Air velocity in trachea</td>
</tr>
<tr>
<td>Blood volume ( V_b )</td>
<td>1 = 1.00</td>
<td>Lung volume</td>
</tr>
<tr>
<td>Circulation time</td>
<td>1/4 = 0.25</td>
<td>Volume flow to lung</td>
</tr>
<tr>
<td>Circulation distance</td>
<td>1/4 = 0.25</td>
<td>Volume of alveolus ( V_A )</td>
</tr>
<tr>
<td>Cardiac stroke volume</td>
<td>1 = 1.00</td>
<td>Tidal volume</td>
</tr>
<tr>
<td>Cardiac frequency ( \omega )</td>
<td>-1/4 = -0.25</td>
<td>Respiratory frequency</td>
</tr>
<tr>
<td>Cardiac output ( E )</td>
<td>3/4 = 0.75</td>
<td>Power dissipated</td>
</tr>
<tr>
<td>Number of capillaries ( N_c )</td>
<td>3/4 = 0.75</td>
<td>Number of alveoli ( N_A )</td>
</tr>
<tr>
<td>Service volume radius ( r_s )</td>
<td>1/12 = 0.083</td>
<td>Radius of alveolus ( r_A )</td>
</tr>
<tr>
<td>Womersley number ( \alpha )</td>
<td>1/4 = 0.25</td>
<td>Area of alveolus ( A_A )</td>
</tr>
<tr>
<td>Density of capillaries</td>
<td>-1/12 = -0.083</td>
<td>Area of lung ( A_L )</td>
</tr>
<tr>
<td>( O_2 ) affinity of blood ( P_{O2} )</td>
<td>-1/12 = -0.083</td>
<td>( O_2 ) diffusion capacity</td>
</tr>
<tr>
<td>Total resistance ( Z )</td>
<td>-3/4 = -0.75</td>
<td>Total resistance</td>
</tr>
<tr>
<td>Metabolic rate ( \beta )</td>
<td>3/4 = 0.75</td>
<td>( O_2 ) consumption rate</td>
</tr>
</tbody>
</table>

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either during ontogeny or phylogenetic diversification, small deviations from quarter-power scaling sometimes occur (3, 23). However, when body sizes vary over many orders of magnitude, these scaling laws are obeyed with remarkable precision. Moreover, the predicted scaling properties do not depend on most details of system design, including the exact branching pattern, provided it has a fractal structure (24). Significantly, nonfractal systems, such as combustion engines and electric motors, exhibit geometric (third-power) rather than quarter-power scaling (1). Because the fractal network must still fill the entire D-dimensional volume, our result generalizes to networks must still fill the entire D-dimensional volume, our result generalizes to

11. K. Shinozaki et al. ibid. 34, 345 (1963; [17, 21]). A generalization to nonuniform branching, where the radii and lengths at a given level may vary, is straightforward. 5

12. The branching of a vessel at level k into nk smaller vessels (Fig. 1) is assumed to occur over some small, but finite, distance that is much smaller than either lk or rk. This relation is similar to that assumed in the Strahler method [A. N. Strahler, Trans. Am. Geo- phy. Union 34, 345 (1963; [17, 21]). A generalization to nonuniform branching, where the radii and lengths at a given level may vary, is straightforward. 5

13. Normalization factors, such as M0, will generally be suppressed, as in Eq. 1. In general, all quantities should be expressed in dimensionless form; note, however, that this does not guarantee that they are size independent and scale as M0. For example, the Womersley number, a of Eq. 8, although dimensionless, scales as M0.5

14. This formula is not valid for plant vessel bundles because plants are composed of multiple parallel vessel elements. Their resistance is given by Z = θm(Nv /Nv)4, where θm is the length of a single vessel element, rv is its radius, and Nv is their total number.


20. See, for example, A. S. Liberal, Math. Biosci. 1, 375 (1967) and T. F. Sherman, J. Gen. Physiol. 78, 431 (1981), which contain summaries of earlier data; also M. Zanir and A. B. N. La Barbera, in: T. Ellenberger, Dept. of Biological Sciences, Boston University, Cambridge, MA 02115, and the Graduate Pro- gram in Biophysics, Harvard University, Cambridge, MA 02138, USA.

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24. This is reminiscent of the invariance of scaling expo- nents to details of the model that follow from renor- malization group analyses, which can be viewed as a generalization of classical dimensional analysis.

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Flexibility in DNA Recombination: Structure of the Lambda Integrase Catalytic Core

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Lambda integrase is archetypal of site-specific recombinases that catalyze intermolec- ular DNA rearrangements without energetic input. DNA cleavage, strand exchange, and relication steps are linked by a covalent phosphorytosine intermediate in which Tyr342 is attached to the 3'-phosphate of the DNA cut site. The 1.9 angstrom crystal structure of the integrase catalytic domain reveals a protein fold that is conserved in organisms ranging from archaeabacteria to yeast and that suggests a model for interaction with target DNA. The attacking Tyr342 nucleophile is located on a flexible loop about 20 angstroms from a basic groove that contains all the other catalytically essential residues. This bipartite active site can account for several apparently paradoxical features of integrase family recombinases, including the capacity for both cis and trans cleavage of DNA.

The integrase protein (Int) of Escherichia coli phage lambda (λ) belongs to a large family of site-specific DNA recombinases from archaeabacteria, eubacteria, and yeast (1–3) that catalyze rearrangements be- tween DNA sequences with little or no sequence homology to each other (4–8). Like λ Int, many of these recombinases function in the integration and excision of viral genomes into and out of the chromo- somes of their respective hosts. Others function in the degradation or segrega- tion of newly replicated chromosomes, conjugative transposition, regulation of plasmid copy number, or expression of cell surface proteins. Integrase family members have the distinctive ability to carry out a complete site-specific recombination reac-