Allometric Scaling in Biology

The design of living beings is not only a matter of molecular biology but also of geometry and physics. This was once more demonstrated with a biophysical model by G. B. West et al. (1) that had been fine-tuned to predict the famous scaling law of metabolism (2), namely a 3/4 power relation between body mass and energy consumption. While to predict the famous scaling law of metabolism, G. B. West demonstrated with a biophysical model by merely may simplify calculations. West may not be an unequivocal prerequisite, but essential for real life. We rather believe that question the view that fractal geometry is crease of the number of small branches (length distributions indicate nongeometric in-
compliance with real patterns, whose branch properties and predictions of a nonfractal blood branching pattern, that is, in segmental arter-
ment, blood vessels do not follow a fractal constant observed, for example in vessels branching off the aorta; moreover, arterial anastomoses, in addition to interconnected venous networks, are common and represent a situation that is not covered by the fractal approach (4, 5). (iii) The scaling law of metabolism, and other putative “fractal” properties like flow heterogeneity and so forth, can also be derived with a nonfractal model, as we have discussed recently (5). (iv) The West et al. model (1) is—strictly speaking—not fractal, because of the finite number of bifurcations, and definitely is not self-similar throughout the entire system, because the diameter relations vary from large vessels (where area-preserving branching is assumed) to smaller vessels (where cubic branching is postulated).

We acknowledge West’s et al. “zeroth order” approach and their cautious interpretation of the model. Nevertheless, in order to assess the influence of a (nearly) fractal as opposed to a nonfractal design, they would have to evaluate the difference. They did not include a 3D visualization of the simulated system, and the geometric properties were not evaluated. Their model does not appear to comply with real patterns, whose branch length distributions indicate nongeometric increase of the number of small branches (5).

Moreover, evolutionary constraints on the design of a vascular system (except in mammals) may come from a developmental bottleneck: eggs are (nearly) closed systems, where parsimony of blood and vessel material, but not of pumping energy, may be required to shape embryonic organs and to maximize fitness (5). Finally, comparable approaches (6) were inspired by Mandelbrot’s famous book (7).

References

G. B. West et al. (1) develop some properties of the cardiovascular system of mammals, starting from the assumption that the dimensions of the capillary blood vessels do not vary with mammal size. Their work also assumes that the blood velocity in the capillaries does not vary with mammal size and that the total blood flow through the capillaries varies with mammal weight raised to the 3/4 power. When the scale-invariant assumption on capillary size was combined with these last two conditions, the resulting conclusion was that the number of capillaries in mammals must scale with mammal size and definitely is not self-similar throughout the system. This means that the number of capillaries in mammals does not vary with mammal size, ever, contrary to my earlier work (2) and to the basic cardiovascular design and physiological processes of mammals. To illustrate this, we let \( n_c, l_c, \) and \( n_r \) denote the characteristic (or typical) radius, length, and number of capillary blood vessels, respectively, and we let \( W \) denote mammal body weight. The associated scaling laws may then be written (2, p. 71) as

\[
r_c \propto W^{1/12}, \quad l_c \propto W^{5/24}, \quad n_r \propto W^{5/8}
\]

where \( \propto \) denotes proportional variation.

These laws refer to changes in dimensions and number of capillary blood vessels accompanying change in mammal size, for example, from the mouse to the human and on to the elephant. The scaling laws were derived by considering basic restrictions associated with similar designs of the cardiovascular system of all mammals. They apply both to the actual beds of capillaries in the individual organs of mammals, as well as to the capillaries in representative single systemic and pulmonary beds. West et al. assume that \( r_c \) and \( l_c \) do not vary with mammal weight and that \( n_r \), with \( n_r \) varying with mammal weight raised to the 3/4 power.

With regard to Eqs. 1 and the basic design of the cardiovascular system, we may consider, for example, the total volume of blood \( V_c \) in the systemic or pulmonary capillaries. This volume is proportional to the product of their characteristic number \( n_r \) and their characteristic individual volume \( \pi r_c^2 l_c \). Thus, we have the proportional relation

\[
V_c \propto n_r \pi r_c^2 l_c.
\]

With the use of Eqs. 1, we see that this volume is predicted to vary directly with mammal weight, in agreement with experimental measurements of pulmonary capillary volume by Gehr et al. (3).

With regard to Eqs. 1 and physiological processes, we may consider, for example, the exchange of oxygen between capillaries and surrounding cells. This matter is of fundamental importance in understanding the scaling relations for capillary dimensions and number. Rate of oxygen transfer is determined by a diffusion operation that is, insofar as geometry is concerned, directly proportional to the product of characteristic surface area \( 2 \pi r_c l_c \) of the capillaries and inversely proportional to their characteristic wall thickness, \( h_c \). Oxygen transfer also depends on the driving force, as measured by the oxygen partial pressure. Thus, if \( \Delta P_o \) denotes difference between oxygen partial pressure inside and outside a capillary vessel, the following proportional relation applies for the oxygen transfer rate \( Q_o \) from a representative systemic capillary bed

\[
Q_o \propto n_r \Delta P_o \frac{r_c l_c}{h_c}
\]
In the absence of reason to the contrary, we may assume that wall thickness $h_c$ and radius $r_c$, vary with mammal size in the same manner, which must be the case if mechanical stress in the capillary walls from blood pressure is the same for all mammals. In addition, similarity requires that $\Delta P_o$ be proportional to $P_o$, the oxygen partial pressure in the blood itself. Thus, we have the relation

$$Q_o \propto n_o P_j c$$  \hspace{1cm} (4)

Variation of the oxygen partial pressure $P_o$ with mammal size has been studied in detail by Schmidt-Nielsen and Larimer (4). Moreover, I have shown that their measurements indicate that $P_o$ varies essentially as mammal weight raised to the negative 1/12 power (2). Thus, comparing Eqs. 1 with Eq. 4, we see that oxygen transfer rate is predictable to scale as mammal weight raised to the 3/4 power, in agreement with extensive well-known measurements of oxygen consumption rate (2, 5).

The rate of oxygen transfer from the capillaries of mammals must, of course, equal the rate of utilization of oxygen by their cells. To describe the latter, we may use the concept of an average body cell (2), with a characteristic number of such cells, $n_o$, assumed to be proportional to characteristic number of capillaries, $n_c$, as mammal size is varied. The volume of an average body cell is then proportional to the ratio $W/n_c$, and the characteristic length, $l_c$, defining the volume (or other external quantity such as surface area) is given by the cube root of this ratio. Thus, using the third of Eq. 1, we see that the scaling relations for average body cells are described by

$$l_c \propto W^{1/3}, \hspace{0.2cm} n_c \propto W^{1/3}$$  \hspace{1cm} (5)

With these results, we are in a position to describe the net rate of oxygen utilization of all body cells. As in the case of oxygen transfer, this is governed by a diffusion process, so that, like Eq. 3, we have the relation for oxygen utilization rate $\dot{Q_o}$, expressible as

$$\dot{Q_o} \propto n_o \Delta P_o \frac{l_c^2}{h_c}$$  \hspace{1cm} (6)

where $\Delta P_o$ denotes the difference between oxygen partial pressure outside and inside the cells, and $h_c$ denotes membrane (wall) thickness of the cells.

If $\Delta P_o$ is assumed independent of mammal size and $h_c$ assumed to vary in the same manner as $l_c$, as in (2), then the scaling Eqs. 5, when combined with Eq. 6, provide the prediction that oxygen utilization rate must vary with mammal weight raised to the 3/4 power, as required from measurement and from oxygen transfer rate. Alternatively, if $\Delta P_o$ is assumed to vary with mammal weight raised to the negative 1/12 power, as in the capillary exchange process described earlier, the same result can be predicted, provided that cell-membrane thickness scales with mammal weight raised to the 1/24 power. In either case, we see that, with $h_c \propto \Delta P_o$, the definition of average body cell as based on the capillary number of Eqs. 1 provides consistent results between oxygen transfer and oxygen utilization.

With respect to Eq. 6, we may also observe that the concept of an average body cell applies directly to cardiac cells because heart weight varies directly with mammal weight (2). The rate of operation of average body cells, say $\omega_c$, can therefore be assumed to be proportional to the heart rate. The amount of oxygen per unit cell volume that is utilized per cell cycle is then expressible from Eq. 6, with $h_c \propto \Delta P_o$, as

$$\dot{Q_o} \propto \frac{n_o \omega_o}{\omega_c} = \frac{1}{\omega_c^3} \propto \omega_c^3$$  \hspace{1cm} (7)

The left-hand side of this relation can be expected to be independent of mammal size for similarly designed mammals, in which case the right-hand side must also be scale invariant. This observation, accordingly, provides the following relation

$$\omega_c^3 \propto \omega_o^3$$  \hspace{1cm} (8)

where $\omega_o$ indicates no dependence on mammal weight. With the use of Eqs. 5, it can be seen from Eq. 8 that the rate of operation of average body cells $\omega_c$ and hence heart rate, is predicted to vary with mammal weight raised to the negative 1/4 power. This is in agreement with extensive measurements of heart rate (2, 5) and provides further evidence for the validity of the scaling laws of Eqs. 1.

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Response: The comments of Kurz and Sandau allow us to address some issues that were omitted from our report because of space constraints. We agree with several of the points that they make. In presenting our general geometric and hydrodynamic model for allometric scaling, we explicitly recognized that the branching architectures of biological distribution networks are not perfect fractals in two respects: (i) there is a fixed size of the terminal branches, and (ii) the scaling changes from area-preserving in major arteries to area-increasing in peripheral vessels.

We were also aware that the branching of real circulatory systems and other biological networks is not perfectly symmetrical, as our zeroth order model assumes. We explored the sensitivity of our results to variations in architecture, including asymmetrical branching and anastomoses. So long as the deviations are not extreme, the scaling exponents do not change. The crucial features are that the branching be predominantly area-preserving and volume-filling. This is reminiscent of phase transitions and scaling exponents in physical systems as derived from normalization group arguments. Other recent studies also show that our model is robust. Zairi (1) has made detailed anatomical and physiological measurements of cardiac arteries, which typically exhibit asymmetrical and anastomosing branching. He finds that the quantitative predictions of our model are still upheld. Turcotte et al. (2) analyze mathematically and by computer simulation the properties of area- and volume-filling networks with nonfractal “side-branches,” and they draw three-dimensional representations. They also find that the deviations from perfect fractal geometries do not appreciably change the predictions and applications our model. Therefore, we are confident that our zeroth order model is relatively insensitive to details of the branching architecture.

We do not agree with several other points made by Kurz and Sandau. First, although the mechanism of formation of cardiovascular and other biological distribution networks during early embryonic development is fascinating, it may be of limited relevance to the geometric and functional properties of well-developed functional networks during later stages of the life history. The cardiovascular systems of mammals and the vessel networks of plants appear to have different ontogenetic mechanisms, but still exhibit similar structural and functional properties. Second, we do not agree that our model has been “fine tuned to predict the famous scaling law of metabolism.” We developed a general model for fractal-like biological distribution networks, based on a simple branching geometry, basic physical principles, and a few well-known facts about mammalian anatomy and physiology.

Without any “fine tuning,” the model predicts a self-similar fractal-like network, 3/4-power allometric scaling of metabolic rate, and many other scaling relationships for structural and functional properties of mammalian cardiovascular and respiratory systems. Basically the same model, modified to incorporate known features of plant biology, predicts many features of the architecture,
Finally, we are not sure how one would perform the “controlled experiment” or make the comparisons to “nonfractal” models that Kurz and Sandau allude to. It is hard to imagine a system that would economically supply billions of cells without some kind of continuously branching network. We did mention that gasoline engines and electric motors, two examples of energy transforming systems without fractal-like resource supply, exhibit simple geometric scaling. Our model is difficult to compare with others that we are aware of, including those cited by Kurz and Sandau, because it considers the geometric structure and hydrodynamic function of an entire network as a single integrated system. The other models either consider the properties of isolated parts of networks, or are much more “fine tuned” by explicitly incorporating some of the empirical allometric scaling relationships that emerge as predictions of our model.

We see two problems with Dawson’s approach. First, in Eqs. 1 he assumes scaling relationships for the radius, length, and number of mammalian capillaries. The justification for the exponents is unclear to us, except that they appear to be required for the consistency of his argument about how the design of the mammalian cardiovascular system changes with body size. We question the empirical support for these values. In particular, while the data indicate that the radii of capillaries and of the red blood cells that travel through them do not vary with body size (3), Dawson assumes that capillary radius scales as M to the 1/12 power. Further, in expression (5) Dawson assumes that the linear dimensions of body cells increase with body size, as M to the 1/8. This relation would require that, when comparing a shrew weighing 2 g with a whale weighing 200,000,000 g, one observes the radii of capillaries and red corpuscles to increase by approximately 4.5 and those of somatic cells by 10. Such a difference has not been reported by mammalian anatomists and physiologists to our knowledge. In contrast, our model assumes that the dimensions of capillaries are invariant with respect to mammalian body size, and it predicts (not assumes, as Dawson seems to imply) that the number of capillaries varies as M to the 3/4. Therefore, our model predicts that the density of capillaries (number per cross-sectional area of tissue) should scale as M to the −1/12 = −0.083. Empirical measurements of four muscles (3) give an average value of −0.095, which we take as support for our model.

Second, this difference in the treatment of capillary anatomy highlights a fundamental difference in approach. In his comment and book (4), Dawson does not appear to treat the mammalian cardiovascular system with a complete model that demands internally consistent values of all parameters. Instead, he seems to make ad hoc assumptions about scaling exponents and other parameters. More fundamentally, Dawson does not explicitly treat the branching architecture of the entire circulatory system, although such an analysis is essential to derive the scaling relationships for such critical parameters as total blood volume, circulation time, and change in pressure and velocity from heart to capillary. In contrast, our zeroth-order model specifies both the geometry and hydrodynamics of the entire fractal-like branching network. Consequently, it is able to make a priori, testable predictions of all the relevant parameters. Whenever our predictions or assumptions differ from Dawson’s, we believe that the best available data support our model.

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