

Fifth dimension of life and the 4/5 allometric scaling law for human brain

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Abstract

Brain cells are not spherical. The basal metabolic rate (B) of a spherical cell scales as $B \sim r^2$, where r is the radius of the cell; that of a brain cell scales as $B \sim r^d$, where r is the characteristic radius of the cell and d is the fractal dimensionality of its contour. The fractal geometry of the cell leads to a 4/5 allometric scaling law for human brain, uniquely endowing humans with a 5th dimension and successfully explains why the scaling exponent varies during rest and exercise. A striking analogy between Kleiber's 3/4 law and Newton's second law is heuristically illustrated. A physical explanation is given for the 4th dimension of life for three-dimensional organisms and the 5th dimension for human brain.

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1. Introduction

There are competing explanations (Riisgard, 1998; White and Seymour, 2003; West et al., 2002; Damuth, 2001; Kuikka, 2002, 2003) for the relationship between animal body size (M) and metabolic rate (B), which is generally expressed as $B \sim M^a$, where a is the scaling exponent, but as yet no agreement has been achieved; allometric scaling remains an intriguing problem. The main contention throughout this body of literature concerns the arguments for and against the Rubner law ($a = 2/3$) (Rubner, 1883) or Kleiber law ($a = 3/4$) (Kleiber, 1932).

The Rubner law, proposed in 1883, derives from the simple geometric analysis of a Euclidean surface-to-volume relationship. It correlates metabolic rate with the body surface. However, metabolic cost does not depend only upon heat exchange through the body surface, so the Rubner 2/3 law has been rebutted by many researchers because of this theoretical pitfall.

Nevertheless, our analysis strongly supports the Rubner law for two-dimensional organisms.

In 1932, Max Kleiber plotted the first accurate measurements of body size versus log metabolic rate for mammals and birds and discovered that the exponent was approximately 3/4. The curve was extended by Brody in 1945, and is now called the mouse-to-elephant curve (Brody, 1945; Mackenzie, 1999). It has since been extended, controversially, to include a wide range of organisms, from mycoplasma ($\sim 10^{-13}$ g) to the blue whale ($\sim 10^8$ g), and it is considered a ubiquitous law in biology (West et al., 2002; Damuth, 2001). The 3/4 law is relevant in medical imaging (Kuikka, 2003), life expectancy (Kuikka, 2002), and many other parameters. A convincing unitary explanation for the allometric scaling laws would have broad implications for our understanding of developmental ontogeny, regeneration, population growth and evolutionary processes, but there is no generally agreed mechanistic model.

West et al. proposed a general model that describes how essential materials are transported through space-filling fractal networks of branching tubes (West et al., 1997). This model is attractive and provides, for the first time,

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a single universal explanation for allometric scalings. But the model has been challenged by some authors (Beuchat, 1997; Dawson, 1998). Dawson (1998) points out that the assumption that capillary dimensions are independent of mammal size is contrary to his early work and to basic cardiovascular design and physiological processes. The most serious pitfall of the theory is the use of the Poiseuille formula in calculating the viscous resistance of a capillary; in fact, blood viscosity depends strongly upon the capillary radius in the form $\mu = \mu_0(1 + C/r^2)$, where C is a constant. Also, contrary to the second assumption (West et al., 1997) that energy dissipation is minimized, the assumed steady laminar flow of a Newtonian fluid in a capillary does not lead to a minimal viscous resistance. Dodds et al. (2001) also pointed out this contradiction in West et al. (1997); the optimization procedure based on Poiseuille formula yields $a \approx 1$ rather than $a = 3/4$.

Recently, Darveau et al. (2002) suggested a multiple-cause cascade model of metabolic allometry, the exponent a is the sum of the influences of multiple contributors to metabolism and control. The basic equation of the cascade model is:

$$MR = a \sum_i c_i M^{b_i},$$

where MR is the metabolic rate in any given state, M is body mass, b_i the scaling exponent of the process i , and c_i the control coefficient of the process i . The model was considered a new perspective on comparative integrative physiology (Weibel, 2002) and scaling relationships (Burness, 2002), but this theory has also been called into question (West et al., 2003; Banavar et al., 2003). West et al. (2003) pointed out that this scaling equation is based on technical, theoretical and conceptual errors, including misrepresentations of their publications. Furthermore, West et al. (2003) concluded that the scaling exponent b depends upon the units of mass: for the basal rate $b \approx 0.76$ when M is in kilograms, and $b \approx 1.08$ when M is in picograms. Banavar et al. (2003) showed that this cascade model is flawed and is therefore meaningless, both for control of metabolic rate in an organism of a given size and for scaling of the metabolic rate.

He and Chen (2003) tried to explain allometry by taking pH values into account, and they predicted $1/2$ -, $2/3$ - and $3/4$ -power laws for, respectively, one-dimensional, two-dimensional and three-dimensional organisms: $B \sim M^{D/(D+1)}$, where D is the dimensionality, B is the basal metabolic rate and M is the mass of the organism.

Taylor et al. (1981) found that the maximal metabolic rate induced by exercise scales as $M^{0.86}$ rather than $M^{0.75}$. Darveau et al. (2002) explained that metabolic rate is a complex combination of functions, and applied the notion of distributed control that is being used in relation to biochemical pathways (Weibel, 2000; Srere, 1993).

A fresh approach, however, is still much needed, and we conclude that fractal cell geometry is the key, and the fractal dimensions of a brain cell satisfactorily explain thoughts and dreams.

2. Of Kleiber's law and Newton's second law

We find a link between Kleiber's law in biology and Newton's second law of motion. We consider first a single particle of mass m moving subject to a force field. The potential and kinetic energies will change, but the total energy is conserved:

$$T + U = \text{constant}, \quad (1)$$

where U is the kinetic energy, and T is the potential energy, $T = 1/2 m \dot{r}^2$.

The equation of motion can be derived in terms of calculus of variations (He, 2003; Hao, 2003; Liu, 2004), i.e.

$$\int_0^t (U - T) dt \rightarrow \max, \quad (2)$$

from which we obtain Newton's second law of motion in the form:

$$m\ddot{r} + F = 0, \quad (3)$$

where the force vector is defined as

$$F = -\frac{\partial U}{\partial r} + \frac{d}{dt} \left(\frac{\partial U}{\partial \dot{r}} \right). \quad (4)$$

Now we turn to metabolism in biology. Natural selection has tended to maximize metabolic capacity by maximizing the surface area available for absorbing resources from the environment.

$$B \rightarrow \max, \quad (5)$$

where B is metabolic rate. But metabolism is constrained by a fixed energy supply and fixed body mass. Note that "fixed energy supply" denotes hereby a total average, the energy supply available depends on blood flow to each organ, the oxygen concentration, the substrate concentration in the blood, and the amount of stored glycogen and lipid in each organ, so our assumption can be considered as first-order approximation.

$$B_0 = \text{constant}, \quad (6)$$

$$M = \text{constant}, \quad (7)$$

where B_0 is the total energy supply and M is the body mass.

Assuming n basal cells with characteristic (or typical) radius r in the organism, we have the following scaling relations:

$$B_0 \sim nB \sim M, \quad (8)$$

$$nr^3 \sim M. \quad (9)$$

Note that (1) in the above relations (8) and (9), M is an invariant; (2) Eq. (9) is not valid for bone tissue.

The metabolic rate B of the organ scales linearly with respect to its total surface:

$$B \sim nr^2. \quad (10)$$

From Eqs. (9) and (10), we can easily obtain the following relation:

$$B \sim n \left(\frac{M}{n} \right)^{2/3} = n^{1/3} M^{2/3}. \quad (11)$$

In view of Eq. (8), we obtain

$$nB \sim n^{4/3} M^{2/3} \sim M, \quad (12)$$

which leads to the result:

$$n \sim M^{1/4}. \quad (13)$$

Substituting Eq. (13) into Eq. (11) results in Kleiber's law (Kleiber, 1932), which reads

$$B \sim M^{3/4}. \quad (14)$$

Kleiber's law is considered a ubiquitous law in biology, but this is not the case. He and Chen (2003) pointed out that the law holds only for three-dimensional organisms. Riisgard (1998) considered that there is no foundation for a "3/4 power scaling law" for respiration in biology; and White and Seymour (2003) concluded that mammalian basal metabolic rate is proportional to body mass^{2/3}.

The diversity of motion patterns in nature suggests different scaling patterns in biology because of differing constraints. Constraining the motion of a particle will change its pattern of motion; similarly, artificial or natural energetic constraints on cell growth may alter the expected scaling patterns.

If we consider a leaf of a plant, an approximately two-dimensional organ, the constraints, instead of Eqs. (8) and (9), become

$$B_0 \sim nB \sim A, \quad (15)$$

and

$$nr^2 \sim A. \quad (16)$$

The area of the leaf, A , is an invariant. By a simple manipulation, as illustrated above, we obtain the following 2/3-law for the leaf:

$$B \sim M^{2/3}, \quad (17)$$

where M is the mass of the leaf.

This perspective explains that both Kleiber's law and Rubner's law can be valid, challenging the notion that Kleiber's law is ubiquitous in biology (West et al., 2002; Damuth, 2001). Kleiber's law is a result of optimal metabolic performance under the constraints of fixed energy supply and fixed body mass.

The power relationship of metabolic rate has been established in single-celled organisms, but little attention has been paid to metabolic scaling in cell culture. He and Chen suggested a cell culture experiment (Fig. 1), where cells are plated on culture dishes or culture bottles. The unattached cells are discarded so that only the attached cells are grown in medium 1640 and 10% fetal bovine serum at 37 °C. During the period of culture the attached cells form a monolayer, which can be regarded as two-dimensional. He and Chen predicted that $B_{\text{cell}} \sim M_{\text{cell}}^{2/3}$, where B_{cell} is the metabolic rate of the cell colony and M_{cell} is its mass.

Nakaya et al. (1998) have studied the relationship between metabolic rate and body size in colonial organisms. They investigated the relationship between metabolic rate and colony size in the colonial ascidian *Botryllus schlosseri*. A small colony was put on a glass slide, which was set in a container submerged in open seawater. The colony spread over the slide to form a sheet. The zooid size did not change during colony growth. The authors measured the oxygen consumption rates of colonies of various sizes (30–800 zooids) using oxygen electrodes. The allometric relationship obtained was: $V_{\text{O}_2} = 0.0643 M^{0.674}$, where V_{O_2} is the oxygen consumption rate (ml/h) and M is the wet weight (g). The experimental data of Nakaya et al. are in good agreement with our prediction.

By analogy with the allometric scaling law in biology, we suggest a similar allometric scaling law for turbulence. Chen et al. (2003) introduced a fresh approach to numerical simulation of turbulence based on the lattice Boltzmann equation. The allometric scaling law suggested it might be quite useful in qualitative analysis.

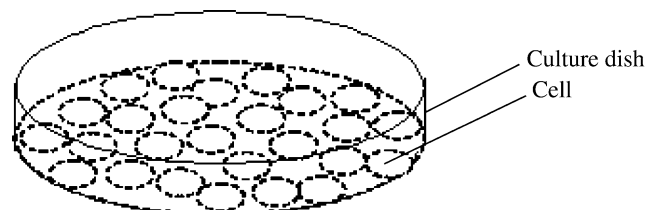


Fig. 1. Two-dimensional life.

Benzi's interesting introduction to turbulence (Benzi, 2003) led us to the following hypothesis: the dependence of a fluid variable Y on the Reynolds number Re is typically expressed using the power function

$$Y \sim Re^b, \quad (18)$$

where b is the power exponent. The Reynolds number is defined as $Re = UD\rho/\nu$, where U and D are the typical velocity and diameter of the flow, respectively, and ν is the kinematic viscosity due to intermolecular forces, ρ fluid density.

When $b = 1$, the relationship is isometric and when $b \neq 1$ the relationship is allometric. Isometry can be found in laminar flow (e.g. the Poiseuille formula). When Re increases, the flow switches from isometry to allometry. We write Eq. (18) in the form:

$$Y \sim Re^{D/(D+1)}. \quad (19)$$

Now considering a particle's motion in turbulence (see Fig. 2), the velocity varies along the pathline. The motion is approximately one-dimensional ($D = 1$), so we predict that

$$\frac{\partial V}{\partial s} \sim Re^{1/2}, \quad (20)$$

where V is the velocity of the particle.

The prediction Eq. (20) is the same as that in Benzi (2003). Similar phenomena arise in everyday observations. The best-known example is the simple pendulum with period $T \sim R^{1/2}$, where R is the length of pendulum. Due to mechanical constraint, it is a one-dimensional motion. Another example is planetary motion. Kepler's third law says that the squares of the periods of revolution around the sun are proportional to the cubes of the distance: $T \sim R^{3/2}$, where T is the orbital period and R is the mean distance between the sun and the planet. Planetary motion can be considered one-dimensional, and the scaling exponent is a multiple of $1/2$.

Fully developed turbulence (see the picture in Benzi, 2003) has a dimensionality of three ($D = 3$), so we have

$$Y \sim Re^{3/4}, \quad (21)$$

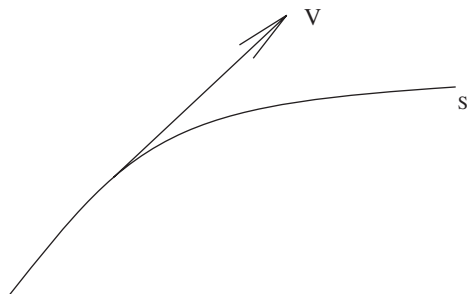


Fig. 2. An approximately one-dimensional flow.

or the scaling exponent b in Eq. (18) characteristically takes a limited number of values, all of which are simple multiples of $1/4$. For example, the Kolmogorov length, η , scales as (Chen et al., 2003; Benzi, 2003)

$$\eta \sim Re^{-3/4}. \quad (22)$$

Allometric scaling laws are found in other systems (Dreyer and Puzio, 2001). One example is the drainage basin of a river. It is shown that the mass of the river and the area of the drainage basin follow a scaling law with an exponent of $2/3$ (Banavar et al., 1999). An example of a one-dimensional system that exhibits scaling is given in Dreyer and Puzio (2001), where the flow through a tube is investigated. The amount of water in the tube is related to its length by a scaling law with exponent $1/2$ (Dreyer and Puzio, 2001). Other scaling phenomena in nature can be found in He et al. (2004); Wan et al. (2004); and He (2004).

3. Fractal approach to multicellular organisms

We consider a multicellular organ and assume that there are n basal cells with characteristic (or typical) radius r . The metabolic rate B of the organ scales linearly with respect to its total surface:

$$B \sim nr^2 = A, \quad (23)$$

where A is the total surface of all cells in the organ. The total cell boundary area is fractal:

$$A \sim r^d, \quad (24)$$

where d is the fractal dimension of the total cell surface. Because the cells are so small we can assume that they are space-filling (thus, for example, nutrients can reach each cell in the organism). So the fractal dimension, d , tends to 3, i.e. $d \rightarrow 3$ for three-dimensional organs $D = 3$. To understand this, we explain as follows: if we have a box to catch cells in the organ, there is one cell in the box with length of $2r$, and there are eight cells in the box with length of $4r$, the fractal dimension reads $d = \ln 8 / \ln 2 = 3$. For two dimensions, please refer to Fig. 3(a).

Combination of Eqs. (23) and (24) leads to the following scaling relationship:

$$n \sim r. \quad (25)$$

The mass M of the organ scales linearly with respect to its total volume of cells:

$$M \sim nr^3. \quad (26)$$

From the scaling relations (23), (25) and (26), we obtain the well-known Kleiber's $3/4$ allometric scaling law (14).

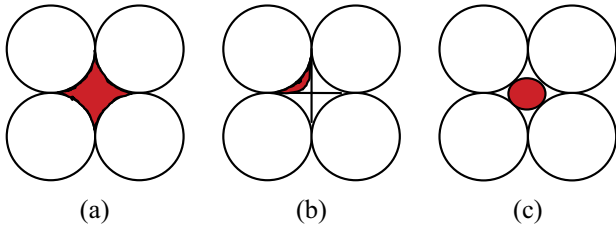


Fig. 3. Each cell in a living body has to enlarge its surface in order to obtain more energy from its environment during exercise. Each cell enlarges its surface by extending into the communal space (the shaded part in (a)). (a) If we use a box to enclose cells and there is one cell in a box of length $2r$, the surface area is πr^2 ; the total surface area becomes $8\pi r^2$ if we use a box of length $4r$; so the fractal dimension of the total cell surfaces is $D = \ln 8 / \ln 2 = 3$. (b) The communal space is defined by eight cells in contact. All the cells invade this space, so they have the same fractal dimensionality. (c) The surface extension for each cell is equivalent to the surface of a sphere with radius of $(\sqrt{2} - 1)r$. The cell's surface area becomes $\pi r^2((\sqrt{2} - 1)^2 + 1)$ if we use a box of length $2(\sqrt{2} - 1)r$. As a result, the fractal dimension of the cell becomes: $D = \ln(1 + 1/(\sqrt{2} - 1)^2) / \ln(1/(\sqrt{2} - 1)) = 2.179$.

For two-dimensional organisms, the fractal dimension, d , tends to 2. So we have $nr^2 \sim r^2$, leading to the result

$$n \sim r^0. \quad (27)$$

We therefore obtain a 2/3-law for two-dimensional organisms:

$$B \sim M^{2/3}. \quad (28)$$

So we prove that the Rubner 2/3-law is valid for two-dimensional lives, and Kleiber's law for three-dimensional lives.

4. The exponent varies during rest and exercise

Fractal cell geometry elucidates the otherwise intractable problem of changes in the exponent between states of rest and exercise. When an animal exercises intensely, each cell in the body needs more nutrition and oxygen to provide the requisite energy output. This can be achieved by increasing the area available for exchange of resources with the environment or by increasing lung performance. At rest, body cells are approximately spherical. During intense exercise, the boundary of each cell tends to occupy the communal empty space (see Fig. 3), so each cell is of fractal construction. Now the metabolic rate scales as

$$B_{\text{motion}} \sim nr^\delta \sim A, \quad (29)$$

where δ is the fractal dimension of the cell. Since the cells fill space in the living body, by a similar fractal

analysis, we have $A \sim r^3$. As a result, we obtain the following scaling law:

$$n \sim r^{3-\delta}. \quad (30)$$

So we obtain:

$$B_{\text{motion}} \sim M^{3/(6-\delta)}. \quad (31)$$

Fig. 3 illustrates the invasion of a cell into the communal space. Fig. 3a heuristically reveals that $A \sim r^3$; Fig. 3b shows part of the fractal construction of the cell (shaded). In order to calculate its approximate fractal dimension numerically, an artificial sphere is inserted into the communal space (Fig. 3c). This simple device enables the value of the fractal dimension of the cell to be determined, i.e. $D = 2.179$. Substituting the result into Eq. (31) yields $B_{\text{motion}} \sim M^{0.785}$, which agrees reasonably with Taylor's data, $B_{\text{motion}} \sim M^{0.86}$ (Taylor et al., 1981).

Each cell has an associated empty space approximately $(2r^3) - 4/3\pi r^3 = 3.81r^3$, which is equivalent to 0.9098 cells. If cells enlarge their surfaces and fill this empty space completely, then the maximal fractal dimension of a metamorphosed cell becomes $D_{\text{max}} = \ln(1.9089/(\sqrt{2} - 1)^2) / \ln(1/(\sqrt{2} - 1)) = 2.7$. Substitution of this result into Eq. (31) gives, for maximal metabolism, $B_{\text{motion}} \sim M^{0.9}$, which also agrees closely with observational data.

5. Fourth and fifth dimension of life and a 4/5-law for the human brain

In 1977, Blum suggested that the 3/4-law can be understood by a four-dimensional approach. In $D + 1$ dimensions, the "area" A of the hypersurface enclosing a $D + 1$ dimensional hypervolume scales as $A \sim V^{D/(D+1)}$, where D is the spatial dimension of the organism. When $D = 3$, we have $A \sim V^{3/4}$, a four-dimensional construction. The 4th dimension of life has received considerable attention since the work of West et al. (1999). So far, however, no satisfactory physical explanation has been given for the 4th dimension of life. We have proved that $n \sim r$ for three-dimensional organisms, so the 4th dimension of life exists only in three-dimensional organs such as heart, liver and kidneys. An isolated rat heart cell displays no four-dimensional attributes. However, if sufficient heart cells are cultured and accumulated in three dimensions, the isolated cardiac cell begins to beat (NASA microgravity research highlights, 2000) and the 4th dimension of life becomes apparent. We have also shown that $n \sim r^0$ for two-dimensional organs, so the 4th dimension does not exist in plant leaves. Animals, in contrast, show characteristics of the 4th dimension.

We will show that human brain has a further dimension. Brain cells are not approximately spherical, in contrast to other human cells. The brain is made up of many cells, including neurons and glial cells. The branching dendrites and the axon of a neuron make the brain cell more geometrically complex than spherical cells.

For a single brain cell, the metabolic rate scales as follows:

$$B \sim r^\delta, \quad (32)$$

where δ is the fractal dimension of the cell surface, and $2 < \delta < 3$, r is the equivalent radius of a brain cell. Since there are large number of (more or less) spherical glial cells in the brain and large number of neurons, which are not all spherical, we must assume that total surfaces of brain cells, including glial cells and neurons, are equivalent to total surfaces of n spheres with radius r .

Fractal dimensions of a Koch curve, the surface of a spherical ball and the surface of a snowflake are, respectively, ≈ 1.26 , 2 and ≈ 2.26 . Natural selection leads most cells to form spheres, which have maximal surface area, so that energy exchange between a cell and its environment is maximized. On the other hand, snowflakes are natural phenomena, with an optimal fractal dimension. Human brain cells have a similar construction to a snowflake, so they can receive as much information as possible from the environment. We, therefore, assume that $\delta \approx 2.26$ for human brain. Note that the human brain is the best-developed system among animals, so the fractal dimension for vertebrate brain, spinal cord, insect brain, or the nerve net of a coelenterate cannot reach this maximal level.

Assuming that there are n basal cells with characteristic radius r in human brain, the overall metabolic rate, B_{brain} , of the brain scales as

$$B_{\text{brain}} \sim nr^\delta \sim A_{\text{brain}}, \quad (33)$$

where A_{brain} is the total surface of all brain cells. By a similar fractal analysis as illustrated above, we have $A_{\text{brain}} \sim r^3$. As a result, we obtain the following scaling law:

$$n \sim r^{3-\delta}. \quad (34)$$

The mass M_{brain} of the brain scales as

$$M_{\text{brain}} \sim nr^3 \sim r^{6-\delta}. \quad (35)$$

So we obtain the following scaling law for brain:

$$B_{\text{brain}} \sim M_{\text{brain}}^{3/(6-\delta)}. \quad (36)$$

The fractal dimension of a cell in human brain is $\delta \approx 2.26 \approx 9/4$. Substituting this into Eq. (36) results in a 4/5-law for human brain:

$$B_{\text{brain}} \sim M_{\text{brain}}^{4/5}. \quad (37)$$

Nature endows humans uniquely with a 5th dimension!

Wang et al. (2001) obtained the following relations for human brain:

$$B_{\text{brain}} = 20.5m^{0.62} \text{ (kJ/d)}, \quad (38)$$

$$M_{\text{brain}} = 0.011m^{0.76}, \quad (39)$$

where m is the body mass. From Eqs. (38) and (39), we have

$$B_{\text{brain}} \sim M_{\text{brain}}^{0.62/0.76} = M_{\text{brain}}^{0.81}, \quad (40)$$

which is in good agreement with our prediction, Eq. (37).

The 0.81 power relationship implies an optimal fractal shape for brain cells, and the fractal shape, in contrast to a sphere, leads to maximal heat exchange due to its extreme surface, this explains why the brain consumes large amounts of energy, and its metabolic rate is near “maximal” even under general BMR conditions in the body, the maximal scaling exponent as illustrated in the above section reaches 0.9. We might call the 4th dimension of life the life-dimension, and the 5th dimension of the brain as the thought-dimension; it originates from the fractal structures of brain cells.

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