The origin of allometric scaling laws in biology

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Abstract

Quantum mechanics postulates a universal relation between the energy and frequency of a charged particle. This is the origin of the allometric relation between metabolic rate P, and body size W, namely $P = aW^{\beta}$. The directionality theory of evolutionary dynamics asserts that the evolutionarily stable states of populations are characterized by extremal states of entropy. This is the origin of the dependence of the scaling exponent β on the phylogenetic status of the organism.

This article shows that (a) in populations subject to bounded growth constraints, the value $\beta = 3/4$ and is characterized by physiological states that maximize metabolic rate, (b) in populations subject to unbounded growth constraints, the value $\beta = 2/3$, and is defined by physiological states which minimize metabolic rate. This model is distinguished from current hypotheses in three main respects: (i) it pertains to prokaryotes, plants and animals, (ii) it explains the empirical fact that the $3/4$ is not a universal property and that deviations from this rule exist at all levels of biological organization (iii) it explains the fact that scaling exponent is highly dependent on body size and phylogenetic condition.

Introduction

A fundamental property of any organism is its body size. This characteristic imposes constraints on the physiology and behavior of the organism and determines its energy expenditure. A large class of empirical studies show that physiological properties of the organism, denoted Y, and body size denoted W, are typically represented by the allometric law; [1], [2], [3], [4], [5], [6]

$$Y = aW^{\beta}$$

Here β is a scaling exponent, and a is a constant which is dependent on the organism: In the case of the physiological variable metabolic rate, P, the exponent β is known to vary from 2/3 to 3/4, with $\beta = 3/4$ representing the value attained by large mammals [7], and $\beta = 2/3$ characterizing many species of birds [7], [8].

Although these scaling relations were documented six decades age and have important ecological [9] and pharmaceutical implications [10], [11] theoretical basis remains highly controversial [12]: no general theory has succeeded in explaining the origin of the relations, the deviations from the dominant 3/4 rule, and the universality of these relations for different kinds of biological systems: uni-cellular organisms, plants and animals. A recent hypothesis, [13], [14], based on the idea that metabolic processes depends on the fractal like nature of distribution networks, has generated considerable interest and invited challenges on several grounds. Alexander [15] has questioned some of the basic assumptions of the model, and in addition has observed that the network structure invoked does not necessarily apply to animals such as crustaceans, snails, which have open blood systems, or to uni-cellular organisms and lower invertebrates which have no blood systems. The claim in [14] that fractal networks need not be a physical system of branching tubes but can be "virtual" does not adequately resolve the objections raised in [15]. Dodds et al. [7] have noted that the network model does not account for the deviation from the 3/4 rule which their analysis of the data has recognized. Indeed, the examination in [7] shows that the exponent β is highly dependent on body size and phylogentic status; a condition which is inconsistent with the network model.

This article proposes a new mechanism, applicable to prokaryotes, plants and animals, which explains the origin of the scaling relation, the deviation from the 3/4 pattern, and the dependency of this deviation on phylogenetic status and body size: Our model is based on a central tenet of the chemiosmotic theory of bioenergetics [16], [17]: the production of

ATP, the energy currency of living organisms, is mediated by the coupling of two dynamical processes (i) the movement of electrons through a series of carriers in biological membranes — the plasma membrane in bacteria, the inner membrane in mitochondria, the thylakoid membrane in chloroplasts, (ii) the translocation of protons across the membrane to produce a proton gradient.

Energy transduction in biological membrane will be constrained by processes of physics which act primarily at the molecular level and unfolds on the time scale of a protonic cycle, and the processes of evolution which act at the population level and unfolds on the time scale of a generation.

In this article we analyse the effect of physical constraints by invoking the quantum mechanical nature of energy transfer in electron flow. We exploit this quanization principle to show that metabolic rate P and body size W are allometrically related. We have

$$P = aW^{\beta}. \tag{1}$$

Here $\beta = \frac{4\mu-1}{4\mu}$, where μ denote the efficiency of the coupling between electron transport and proton translocation.

We analyze the effects which evolutionary constraints impose on energy transduction by appealing to directionality theory [18], [19], a dynamical theory of evolution based on the concept evolutionary entropy, a measure of the variability in the age of reproducing individuals in the population. Directionality theory analyses evolutionary changes in entropy in populations subject to two classes of ecological constraints (a) *bounded growth* — this property describes populations whose average growth rate is stationary or is bounded by the fluctuation decay rate in population numbers; (b) *unbounded growth* — this condition characterizes populations whose average growth rate exceeds the fluctuation decay rate. We will show that evolutionary changes in the parameters entropy and metabolic rate are positively correlated. We will then appeal to the main tenets of directionality theory to predict the following dependencies between the ecological constraints and scaling exponents.

(I) *Bounded growth constraints:* Physiological states of organisms are described by energetic processes which maximize metabolic rate, which scales according to the relation: $P \sim W^{3/4}$.

(II) *Unbounded growth constraints:* Physiological states are described by energetic relations which minimze metabolic rate, which scales according to the relation $P \sim W^{2/3}$.

These predictions indicate that the scaling exponent will not only be constrained by physical factors, in this case the quantum nature of energetic interactions, but will be contingent on the evolutionary history or the phylogenetic status of the population. Our model entails that in lineages generated by large mammals or perennial plants where bounded growth constraints prevail, scaling will be described by the 3/4 rule; whereas in lineages defined by small mammals or annual plants — organisms subject typically to unbounded growth constraints — the 2/3 scaling rule will obtain. The empirical analysis delineated in Dodds, Rothman and Weitz [7] concords with these general predictions.

Energy Transduction and Allometric Relations

In our mathematical analysis of the coupling between electron transport and proton translocation which defines the energy transduction process, we will focus on the operations of bacteria, which in general consist of a single compartment bounded by a cytoplasmic membrane. In view of the chemiosmotic theory [16], [17] the same principles of energy transduction apply to chloroplasts and mitochondria. Accordingly the scaling relations we derive will also pertain to plants and animals.

We will consider energy transduction as a two stage process: (a) An energy source is used to transport protons uphill across the hydrophobic barrier of the cytoplasmic membrane. As a result the energy is transduced to an electrochemical potential difference, Δp, of hydrogen ions composed of differencies in electrical and chemical potential. (b) The energy accumulated is utilized for ATP synthesis coupled to downhill H^+ movement, see Fig. 1.

Fig. (1)

We are interested in analytically describing the energy generated by the coupling of these two processes. As electrons pass along the electron transport chain, Δp is generated as a result of the translocation of protons across the bacterial plasma membrane. The electrochemical gradient Δp is used, to drive ATP synthesis.

In view of the resistance of the membrane to the traanslocation of electric charge, the coupling of the electron transport chain to ATP production will not be perfect: it will be characterized by a certain efficiency which represents the extent to which electron transport and proton translocation are coupled.

Constraints of Physics: Quantization of effects

We will consider the electrons in the electron transport chain as a collection of oscillators with frequency ν whose energy can only be contained in discrete units of energy $h\nu$. We write $E_1 = h\nu$, where h the *quantum of action* denotes Planck's constant.

The protons in the proton translocation system is described in terms of a proton cycle time, denoted τ, the mean time it takes proton to traverse the pathway linking electron flow with the ATP synthase. The mean metabolic energy E_2 generated by this process will be proportional to τ, with constant of proportionality g. We call g the *quantum of metabolism* and we write $E_2 = g\tau$.

We now consider the coupling between the electron transport system and proton translocation. We take account of the fact that the electrons can assume only discrete energy values: $E_1 = 0,\ h\nu,\ 2h\nu, \ldots kh\nu \ldots$. These energy levels, in a system coupled to a proton translocation system with cycle time τ, have probabilities defined by

$$p_k = A \exp\left[-\frac{kh\nu}{g\tau^{\mu}}\right],\ k = 0, 1, 2, \ldots \tag{2}$$

Here μ, $0 < \mu \leq 1$, denote the efficiency of the coupling between the electron transport and proton translocation systems.

The coefficient A is determined by the condition that the sums of the probabilities p_k must be unity. This condition yields

$$A = 1 - \exp\left[-\frac{h\nu}{g\tau^{\mu}}\right], \ldots \tag{3}$$

The energy $\tilde{E}(\nu)$ of the quantized process will be given by $\tilde{E}(\nu) = \tilde{n}h\nu$, where $\tilde{n} = \sum_k kp_k$, denote the average number of quanta.

We have, using (2) and (3)

$$\tilde{E}(\nu) = \frac{h\nu}{\exp[\frac{h\nu}{g\tau^{\mu}}] - 1} \tag{4}$$

In view of (4), the total energy generated by the coupling of the electron transport system with the translocation of protons is given by

$$U = \int_0^{\infty} \tilde{E} f(\nu) d\nu$$

where $f(\nu)$ denotes the frequency density of modes.

The density of modes plays the same role as the density of single-particle states in the perfect gas problem, [20], accordingly, we can assume that $f(\nu) = a\nu^2$ where a is a constant.

We thus obtain

$$\begin{aligned} U &= a \int_0^{\infty} \frac{h\nu^3\ d\nu}{\exp(\frac{h\nu}{g\tau^{\mu}}) - 1} \\ &= \left(\frac{a}{h^3}\right) (g\tau^{\mu})^4 \int_0^{\infty} \frac{x^3 dx}{e^x - 1} \end{aligned}$$

This yields

$$U = c\tau^{4\mu} \tag{5}$$

where $c = ag^4/h^3$

The expression for the total energy given by (5) can be exploited to derive an analytical representation of the metabolic rate in terms of body size.

We first observe that at steady state the total energy U will be proportional to the volume of the cell. Assuming that the density of the cell is uniform, we have $U = kW$. In view of (5), the cycle time τ we be given by the allometric relation

$$\tau = \alpha W^{\frac{1}{4\mu}} \tag{6}$$

where $\alpha = \left(\frac{k}{c}\right)^{\frac{1}{4\mu}}$.

Since the metabolic rate $P = \frac{dU}{d\tau}$, we obtain

$$P = 4\mu c\alpha^{4\mu-1} W^{\frac{4\mu-1}{4\mu}} \tag{7}$$

One of the central assumptions that underlie the model is that the physiological properties of organisms are determined by both physical and evolutionary constraints. The expresson for the metabolic rate P given in (5) derives from physical constraints, namely the quantized nature of energy in the electron transport system. We will now invoke directionality theory to determine the set of constraints evolutional evolutionary forces will impose on metabolic rate.

Evolutionary constraints: directionality theory.

Directionality theory is a dynamical theory of evolution which integrates Mendelian genetics with demographic factors to study the dynamics of gene frequency change under different modes of ecological constraints. The central concept in the theory is the demographic parameter evolutionary entropy, which describes the heterogeneity in birth and death rates among individuals in a population of replicating organisms. Demographic heterogeneity has its origins in the instability of the ontogenetic process: the small variations in timing and in the sequence of developmental events that translate the genetic program into the adult state. This instability entails that any genetically homogeneous population of individuals will be characterized by a variability in their phenotypic states — size, age, metabolic energy — and hence variability in terms of their reproduction and survivorship rates. In populations

in which the state of individuals is parametrized by age, we have shown that evolutionary entropy, denoted H is uniquely characterized by [18],

$$H = -\frac{\int_0^\infty p(x)\log p(x)dx}{\int_0^\infty xp(x)dx} \equiv \frac{S}{T} \tag{8}$$

Here $p(x)$ represents the probability distribution of the age of reproducing individuals in the population; and T describes the generation time, the mean age of individuals at the birth of their offspring.

Evolution entropy has an important dynamic attribute: it describes demographic stability, the rate of decay of the fluctuations in population numbers which are induced by small variations in the individual birth and death rate.

The main tenets of directionality theory are a set of principles which relate the ecological constraints, bounded and unbounded growth, with evolutionary changes in entropy under mutation and natural selection. The correspondence between ecological constraints and evolutionary trends can be qualitatively annotated as follows, [19]:

(I) *Bounded growth constraints:* (large population size): a uni-directional increase in entropy

(II) *Unbounded growth constraints:* (large population size): a uni-directional decrease in entropy.

(III) *Unbounded growth constraints:* (small population size): random, non-directional change in entropy.

These principles can be invoked to predict evolutionary trends in metabolic rate. We first observe, as shown in [21], that up to additive constants, the entropy function S defined in (8), can be expressed in terms of the metabolic rate P of an adult individual in the population, and the generation time T. We have

$$S = \gamma PT \tag{9}$$

where γ denotes a numerical constant.

In view of (8) and (9), changes in the metabolic rate P and evolutionarly entropy H will be positively correlated. Consequently, evolutionary trends in the metabolic rate will be described by patterns similar to A(I), A(II) and A(III). We can therefore delineate the following principles relating ecological norms with evolutionary trends in metabolic rate.

B(I) *Bounded growth constraints:* A uni-directional increase in metabolic rate

B(II) *Unbounded growth constraints:* (large population size): A uni-directional decrease in metabolic rate.

B(III) *Unbounded growth constraints:* (small population size): random, non-directional change in metabolic rate.

The principles described by B(I), B(II), and B(III) entail that the metabolic rate of an organism, and consequently, the scaling exponent $\beta = \frac{4\mu-1}{4\mu}$, will be modulated by the ecological situation the population endures during its evolutionary history. We can therefore distinguish between the following two perspectives:

(A) *Bounded Growth:* In populations subject to these ecological constraints, the evolutionarily stable state of the population will be described by organisms with physiological states that maximize the metabolic rate. The maximal metabolic rate will be characterized by an efficiency $\mu = 1$. In this case, we have $\beta = 3/4$, and $P \sim W^{3/4}$.

(B) *Unbounded Growth:* In populations evolving under these constraints, the evolutionarily stable states will be defined by organisms with physiological states that minimize the metabolic rate.

Now for a given body size W, the minimal metabolic rate will be that rate which balances the rate of heat loss. However, in a resting state, heat is predominantly lost through the surface area, which scales as $V^{2/3}$ where V denotes the volume. Assuming a size invariant uniform density, we obtain that the minimal metabolic rate will described by the exponent $\beta = 2/3$ and we have $P \sim W^{2/3}$. This minimal condition corresponds to an efficiency $\mu = 3/4$.

The predictions relating ecological constraints, scaling exponents and metabolic condition are summarized in Table (1).

Table 1

Relations between ecological constraints, scaling exponent and metabolic rate

Ecological condition	*Scaling exponent*	*Metabolic Rate*
Bounded growth	$\beta = 3/4$	Maximal value
Unbounded growth	$\beta = 2/3$	Minimal value

The model we have described is restricted to unicellular organisms. It can be easily extended to plants and animals. Energy transduction in plants is mediated by means of the thylakoid membrane in chloroplasts; in animals, by means of the inner membrane in mitochondria: ATP production in these organelles is also generated by the coupling of electron transport and proton translocation: Accordingly the model for uni-cellular organisms applies to these systems provided we assume that body size is related to the number of chloroplasts in plants and the number of mitochondria in animals.

Conclusion

The model we have proposed provides a mechanism for understanding the central role of body size at all levels of biological organization, prokaryotes, plants and animals. The model rests on the idea that energy transduction in biological organisms is constrained by two classes of processes which operate on two distinct scales. The first process derives from Physics. This process has its origin in quantum mechanics and the constraints which the discrete nature of energy interactions impose on the relation between size and metabolic energy. This process unfolds on the time scale of molecular interactions. The second process derives from evolutionary dynamics and the constraints which ecological forces impose on changes in the demographic properties of populations by natural selection. This dynamic is registered on the time scale of population interactions, namely, a generation.

The relationship between metabolic rate and body size depends on the number of degrees of freedom a given quantity of metabolic energy may express in a body of a given size. Quantum interaction entails that the number of degrees of freedom over which metabolic energy can spread is large; a property which means that metabolic rate will be allometrically and not linearly related to body size. Evolutionary interactions impose further bounds on the number of degrees of freedom: the scaling exponents 3/4 and 2/3 are consequencies of the effects of these interactions.

References

[1] Kleiber, M., (1961), The fire of life. An introduction to animal energeties. New York. Wiley

[2] Kleiber, M., (1932), Body size and metabolism. Hilgardia 6, 315-353

[3] Brody, S. (1945). Bioenergetics and Growth. New York Ranhold.

[4] Hemmingsen, A. (1960) Energy metabolism as related to body size and respiratory surfaces, and its evolution. Rep. Steno. Mem. Hosp. 9, 1-110.

[5] Heusner, A. , (1987), What does the power function reveal about structure and function of animals of different size? Ann. Rev. Physiol. 49, 121-133.

[6] Bartels, H. (1982), Metabolic rate of mammals equals 0.75 power of their body weight.

[7] Dodds, P.S., Rothman, D. H., and J.S. Weitz (2001), Re-examination of the 3/4 law of metabolism. Jour. Theor. Biol. 209, 9-27.

[8] Bennett, P. and Harvey P. (1987), Active and resting metabolism in birds — allometry, phylogeny and ecology. J. Zool. 213. 327-363.

[9] Damuth, J. (1981), Population density and body size in mammals. Nature 290. 699-700.

[10] Mordenti, J. (1986), Man versus beast: pharmacokinetic scaling in mammals. J. Pharmaceut. Sci. 75. 1028-1040.

[11] Mahmood, I. (1999), Allometric issues in drug development. J. Pharmaceut. Sci. 88, 1101-1106.

[12] Whitfield, J. (2001), All creatures great and small. Nature 413. 342-344.

[13] West, G.B., Brown T. H., and Enquist, B.J. (1997), A general model for the origin of allometric scaling laws in biology. Science 276, 122-126.

[14] West, G.B., Brown T. H., and Enquist, B.J. (1999), The fourth dimension of life: fractal geometry and allometric scaling of organisms. Science 284, 1677-1679.

[15] Alexander, R.M. (1999), Energy for animal life. Oxford.

[16] Mitchell, P. (1971), From energetic abstraction to biochemical mechanism. Symp. Soc. Gen. Microbiol. 27, 383-423.

[17] Brand, M. D., and Morphy, M. (1987), Control of electron flux through the respiratory chain in mitochondria and cells. Biol. Rev. 62, 141-193.

[18] Demetrius, L. (1997), Directionality principles in thermodynamics and evolution. Proc. Natl. Acad. Sci. U.S.A. 94, 3491-3498.

[19] Demetrius, L. (2000), Thermodynamics and evolution. Jour. Theor. Biol. 706, 1-16.

[20] F. Mandl, (1988), Statistical Physics. 2nd Edition. John Wiley and Sons.

[21] Demetrius, L. (2000), Directionality theory and the evolution of body size. Proc. Roy. Soc. 267, 1-7.