Quantum statistics and allometric scaling of organisms

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Abstract

This article proposes a mechanism to explain allometric relations between basal metabolic rate and the body size of organisms. The model postulates that energy transduction in biological organisms is constrained by two classes of dynamical processes: The first process has its origin in quantum mechanics and the constraints which the coupling of electron transport and proton translocation impose on metabolic activity. The second derives from evolutionary dynamics and the constraints which ecological and demographic forces impose on metabolic rate. These two processes are invoked to show that the scaling exponent between basal metabolic rate and body size follows a $\frac{3}{4}$ rule, in the case of organisms subject to ecological constraints defined by scarce but dependable resources, and a $\frac{2}{3}$ rule when constraints are defined by ample but only temporarily available resources. Our conclusions are based on general arguments incorporating the molecular mechanisms that determine metabolic activity at all levels of biological organization. Hence the model applies to uni-cellular organisms, plants and animals.
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1. Introduction

The body size of an organism is a fundamental property as it constraints several different features of the organism's physiology and behavior. Body size affects all biological structures and processes by regulating the rates at which the organism absorbs nutrients and also the rate at which it converts these nutrients or metabolites into

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reproduction. The dependence of the basal metabolic rate, P, on body size, denoted W, is typically described in terms of the allometric relation

$$P = aW^\beta .$$ (1)

Here a is a constant, which is a characteristic of the phylogenetic status of the organism, and β is a scaling exponent.

The empirical basis for (1) has its origin in studies of the metabolic rate of several different species of domesticated mammals [1]. These studies, and later work by Brody [2] on a larger range of mammals, and by Hemmingsen [3] on uni-cellular organisms, showed that $\beta = \frac{3}{4}$. Accordingly, the $\frac{3}{4}$ rule was considered as a universal property of organisms. More recent studies, however, have shown that the scaling exponent is highly dependent on the phylogenetic status of the organisms: mammalian lineages are typically characterized by $\beta = \frac{3}{4}$, whereas most species of birds [4] are defined by the exponent $\beta = \frac{2}{3}$. Recent reviews of the empirical literature [5], using highly refined statistical methods, now indicate that, although the $\frac{3}{4}$ rule is dominant among large mammals, significant deviations, as represented by $\beta = \frac{2}{3}$, do obtain among small mammals and birds.

This article proposes a mechanism, based on quantum statistics, to explain the origin of allometric relations as defined by (1). Our model aims to explain the incidence of scaling relations in both uni-cellular and multicellular organisms, the dependence of the scaling exponent on body size, and the presence of both two-thirds and three-quarter power scaling laws.

Previous efforts to elucidate (1) in terms of mechanistic models have been based on hypotheses such as resistance to elastic buckling in terrestrial organisms [6], the alleged fractal-like nature of distribution networks [7]. These studies have failed to account for the fact that (1) pertains not only to multicellular organisms, but also to uni-cells, where the phenomena of elastic buckling and fractal networks are questionable. The works in Refs. [6,7] also do not account for the dependency of the scaling exponent on the phylogenetic status of the organism. The model we now propose rests on the observation, enshrined in the chemiosmotic theory of bioenergetics [8], that 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.

In this article we will analyze the action of these dynamical processes by invoking a quantum mechanical nature of energy transfer in electron flow and proton translocation. We will exploit the fact that quantum theory restricts the energy in any given standing wave mode defined by an electron or proton to be of the form

$$\varepsilon_n = nh\omega$$ (2)

when $n = 0, 1, \ldots, h$ is Planck's constant and ω the frequency of the mode, to show that the scaling exponent, β, in the allometric relation (1) is given by

$$\beta = \frac{4\mu - 1}{4\mu} \; .$$

The parameter μ denotes metabolic efficiency, defined by the ratio of the rate of energy-accepting processes, that is, ATP synthesis, to the rate of the energy-donating process, substrate oxidation.

We will show that maximal and minimal values of the basal metabolic rate are obtained when $\mu = 1$ and $\frac{3}{4}$, respectively. In view of the corresponding values for the scaling exponent β, we have $P_{\max} \sim W^{3/4}$; $P_{\min} \sim W^{2/3}$. We will invoke this observation in the context of an evolutionary argument, to explain the dependence of the scaling exponent on the phylogenetic status of organisms, in particular, the dominance of the $\frac{3}{4}$ rule in large mammals, and the incidence of the $\frac{2}{3}$ rule in certain species of birds. The evolutionary argument we apply derives from directionality theory, an analytical model which studies changes in the genotypic and phenotypic composition of populations under mutation and natural selection [9]. This theory predicts that the evolutionarily stable states of populations are characterized by patterns of fecundity and mortality distributions which are extremal states of the demographic variable entropy, a measure of the uncertainty in the age of reproducing individuals in a population: Life history distributions will maximize entropy, when evolution occurs under limited but constant resource conditions, and minimize entropy when resources are ample but inconstant. The analytical fact that evolutionary changes in entropy and metabolic rate are positively correlated [10] entails that the physiological conditions that describe the evolutionarily stable states of natural populations will also be characterized by extremal states—maxima and minima—of metabolic rate.

The concepts in bioenergetics and the chemiosmotic theory described in this article are drawn extensively from Ref. [11]. This text provides a critical review of the various mechanisms which have recently been proposed to model energy transduction in organisms. The review paper [9] provides the basic ideas which underlie the main tenets of directionality theory.

2. Metabolic rate and energy transduction

The engines that perform energy transduction in plants and animals are chloroplasts and mitochondria, respectively. In chloroplasts, energy is transduced by electron carriers in the thylakoid membrane; in mitochondria, the inner membrane is the mediating factor. These processes are similar in bacteria where transduction occurs within the plasma membrane. Whereas plants and animals are highly complex structures, a bacterial cell typically consists of a single compartment, a minute blob of protoplasm encased within its plasma membrane and shielded by an inert cell wall. In view of the simplicity of the bacterial system we will use this model in our analysis, and show later that the results obtained in this context can be extended to multicellular organisms.

We will consider energy transduction as a two-stage process:

(i) An energy source is used to power the movement of electrons through a series of carriers in the cytoplasmic membrane. These movements are coupled to the pumping of protons across the membrane generating a transmembrane electrochemical proton gradient.
(ii) The energy accumulated is used to move protons across the membrane, down their concentration gradient. This movement is coupled to the synthesis of ATP from ADP and P_i.

Our analysis rests on the distinction between heat engines, that is, machines that convert thermal energy into mechanical energy, and non-thermal engines, that is, machines that do work at a single temperature. Most physical systems operate as heat engines and changes in energy in these systems can be parametrized by temperature.

Living organisms are essentially isothermal—there are no significant differencies in temperature between parts of a cell or between different cells in a tissue; chemical energy is converted by the processes of energy transduction directly into biological work. Energy transfer between parts of a cell generally results from differencies in the turnover rates of metabolites at different locations within the cell. Energy transformation between different cells in a tissue is mediated by differencies in the replication rates of the various cells.

Now the fundamental processes which drive the dynamics of energy transformation at the molecular and cellular levels are: (a) the set of redox reactions that transfer electrons from a reduced substrate to a terminal acceptor and (b) the chemiosmotic reactions that translocate protons across the energy-transducing membranes. A measure of the temporal organization of these processes is the mean transit time for the circuit of protons linking the primary proton pump with ATP synthesis. This index of turnover rate, which we call the protonic cycle time, will play a fundamental role in our study of the metabolic process.

The significance of the different time scales that characterize metabolic activity at cellular, organismic and population levels has been recognized in several empirical studies [12,13]. Physiological time, the generic term used to describe the different turnover times of metabolic events at the molecular and cellular level, includes properties such as the duration of heart beat, turnover time of insulin, twitch contraction time of muscle, and duration of one breath. The cycle times, denoted τ, for these processes are quantitatively related. We have the allometric relation [12]

$$\tau = \tilde{a} W^{\tilde{\beta}} \ .$$

Here $\tilde{a}$ is a constant, which depends on the phylogeny and the level of biological organization, and $\tilde{\beta}$ is a scaling exponent. The scaling exponent in most cases studied concentrates around the value one-quarter. The robustness of the empirical scaling rules for physiological time and metabolic rate suggests that these two processes are regulated by the same physiological mechanisms. The analysis we develop in this article will provide support for this hypothesis.

2.1. Quantization effects

In our analysis of the electron-transport process we will appeal to certain pioneering studies on electron transfer reactions [14]. These studies applied a theory of potential energy surfaces and equilibrium statistical mechanics to develop a detailed model of electron transfer in chemical systems. The analysis showed that, provided a change in charge on the reactants produced a proportional change in the dielectric polarization of the surrounding medium, many dimensional potential energy surfaces for the reactants and products could be reduced to harmonic free energy curves that are functions of a single-reaction coordinate.

Now electron transfer in the redox reactions in biological systems are from one molecular center to another, as in the chemical case. However, these reactions do not depend strongly on environmental fluctuations since the centers are embedded in a lipid–protein membrane, which is relatively rigid. Accordingly, the formalism in Ref. [14] can be applied to these redox reactions.

Within this framework, the distortions of electron donors and acceptors from their equilibrium configurations can be described by free energy parabolas with identical force constants. Hence the rate constant $\tilde{k}$ for the electron transfer from donor to acceptor is given by [14]

$$\tilde{k} = \kappa(r)\theta \exp\left[-\frac{\Delta G^{\#}}{RT}\right] \ . \tag{3}$$

Here $\kappa(r)$ is the transmission coefficient for electron transfer which is dependent on the distance, r, between donor and acceptor, R is the gas constant, θ is an effective frequency parameter and T the absolute temperature. $\Delta G^{\#}$ is the free energy of reactants necessary to accomplish the electron transfer.

Now let τ denote the protonic cycle time, the mean time which elapses from the extrusion of a proton to its return in the membrane through one of its pores. The mean number of protons (N) generated per cycle by the electron transfer process will be given by $N = \tilde{k}\tau$, where $\tilde{k}$ denote the reaction rate given by (3).

Now let $\Delta\tilde{\mu}_{H^+}$ denote the free energy change as protons move back into the cell down along both the electrical and chemical gradients. The free energy of the driving reaction ΔG^* will be given by $\Delta G^* = N\Delta\tilde{\mu}_{H^+}$ [11]. We will rescale this quantity using the counting index, Avogadro's number, N_A, the number of atomic mass units per mole. The corresponding free energy change at steady state, denoted E, becomes

$$E = \left(\frac{N}{N_A}\right)\Delta\tilde{\mu}_{H^+} \ ,$$

which can be expressed in the form

$$E = g\tau \ , \tag{4}$$

where $g = (\tilde{k}/N_A)\Delta\tilde{\mu}_{H^+}$.

The free energy change given by (4) describes the metabolic energy released by the transfer of electrons along the electron transport chain and the concomitant translocation of protons across the energy-transducing membrane. Eq. (4) resides on the relation $N = \tilde{k}\tau$, for the mean number of protons generated per cycle. This characterization

implicitly assumes that the circulation of protons across the membrane is a continuous process.

The continuity assumption will now be relaxed. The studies reviewed in Refs. [15,16] indicate that the Marcus theory of electron transfer can be applied to the proton-transfer process. Accordingly, the multidimensional potential energy surfaces for the donor and acceptor states in proton-transfer reactions can also be reduced to harmonic free energy curves which depend on a single-reaction coordinate.

We will now assume that the behavior of the proton is quantized: We postulate that:

(a) The potential energy curve for the proton can be characterized in terms of a harmonic oscillator.
(b) The energy that can be stored by the oscillator with natural frequency is an integral multiple of a basic energy unit and directly proportional to the oscillator's characteristic frequency ω.

The quantization hypothesis entails that the electron transfer–proton translocation process will now be stochastic. Hence, in order to determine the mean metabolic energy generated, we must first characterize the probability, $\hat{v}_n$, that the proton is in energy state ε_n when steady-state conditions are attained.

We will appeal to the statistical mechanics formalism developed in Ref. [17].

Write $\varphi_n = \exp[-\varepsilon_n/E]$, and let $v = (v_n)$ denote an arbitrary probability distribution on the set of energy states. The entropy $S(v)$ of the state $v = (v_n)$ is given by

$$S(v) = -\sum_n v_n \log v_n .$$

The mean energy of the system in state v is denoted $v[\varphi]$, and is defined by

$$v[\varphi] = \sum_n v_n \log \varphi_n .$$

The steady-state distribution, $\hat{v} = (\hat{v}_n)$, is the unique state that maximizes

$$S(v) + v[\varphi] ,$$

which, as shown in Ref. [17], is given by

$$\hat{v}_n = \frac{\exp(-\varepsilon_n/E)}{Z} ,$$

where

$$Z = \sum_n \exp\left(\frac{-\varepsilon_n}{E}\right) .$$

Hence the mean energy $\tilde{E}$ now becomes

$$\tilde{E} = \sum_n \varepsilon_n \hat{v}_n = \sum_n nh\omega \frac{\exp(-nh\omega/E)}{Z} .$$

The above expression yields, on algebraic manipulation,

$$\tilde{E} = \frac{h\omega}{\exp(h\omega/g\tau) - 1} \ . \tag{5}$$

Now, when $g\tau \gg h\omega$,

$$\exp\left(\frac{h\omega}{g\tau}\right) - 1 \approx \frac{h\omega}{g\tau} \ .$$

Hence,

$$\tilde{E} = g\tau \ .$$

We note that when the cycle time τ is large, the mean energy $\tilde{E}$, defined by (5), reduces to the expression for the classical case. These observations indicate that a quantum-mechanical or a classical behavior is not an inherent property of the metabolic system under any conditions, but depends critically on the cycle time τ.

Now the energy $\tilde{E}$ given by (5) depends on the frequency. We write $\tilde{E} = \tilde{E}(\omega)$, to denote this dependency. In order to determine the total metabolic energy generated by the process, we will now consider the density of states $f(\omega)$, that is, the number of states in which the electron has frequency in the range ω, $\omega + d\omega$.

Assuming that the electron behaves as an infinite set of harmonic oscillators, the density $f(\omega)$ will be given by $f(\omega) = aV\omega^2$, where V denotes the total volume of the cell and a a constant (see Ref. [18]).

Hence the mean energy U generated by the metabolic transfer process is now given by

$$U = \int_0^\infty E^*(\omega) f(\omega) \, d\omega \ ,$$

where $E^*(\omega) = (1/V)\tilde{E}(\omega)$, the mean energy per unit volume.

Using (5), we thus obtain

$$U = a \int_0^\infty \frac{h\omega^3 \, d\omega}{\exp(h\omega/g\tau) - 1}$$

$$= \left(\frac{a}{h^3}\right) (g\tau)^4 \int_0^\infty \frac{x^3 \, dx}{e^x - 1} \ ,$$

which yields

$$U = c\tau^4 \ , \tag{6}$$

where $c = a\pi^4 g^4 / 15h^3$.

The above expression for the metabolic energy U released by the electron-transfer process, as given by (6), is analogous to the Stephan–Boltzmann law: the rate of energy transmission of a hot body is proportional to the fourth power of the absolute temperature. The law was originally discovered empirically by Stephan in 1879. Boltzmann later showed that the empirical law could be derived using thermodynamic

and electromagnetic arguments. Planck, in efforts to construct a statistical mechanics–electromagnetic theory of black body radiation, showed that the Stephan–Boltzmann law could be derived by postulating that when heated matter emits radiant energy, it does so in discrete bundles rather than continuously.

The derivation of (6) is based on the proposition that Planck's quantization rule may also apply to the energy generated by cellular metabolism, a non-equilibrium process. Planck's prescription $\varepsilon_n = nh\omega$ for the energy of a harmonic oscillator assumes that the energy associated with photons, electrons, protons occur in discrete bundles. Electromagnetic radiation is generated by the energy of photons. Radiant energy is due to the random thermal motion of the individual photons. Hence radiant energy at thermal equilibrium will depend on temperature. Metabolism is generated by the energy released by electrons and protons as the particles are transferred from donor to acceptor states within and across the energy-transducing membranes. Metabolic energy is due to the coupling of the dynamic events—electron transfer and proton translocation. This is a non-equilibrium process which is essentially isothermal. The metabolic energy at steady state will therefore depend on the temporal organization of the individual particles, a property which can be measured by the protonic cycle time.

The thrust of our analysis derives from the observation that physical processes at thermal equilibrium, where temperature is the organizing parameter, and biological processes at non-equilibrium steady states, where cycle time is the organizing variable, can be analyzed within the same statistical mechanics formalism. This observation has an analytical basis. It issues from the following mathematical fact: The growth rate parameter in population dynamics satisfies a variational principle which is formally analogous to the minimization of the free energy in thermodynamic systems [17,19]. This fact implies a formal correspondence between temperature, in thermodynamic theory, and cycle time in population dynamics. The methods we invoke to derive (6) are an application of this idea to metabolic systems.

2.2. Metabolic rate and cell size

The expression for the metabolic energy U given by (6) pertains to the electron-transfer process, that is, the energy-donating system. Let $\tilde{U}$ denote the metabolic energy associated with ADP phosphorylation, the energy-accepting process. According to the chemiosmotic theory, there is no direct connection between the enzymes of the respiratory chain and the phosphorylation enzymes. Respiration and phosphorylation are coupled via the energy-transducing membrane. When protons are transferred across the membrane it is converted to an energized state due to the proton concentration gradient formed and the electrical potential difference across the membrane.

Let μ denote the metabolic efficiency that defines the coupling between the respiratory and phosphorylating systems. This is represented by the ratio of the rate of the energy-accepting process, that is, ADP phosphorylation, to the rate of the energy-donating process, electron transport. Hence the parameter μ is given by

$$\mu = \frac{\log \tilde{U}}{\log U} \ .$$

As noted in Ref. [20], $\mu = qZ$, where $q, 0 \leqslant q \leqslant 1$, is a measure of the degree of coupling between electron transport and proton phosphorylation, with $q = 1$ and 0 for completely coupled and uncoupled systems, respectively. The quantity Z is a stoichiometry parameter which is equal to the ATP/electron transport flux ratio.

In view of (6), we have

$$\tilde{U} = c\tau^{4\mu} \ .$$

The expression for the metabolic energy $\tilde{U}$ derives from the quantum effects we postulate and the statistical mechanics argument we invoke. We can also consider cellular metabolism as a thermodynamic process and appeal to ideas from non-equilibrium thermodynamics to characterize $\tilde{U}$. Assuming a steady-state condition for the cell, we have $\tilde{U} = \tilde{S}T$, where $\tilde{S}$ denote the thermodynamic entropy of the cell.

The entropy $\tilde{S}$ is an extensive quantity which will be proportional to the volume V. Assuming that the density of the cell is uniform, we obtain, since the temperature is an intensive parameter, that

$$\tilde{U} = \gamma W \ ,$$

where W denotes the cell size and γ a proportionality constant. We can now appeal to the quantized and thermodynamic descriptions of the energy $\tilde{U}$ to infer that the cycle time τ will be given by the allometric relation

$$\tau = \alpha W^{1/4\mu} \ , \tag{7}$$

where $\alpha = (\gamma/c)^{1/4\mu}$.

Since the metabolic rate $P = \mathrm{d}\tilde{U}/\mathrm{d}\tau$, we obtain

$$P = 4\mu c \left(\frac{\gamma}{c} W \right)^{(4\mu-1)/4\mu} \ .$$

This yield the general scaling relation

$$P \sim W^{(4\mu-1)/4\mu} \ . \tag{8}$$

2.3. Multicellular organisms

The analysis I have described pertains to uni-cellular organisms. The argument can be extended to plants and animals. Energy transduction in plants is mediated by 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 will also apply to these multicellular systems.

In the case of animals, the model we will now consider, we assume that the metabolic energy is due exclusively to processes that occur in mitochondria. For an organism with m mitochondria, the energy associated with each mitochondrion, denoted X_i, is given by $\tilde{U}_i = c\tau_i^{4\mu}$ where τ_i is the protonic cycle time. The mean energy $\tilde{U}$ is given by $\log \tilde{U} = (1/m) \sum_{j=1}^{n} \log \tilde{U}_j$. Hence $\tilde{U} = (\tilde{U}_1 \tilde{U}_2 \ldots \tilde{U}_m)^{1/m}$. The cycle time associated

with the coupling of the different processes is given by $\tau = (\tau_1 \tau_2 \ldots \tau_n)^{1/m}$. These relations yield $\tilde{U} = c\tau^{4\mu}$.

We can exploit the argument described in the uni-cell model to show that $\tilde{U} = \tilde{\gamma}\tilde{W}$, where $\tilde{W}$ denote the mean mitochondrial mass. In view of the expressions for $\tilde{U}$ in terms of cycle time and mitochondrial mass, we conclude that for mitochondria, scaling relations analogous to (7) and (8) will also hold.

In order to determine a scaling relation for the overall metabolic rate, $\hat{P}$, of a multicellular organism as a function of its body size $\hat{W}$, we will consider the allometric relations for its constituent cells and their mitochondria. We will appeal to ideas described in Ref. [21]. We first note that $\hat{P}$ will be a function of the masses characterizing the various levels—mitochondrial, cellular, and individual: We write

$$\hat{P} = \hat{P}(\hat{W}, W_c, W_m) ,$$

where W_c and W_m denote the mean cell size and mean mitochondrial size, respectively. We consider a multicellular organism, to be composed of N_c closely packed identical cells; each with metabolic rate $P_c(\hat{W}, W_c, W_m)$ such that $N_c \approx \hat{W}/W_c$. In this model, the metabolic rate of an average cell in the organism will depend on the overall body mass. Each cell will be composed of N_m mitochondria, each with metabolic rate $P_m(\hat{W}, W_c, W_m)$ such that $N_m \approx W_c/W_m$.

From the conservation of energy for flow through the circulatory system that supplies cells, we have

$$\hat{P}(\hat{W}, W_c, W_m) = N_c P_c(\hat{W}, W_c, W_m) . \tag{9}$$

An analogous relation is obtained for P_c by considering energy flow through the mitochondria. We have

$$P_c(\hat{W}, W_c, W_m) = N_m P_m(\hat{W}, W_c, W_m) . \tag{10}$$

Combining (9) and (10), we have

$$\hat{P} = N_c N_m P_m . \tag{11}$$

Now $N_c W_c \approx \hat{W}$ and $N_m W_m \sim W_c$.
Hence

$$N_c N_m W_m \approx \hat{W} . \tag{12}$$

Since $P_m \sim W_m^{(4\mu-1)/4\mu}$, we conclude from (11) and (12), that the overall metabolic rate $\hat{P}$ will also satisfy a scaling relation of the form

$$\hat{P} \sim \hat{W}^{(4\mu-1)/4\mu} .$$

3. Metabolic rate: optimality principles

The expression for the metabolic rate given by (8) derives from physical constraints, namely the quantized nature of energy transformations. We will now apply an analytic

model of the evolutionary process to determine a complementary set of constraints which evolutionary forces will impose on the metabolic rate.

Analytical studies of the evolutionary process show that the metabolic rate of an organism, as is the case with other physiological variables, is subject to evolutionary change by mutation and natural selection. The trends in metabolic rate can be inferred from directionality theory, an analytic model which integrates Mendelian genetics with demography [9].

Directionality theory classifies populations according to the ecological forces that impinge on the population dynamics. The theory distinguishes between two classes of ecological constraints.

(a) *Bounded growth*: This pertains to populations existing in environments in which resources are limited but in constant supply. Population size under this constraint will be either stationary or fluctuate around some constant value.
(b) *Unbounded growth*: This condition refers to populations existing in environments in which resources are ample but are available only intermittently. Population size under this constraint will be characterized by alternating episodes of rapid increase and decline.

Directionality theory parametrizes the state of the population by the complexity of its life-history, a property which is measured by evolutionary entropy, denoted H, and given by

$$H = -\frac{\int_0^\infty p(x)\log p(x)\,\mathrm{d}x}{\int_0^\infty x\,p(x)\,\mathrm{d}x} \equiv \frac{S}{\tilde{T}} \ . \tag{13}$$

Here $p(x)$ denotes the probability density function of the age of reproducing individuals in the population. The function $p(x) = \exp(-rx)V(x)$. The quantity, r, denotes the population growth rate. The function $V(x)$, called the net reproductive function at age x, is defined by the product $l(x)m(x)$, where $l(x)$ is the probability that an individual born at age zero will survive to age x, and $m(x)$ the mean number of offspring produced at age x.

The main tenets of the theory are a set of directionality principles which relate ecological constraints—bounded and unbounded growth—to changes in entropy under mutation and natural selection.

In the case of large populations, these tenets can be described as follows:

I(a) In populations subject to bounded growth constraints, evolution is described by a uni-directional increase in entropy.
I(b) In populations subject to unbounded growth constraints, evolution is described by a uni-directional decrease in entropy.

We will now show that the metabolic rate, P, is characterized by directionality principles analogous to (I). We observe from (13) that $S = -\int_0^\infty p(x)\log p(x)\,\mathrm{d}x$ and $\tilde{T} = \int_0^\infty x\,p(x)\,\mathrm{d}x$. The quantity S describes the uncertainty in the age of the mother of

a randomly chosen newborn, whereas $\tilde{T}$ denotes the generation time, the mean age of mothers at the birth of their offspring.

The studies given in Ref. [10] applied energetic arguments to show that the entropy function S is, up to additive constants, isometrically related to body size. We have

$$S = \tilde{c}W + \tilde{d} \, ,$$

where $\tilde{c}$ and $\tilde{d}$ are constants which depend on the phylogenetic status of the organism.

In view of (13), we conclude that

$$H\tilde{T} = \tilde{c}W + \tilde{d} \, . \tag{14}$$

Now since cycle times at different levels of biological organization satisfy allometric relations with similar exponents [12], we can conclude that the generation time $\tilde{T}$ will satisfy the allometric relation (7). Using (7) and (8) we can therefore infer that

$$P\tilde{T} \sim W \, . \tag{15}$$

The perturbation methods in Ref. [10] can now be applied to (14) and (15) to show that

$$\Delta H \cdot \Delta P > 0 \, , \tag{16}$$

where ΔX denotes a change in the parameter X due to a change in the net reproductive function that defines the life table. Relation (16) implies that evolutionary changes in entropy and evolutionary changes in the metabolic rate are positively correlated.

Relation (16) can be integrated with (I) to derive, in the case of large populations, the following series of correlations between ecological constraints and evolutionary changes in metabolic rate. We have

II(a) *Bounded growth constraints*: a uni-directional increase in metabolic rate.
II(b) *Unbounded growth constraints*: a uni-directional decrease in metabolic rate.

Principles (II) entail that the metabolic rate of an organism, and consequently the scaling exponent $\beta = (4\mu - 1)/4\mu$, will be regulated by the ecological situation the population contends throughout its evolutionary history. We can exploit (II) to infer the following extremal principles for metabolic rate:

We have

(A) In populations subject to *bounded growth* constraints, the evolutionarily stable state of the population will be described by organisms with physiological states that *maximize* the metabolic rate.
(B) In populations subject to *unbounded growth* constraints, the evolutionarily stable state will be described by physiological states which *minimize* the metabolic rate.

Invoking principle (A) and expression (8) for metabolic rate, we observe that maximal metabolic rates will correspond to an efficiency $\mu = 1$. When this condition holds, $\beta = \frac{3}{4}$ and we obtain the scaling relation $P \sim W^{3/4}$.

In our application of principle (B) we note that, in the case of homeotherms of 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 of homeotherms will be described by the exponent $\beta = \frac{2}{3}$, and we have $P \sim W^{2/3}$. This minimal condition corresponds to an efficiency $\mu = \frac{3}{4}$.

4. Conclusion

The size of an organism imposes constraints on its physiology and determines its life-history and ecological traits. The metabolic rate of an organism, that is, the rate at which chemical energy is being transformed from nutrients into osmotic and chemical work, regulates its physiological activities. Empirical studies show that metabolic rate and body size satisfy an allometric relation whose exponent depends on the phylogenetic status of the organism. This article has proposed a model to explain these empirical laws. The model rests on the idea that energy transduction in a biological organism is determined by two classes of dynamical processes. The first operates on the time scale of chemical kinetics—the transit time of molecules in the electron- and proton-transfer reactions. This dynamic is concerned with the energy released as electrons are transferred from a substrate to oxygen and protons are translocated across membranes. Our model assumes that these processes are quantized and exploits Planck's quantization rule to show that the relation between metabolic rate P and body size W will be given by

$$P = aW^{\beta} \,,$$

where the scaling exponent, β, depends on the metabolic efficiency.

The second process we consider operates on the time scale of a generation—the mean age at which individuals in the population produce offspring. This dynamical system describes evolutionary changes in the population under different ecological constraints. The model exploits a new analytical theory of evolution to show that the scaling exponent β will be contingent on the evolutionary history of the population. The scaling exponent $\beta = \frac{3}{4}$, which maximizes metabolic rate, and $\beta = \frac{2}{3}$, which minimizes metabolic rate, are consequences of these evolutionary constraints.

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