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Allometric scaling of biological rhythms in mammals

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ABSTRACT

A wide spectrum of cyclic functions in terrestrial mammals of different size, from the 3-gram shrew to the 3-ton elephant, yields an allometric exponent around 0.25, which is correlated – as a kind of common denominator – with the specific metabolic rate. Furthermore, the applicability of these empirical findings could be extrapolated to chronological events in the sub-cellular realm. On the other hand, the succession of growth periods (T98%) until sexual maturity is reached also follows the 1/4 power rule. By means of Verhulst's logistic equation, it has been possible to simulate three different biological conditions, which means that by modifying the numerical value of only one parameter, revertible physiological and pathological states can be obtained, as for instance isostasis, homeostasis and heterostasis.

Key terms: growth, dimensional analysis, specific metabolic rate, logistic equation, homeostasis, heterostasis

INTRODUCTION

Since Lambert and Teissier (1927), a mathematician and a zoologist, introduced the dimensional analysis in the biological sciences with the aim to obtain new relationships among different variables, such as heart rate, respiratory rate and specific metabolic rate of mammals of different size, the subsequent advancement was made by Julian Huxley (1932) by introducing the allometric equation ($Y = a \cdot M^b$) in Comparative Physiology, where: Y = any biological variable; a = an empirical parameter; M = body mass; and b = characteristic allometric exponent.

On the other hand, several theories of biological similarity, which are based on dimensional analysis of the physical sciences (MLT-system, where M = mass, L = length, and T = time), are able to predict satisfactorily the numerical values of the above-mentioned empirical allometric exponents (b) (Günther, 1975a; 1975b; Günther & Morgado, 1984; 2003a; 2003b; 2004; Günther, González & Morgado, 1992; Günther, Morgado & Jiménez, 2003).

There is little doubt, that cyclic activities permeate almost all biological functions, as shown in Table I and Figure 1, comprising a wide spectrum, from the activity of cytochrome oxidase – the master reaction of oxidative metabolism – (West et al., 2002) to the frequency of sleep cycles (Zepelin & Rechtschaffen, 1974), since the logarithms of parameter a vary from +4.50 to -3.18, corresponding to 7.68 decades, or to a 47.86 million-fold difference.

The common denominator of all biological rhythmcities may be the "specific metabolic rate" of each organism (Schmidt-Nielsen, 1997), which has been defined as total oxygen consumption per unit body weight and per unit of time.

Since ancient times, heart rate (HR) has been the paradigm of biological rhytmicities, particularly in human medicine, where any abnormality of the

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TABLE I

Seven cyclic functions (given in Hertz) of mammals
(data from Peters, 1983; Calder, 1984)

Item	Function	Parameter (log a)	Exponent (b)	References
1	Flicker-fusion-frequency	1.75	- 0.25	Günther & Morgado (2004)
2	Muscle twitch frequency	1.72	- 0.21	Syrovy & Gutman (1975)
3	Heart rate	0.60	- 0.25	Stahl (1967)
4	Respiratory rate	- 0.05	- 0.26	Stahl (1967)
5	Gut beat rate	- 0.45	- 0.31	Adolph (1949)
6	Blood flow turnover	- 1.32	- 0.21	Stahl (1967)
7	Sleep cycle frequency	- 3.18	- 0.24	Zepelin & Rechtschaffen (1974)
A common reference system	Specific metabolic rate ($VO_2 \cdot kg^{-1} \cdot h^{-1}$)	- 0.15 - 0.15	- 0.25 - 0.25	Schmidt-Nielsen (1997) Schmidt-Nielsen (1997)

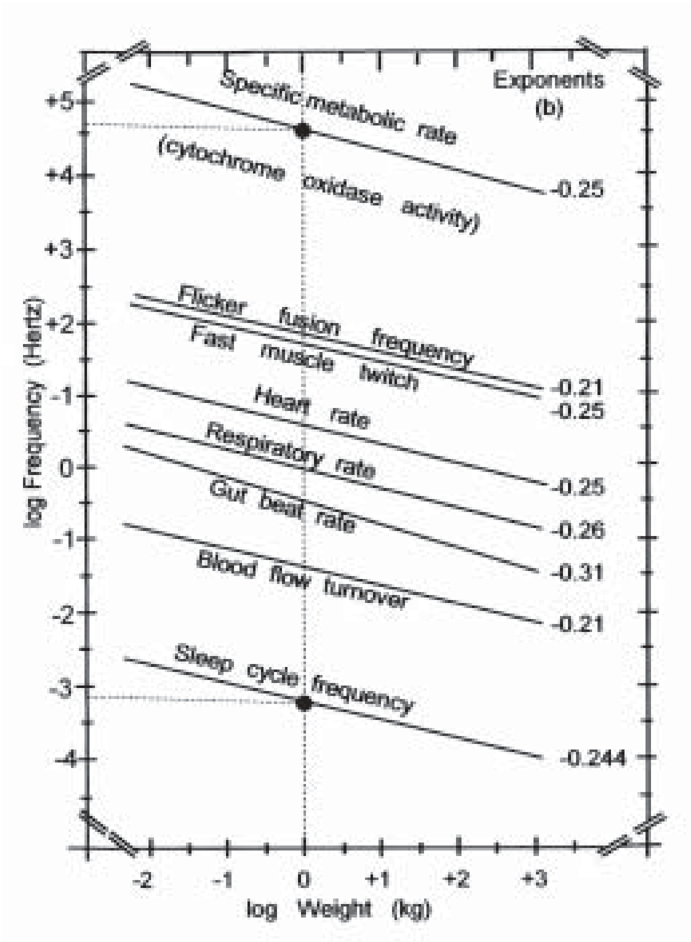

Figure 1: The inverse correlation between the logarithms of eight chronological events (given in Hertz) and the logarithms of the corresponding body weights, given in kilograms.

arterial pulsations is a matter of concern. The corresponding allometric equation ($HR = 202 \cdot W^{-0.25}$), as illustrated in Table II is applicable to a wide spectrum of terrestrial mammals, from the 3-gram shrew to the 3-ton elephant, which represents a million-fold body weight (W) difference, despite the fact the heart as a pump is morphologically and physiologically almost identical in all mammals. More recently, West et al. (2000) were able to extrapolate these conclusions to the sub-cellular realm (see Table II).

In sum, representative theories and experiments have confirmed the paramount importance of Fraser's (1966) dictum: "Cycle repetition is the rule of living".

BIOLOGICAL TIME AND ITS LOGISTIC EQUATION

The study that follows intents to show that, by means of Verhulst's logistic equation, known since 1845, it has been possible to obtain three different solutions for biological time events: 1) a constant output signal with only one attractor, which can be defined as "isostasis" in the sense of Claude Bernard's "fixité du milieu intérieur"; 2) a steady state of rhythmic output with two attractors, which resembles Walter Cannon's concept of "homeostasis", and finally 3) a "chaotic" outcome without any attractor, which can be defined as "heterostasis" in the sense of Hans Selye (1973).

We must emphasize that the Verhulst's logistic equation (Figure 2) yields: 1) a set of successive numerical solutions, which may be equal or very similar when the equation $X_{n+1} = f(X_n) = a \cdot X_n(1-X_n)$ or else, when $X_{n+1} = X_n \pm DX$, where DX is a small difference, which can be of positive or negative sign, as commonly happens with any physiological variable as a function of time, and 2) three significantly different behaviors, depending upon the numerical value of parameter (a), because: i) when the parameter (a) is less than 3.0, the result will be a constant value (isostasis); ii) when parameter (a) varies between 3.0 and 3.45, the output will be oscillatory (homeostasis); and finally, iii) when parameter (a) is greater than 3.45, the resulting values will be predominantly of chaotic nature, which is equivalent to the "heterostasis" of Selye (1973).

TABLE II

Heart rate (min^{-1}) in mammals of different body weights (kg) and chronological characteristics of sub-cellular items (in Hertz). Data from West et al. (2002)

Item	Macroscopic and microscopic entities	Weight (W) in kg	Log period $f(W^{1/4})$	Log frequency $f(W^{-1/4})$	Heart rate (min^{-1}) $HR = 202 \cdot W^{-1/4}$ (W in kg)	Estimated turnover number (Hz)
1	Blue whale	100,000	1.25	- 1.25	11.4	-
2	Elephant	3,000	0.87	- 0.87	27.3	-
3	Man	70	0.46	- 0.46	70	-
4	Shrew	0.003	- 0.63	0.63	862	-
5	Mammalian cell	10^{-8}	- 2.0	2.0	-	1.0
6	Mitochondria	$10^{-12.5}$	- 3.125	3.125	-	1,333
7	Cytochrome-oxydase	$10^{-18.5}$	- 4.625	4.625	-	42,170

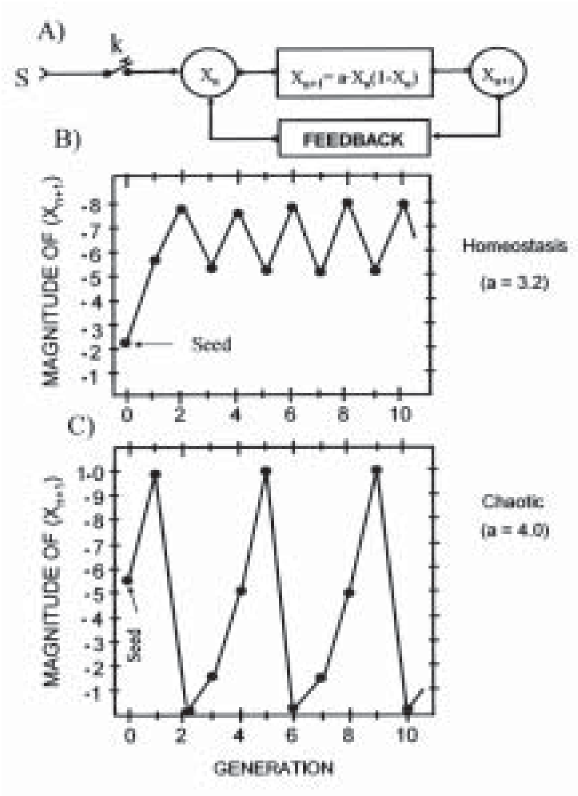

Figure 2: A) Feedback circuit of a biological iterator ($X_{n+1} = a \cdot X_n \cdot (1 - X_n)$). The first cycle starts when key (k) introduces the seed (S) into the circuit.
B) Oscillatory response of the iterator in the homeostatic range, when parameter a = 3.2.
C) Output of the iterator in the chaotic realm (heterostasis), when parameter a = 4.0.

Concerning the first theoretical alternative or the "isostasis" phenomenon of Claude Bernard (Figure 3), it is note worthy that the empirical findings have confirmed the validity of Bernard's theoretical assumption, because the electrolyte concentrations in the plasma of all terrestrial mammals (in accordance to data from Altman and Dittmer, 1974) yield the following figures (mean ± SEM): a) sodium: 141.41 ± 2.2; b) chloride: 105.72 ± 1.22; c) potassium: 4.07 ± 0.18; d) calcium: 4.91 ± 0.12.

Surprisingly, isostasis in mammals could be extrapolated to each individual, irrespective of their body size. Furthermore, the periodicity of the homeostatic processes is restricted to narrow ranges, whereas in the case of heterostasis, the oscillations are beyond the normal ranges for each specific function. They are of greater amplitude and occur in irregular patterns, which is characteristic of pathology.

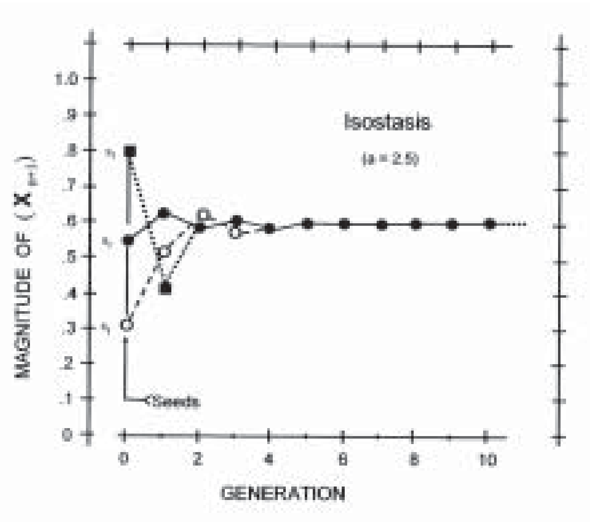

Figure 3: Response of the iterator in isostasis, irrespective of the original value of the seeds (s_1 – s_3). A numerical example of "isostasis" is given in the text.

THE ALLOMETRY OF GROWTH

Another distinctive feature of living beings is their capacity to increase both in size and in number, either as single individuals or as a population. It is of great interest that Calder (1984) summarized the meaning of growth as follows: "Growth is, after all, a physiological process, both during post-natal life, maturation, maintenance and aging, periods which should be regarded as a continuum." In Table III, five biological growth periodicities are defined in accordance with allometric criteria, and in almost all instances, an allometric exponent (b) around 0.25 was obtained. As shown in Table III, items 2 and 3, a succession of generations in a given species, means a series of T98 growth periods, where T98 is the time span required to reach 98% of reproductive maturity (item 4, Table III), as illustrated in Figure 4. The history of a species is precisely equivalent to the succession of T98 periods, which is just the substrate of natural selection.

TABLE III

Growth times and periods that are associated with phases of reproduction (data from Calder, 1984; Peters, 1983)

Item	Independent variable	Body weight range (kg)	Parameter (a) in days; the value of (a) when W = 1 kg	Exponent (b) $\pm S_b$	Determination coefficient (r^2)
1	Gestation time	0.017 - 2750	65.3	0.258 ± 0.032	0.72
2	50% growth (T50)	-	130.5	0.25	-
3	98% growth (T98)	-	447	0.26	-
4	Reproductive maturity	-	274	0.29	0.57
5	Maximum longevity in captivity	-	4234	0.20	0.59

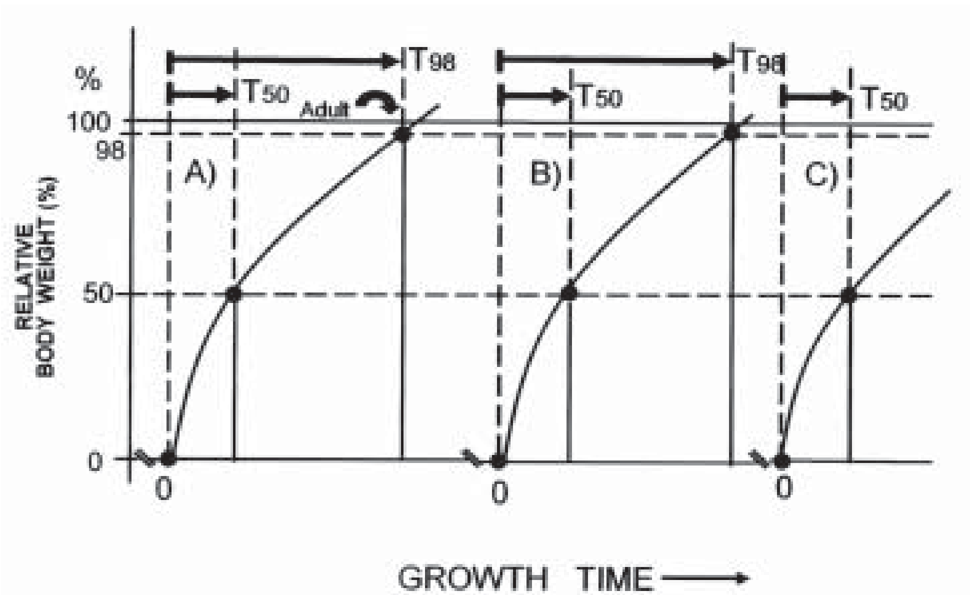

Figure 4: Sequence of three growth periods, with indication of the relative body weight given as a percentage of the adult value (100%). As shown in Table III, items 3 and 4, means that reproductive maturity is attained at the 98% growth condition.

DISCUSSION

The present study dealt with the quantitative analysis of the comparative physiology of terrestrial mammals, from the 3-gram shrew to the 3-ton elephant – a million-fold body weight difference – which can be extrapolated to the 100-ton whale.

From the chronological analysis of rhythmic phenomena in mammals, a general $^1/_4$-power of body weight could be obtained from lifetimes, growth periods, heart and respiratory rates to sleep cycles. On the other hand, West and colleagues (2002) extrapolated the above-mentioned power law, to sub-cellular periodicities of redox cycles of mitochondrial oxidases, whereas Sernetz and colleagues (1985) correlated the specific metabolic rate with the fractal nature of biological times.

Verhulst's logistic equation, from 1845, yielded a sequence of self-similar results through a feedback circuit which is governed by a single parameter, whose numerical value determines the outcome; in one instance, the final result was "isostasis" (C. Bernard); in the other, "homeostasis" (W. Cannon), and finally, a pathological sequence could be simulated as "heterostasis" (H. Selye).

Finally, growth phenomena could be analyzed from a quantitative point of view, while two types of increasing size of an organism should be distinguished, one, during the intrauterine gestation period (Table III, item 1), and second, the post-natal growth until the 98% of adult size (Table III, item 3) is reached. In both cases, the allometric exponent varies around b = 0.25. The survival of a given species depends upon the sequence of T98 periodicities until in each instance sexual maturity is achieved.

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