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A Novel Allometric Approach to Xenobiotic Clearance

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Abstract: Derivation of an allometric equation should be based on the assumption of homogeneous or hierarchical structure, thus an organ-based scaling law is much suitable for physiological processes. A new allometric law is established for Xenobiotic Clearance and the prediction agrees excellently with the experimental observation.

Key words: Allometric scaling law, kidney function, clearance, approach, xenobiotic

INTRODUCTION

The scaling of physiological processes versus body-size has now become a focus of interest in biology (West *et al*., 1997; Darveau *et al*., 2002; He and Huang 2006). It has been observed that many physiological process and organ sizes scale with increasing body size, as described by the following simple power law:

$$B \propto M^b \quad (1)$$

Where, B is physiological property or anatomic size, M is body size, b is the scaling exponent. In a strict mathematical view, the scaling (1) is valid only for the case when the discussed body is homogeneous or hierarchical, otherwise it becomes mathematically meaningless.

Let us consider the Cantor triadic set, the totally length depends the scale, Δx, used.

$$L \propto (\Delta x)^D, \quad D = \ln 2/\ln 3 \quad (2)$$

The triadic Cantor set is hierarchical and its basic character can be expressed in a scaling formulation (Fig. 1). Let us consider the first iteration of the Cantor triadic set. In this case $\Delta x = 1/3$ of the length of the unit interval while the number of parts left is $n = 3-1 = 2$. The scaling exponent is calculated as $D = -\ln n/\ln \Delta x = -\ln 2/\ln(1/3) = \ln 2/\ln 3$.

The biological processes underlying allometric scaling relations for metabolic rates in biology have been a topic of long-standing interest and speculation. The scaling exponent is a point of contention throughout the open literature. Animal's whole body is inherently inhomogeneous and has no hierarchical structure, so such debate is mathematically incorrect and biologically irrelevant. West *et al*. (1997) claimed that they obtained a universal exponent (i.e. b = 3/4) for all animals and plants, however, their derivation has no mathematical basis (Kozlowski and Konarzewski, 2004, 2005; Etienne *et al*., 2006).

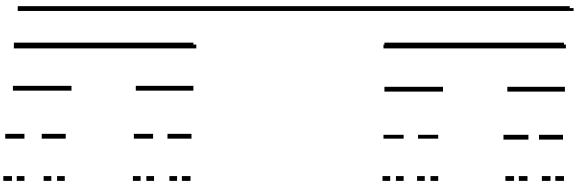

Fig. 1: The hierarchical triadic cantor set

ORGAN-BASED ALLOMETRY

There are many methods to explain various phenomena in biology, such as allometrical method (West *et al*., 1997; Kuikka, 2006), statistical method (Al-Suwaiyel *et al*., 2006) and E-infinity theory (El Naschie, 2006, 2007). In particular, using a blend of the methodology of allometrical scaling and E-infinity theory it was possible to solve various basic problems in biology (He, 2006a-c, 2007).

We know that brain, liver, kidneys and heart together account for ~60% of resting energy expenditure in humans, even though the 4 organs represent <6% of body mass (Wang *et al*., 2001), different organs obey different scaling laws.

To analyze the allometric scaling of many physiological phenomena, we should begin with an organ with homogeneous structure (e.g., heart) or hierarchical structure (e.g. airway in lung). We assume that that some a physiological parameter scales allometrically with the organ mass as (He, 2006a- c, 2007).

$$B_{organ} \propto T_{organ}^{\alpha} \quad (3)$$

Where, B_{organ} is the physiological property (e.g., metabolic rate) of an organ, T_{organ} its mass, α the scaling exponent.

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

$$B_{organ} \propto nr^2 \quad (4)$$

The mass T_{organ} of the organ scales linearly with respect to its total volume of cells:

$$T_{organ} \propto nr^3 \quad (5)$$

It is obvious that the scaling exponent α depends upon the cells' structure and cells' distribution, or fractal dimension of the cells in the organ (He and Huang, 2006). Due to different structures of various organs in a living body, there must be different scaling laws. There is not a ubiquitous law that relates size and metabolic rate across all organisms. Different organs in a living body, organisms at different motion states or at different life periods, obey different scaling laws as well. By a simple fractal analysis, He and Huang (2006) obtained a novel scaling law in the form

$$B_{organ} \propto T_{organ}^{(D+N/6)(D+1)} \quad (6)$$

Where, D is cells' fractal dimension of the studied organ. For kidney D = 3 and N = 4 (He and Huang, 2006) we predict

$$B_{kidneys} \propto T_{kidneys}^{0.91} \quad (7)$$

The mass of kidney scales as Wang *et al.* (2001)

$$T_{kidneys} \propto M^{0.85} \quad (8)$$

From the scaling relationships (7) and (8), we have

$$B_{kidneys} \sim M^{0.77} \quad (9)$$

Which agrees excellently with the experiment observation (Wang *et al.*, 2001).

A NOVEL ALLOMETRIC APPROACH TO XENOBIOTIC CLEARANCE

Allometric scaling has been applied in pharmacokinetics for approximately 2 decades (Hu and Hayton, 2001; Maxwell and Jacobson, 2004). The major interest has been prediction of pharmacokinetic parameters in man from parameter values determined in animals. Clearance has been the most studied parameter, as it determines the drug-dosing rate. In most cases, the pharmacokinetics of a new drug was studied in several animal species and the allometric relationship between pharmacokinetic parameters and body weight was determined using linear regression of the log-transformed data.

$$CL \propto M^{\beta} \quad (10)$$

Hereby CL is the clearance rate, M is the body mass, β is the scaling exponent, which is determined experimentally.

As we point out above, we can not deduce the above scaling law directly, for the body mass is not homogeneous and not all parts of body organs contribute to clearance explicitly. However, considering the relationship between the Clearance rate (CL) and kidney's mass (T), we can immediately obtain the following scaling law similar to (7)

$$CL \propto T^{0.91} \quad (11)$$

The kidney's mass (T) is related allometrically to body Mass (M) in the form Wang *et al.* (2001)

$$T \propto M^{0.85} \quad (12)$$

Combining (11) and (12), we have the following scaling related to body mass:

$$CL \propto M^{0.77} \quad (13)$$

Which is very closed to Hu and Hayton's (2001) observation: $CL \propto M^{0.74}$ and Maxwell and Jacobson's (2004) observation: $CL \propto M^{0.759}$.

CONCLUSION

As pointed out by Kozlowski and Konarzewski (2004, 2005) and West *et al.* (1997) model of allometric scaling is mathematically incorrect and biologically irrelevant, so it has no mathematical meaning for us to deduce a body-size allometric scaling: $B \propto M^b$. The most suitable scaling law should be deduced from an homogeneous organ in the form: $B_{organ} \propto T^b{}_{organ}$ Our theoretical prediction agrees well with experimental data in open literature (Hu and Hayton, 2001; Maxwell and Jacobson, 2004).

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REFERENCES

Al-Suwaiyel, M.I., A. Alani and A. Al-Swailem, 2006. An investigation of Fibonacci-like sequences in biology and mathematics. Int. J. Nonlinear Sci., 7: 133-136.

Coutinho, E.M., F.L. Silva, A.F. Barros, R.E. Araújo, S.A. Oliveira, C.F. Luna, A.A. Barbosa and Z.A. Andrade, 2007. Repeated infections with Schistosoma mansoni and liver fibrosis in undernourished mice. Acta Trop., 101: 15-24.

Darveau, C.A., R.K. Suarez, R.D. Andrews and P.W. Hochachka, 2002. Allometric cascade as a unifying principle of body mass effects on metabolism. Nature, 417: 166-170.

El Naschie, M.S., 2006. The brain and E-Infinity. Int. J. Nonlinear Sci., 7: 129-132.

El Naschie, M.S., 2007. A review of applications and results of E-infinity theory. Int. J. Nonlinear Sci., 8: 11-20.

Etienne, R.S., M.E.F. Apol and H. Olff, 2006. Demystifying the West, Brown and Enquist model of the allometry of metabolism. Functional Ecol., 20: 394-399.

He, J.H., 2006a. Cell size and cell number as links between noncoding DNA and metabolic rate scaling Chaos. Solitons and Fractals, 28: 1026-1028.

He, J.H., 2006b. An allometric scaling law between gray matter and white matter of cerebral cortex. Chaos, Solitons and Fractals, 27: 864-867.

He, J.H., 2006c. Application of E-infinity theory to biology. Chaos, Solitons and Fractals, 28: 285-289.

He, J.H. and Z.D. Huang, 2006. A novel model for allometric scaling laws for different organs. Chaos, Solitons and Fractals, 27: 1108-1114.

He, J.H., 2007. Shrinkage of body size of small insects: A possible link to global warming?. Chaos, Solitons and Fractals, 34: 727-729.

Hu, T.M. and W.L. Hayton, 2001. Allometric scaling of xenobiotic clearance: Uncertainty versus universality, Aaps Pharmsci., 3: Art. No. 29.

Kozlowski, J. and M. Konarzewski, 2004. Is West, Brown and Enquist's model of allometric scaling mathematically correct and biologically relevant?. Func. Ecol., 18: 283-289.

Kozlowski, J. and M. Konarzewski, 2005. West, Brown and Enquist's model of allometric scaling again: The same questions remain. Func. Ecol., 19: 739-743.

Kuikka, J.T., 2006. Fractal analysis of organ structure, function and interactions. Int. J. Nonlinear Sci., 7: 239-243.

Maxwell, L.K. and E.R. Jacobson, 2004. Allometric scaling of kidney function in green iguanas. Comparative Biochem. Physiol. Part A., 138: 383-390.

Wang, Z.M., T.P. O'Connort, S. Heshka and S.B. Heymsfield, 2001. The reconstruction of Kleiber's law at organ-tissue level. J. Nutr., 131: 2967-2970.

West, G.B., J.H. Brown and B.J. Enquist, 1997. A general model for origin of allometric scaling laws in biology. Science, 276: 122-126.